UDK 61(061.231)=862=20

CODEN LIVJA5
ISSN 0024-3477 (TISAK)
ISSN 1849-2177 (ONLINE)

LIJEČNIČKI VJESNIK

GLASILO HRVATSKOGA LIJEČNIČKOG ZBORA
THE JOURNAL OF THE CROATIAN MEDICAL ASSOCIATION
Utemeljen 1877. Founded 1877

22nd ZIMS Zagreb International Medical Summit

for students and young doctors

ZIMS
ZAGREB INTERNATIONAL MEDICAL SUMMIT

Liječ Vjesn God. | Vol. 144 [2022] Broj | Num. Supl. 7 Str. | Pag. 1–51 Zagreb, Hrvatska | Croatia

LIJEČNIČKI VJESNIK

GLASILO HRVATSKOGA LIJEČNIČKOG ZBORA

Utemeljen 1877.

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https://hrcak.srce.hr/lijecnicki-vjesnik


ORGAN

BORA LIEČNIKÁ KRALJEVINÁ HRVATSKE I SLAVONIJE.

UREDNIKOM MU

ODBOR LIEČNIČKOGA SBORA.

I. GODINA.

U ZAGREBU 1877.

UDK 61(061.231)=862=20
Liječnički vjesnik citiraju: Scopus, EMBASE/Excerpta Medica, EBSCO, Hrčak, DOAJ, CROSSREF

Liječnički vjesnik tiskano izdanje ISSN 0024-3477
Liječnički vjesnik online izdanje ISSN 1894-2177

Osnivač i izdavač
HRVATSKI LIJEČNIČKI ZBOR
Za izdavača
ŽELJKO KRZNARIĆ
Glavni i odgovorni urednik
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„Gredice" – Horvaćanska 67, Zagreb, Hrvatska
Tisak
PRINTERA grupa – Franje Tuđmana 14, Sveta Nedelja, Hrvatska
Web stranica
Alen Babacanli
Naklada
1000 primjeraka

Zagreb, 2022.

Opis

Liječnički vjesnik je najstariji hrvatski medicinski časopis koji neprekidno izlazi od 1877. te redovito bilježi sva važna stručna i strukovna dostignuća u hrvatskoj i svjetskoj medicini. U *Liječničkom vjesniku* objavljuju se uvodnici, stručni i znanstveni radovi, pregledni članci, prikazi bolesnika, lijekova i metoda, preliminarna znanstvena i stručna priopćenja, osvrti, pisma uredništvu, prikazi knjiga, referati iz literature i drugi prilozi. Svi rukopisi podvrgnuti su procesu recenzija.

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Osnivač i izdavač / Founder and Publisher
HRVATSKI LIJEČNIČKI ZBOR

Za izdavača / For Publisher
Željko Krznarić

Glavni i odgovorni urednik / Editor-in-Chief
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Deskriptori / Descriptors
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Naslovnica / Front Page
KONTRAST

Tehnički urednik / Technical Editor
Josip Vlahović

Slog / Typesetting
„Gredice" – Horvaćanska 67, Zagreb, Hrvatska

Tisak / Printed by
PRINTERA grupa – Franje Tuđmana 14, Sveta Nedelja, Hrvatska

Web stranica / Web page
Alen Barbacanli

Naklada
n primjeraka

Rukopis i svi članci šalju se Uredništvu Liječničkog vjesnika, Zagreb, Šubićeva ul. 9, tel. (01) 46-93-300, e-mail: lijecnicki-vjesnikhlz.hr. Članarina, pretplata i sve novčane pošiljke šalju se Hrvatskomu liječničkom zboru, Zagreb, Šubićeva ulica 9, odnosno na žiro račun br. 2360000-1101214818 ili devizni račun br. 2100060384, Zagrebačka banka d.d., Savska c. 60, Zagreb, Swift: Zaba HR 2X, IBAN HR7423600001101214818, OIB 60192951611. Članarina Hrvatskoga liječničkog zbora iznosi 200 kuna; za liječnike pripravnike i obiteljska članarina iznosi 100 kuna. Pretplata za Liječnički vjesnik je 315 kuna (inozemstvo 84 eura). Radi redovitog primanja časopisa svaku promjenu adrese potrebno je javiti Uredništvu. Svaki član Hrvatskoga liječničkog zbora ima pravo besplatno objaviti članak u Liječničkom vjesniku; autori koji nisu članovi Zbora moraju platiti naknadu u iznosu od 187,50 kuna + PDV.
Liječnički vjesnik citiraju: MEDLINE/Index Medicus i EMBASE/Excerpta Medica.

ZIMS 22nd Zagreb International Medical Summit

for Medical Students and Young Doctors

15th December 2022 – 18th December 2022

Zagreb, Croatia

22nd ZIMS Abstract Book

EDITORS

Barbara Borojević, Rea Novak

DESIGN AND LAYOUT

Barbara Borojević

PUBLISHERS

Croatian Medical Association – Student Section
Local Committee Zagreb,
Šubićeva 9, HR-10000 Zagreb, Croatia

European Medical Students' Association Zagreb
Šalata 3, HR-10000 Zagreb, Croatia

Printera grupa
Ul. Dr. Franje Tuđmana 14, 10431, Sveta Nedelja

ZIMS Abstract Book is published annually in conjunction with ZIMS.
Published so far 1st ZIMS Abstract Book (2001), 2nd ZIMS Abstract Book (2002), 3rd ZIMS Abstract Book (2003), 4th ZIMS Abstract Book (2004), 5th ZIMS Abstract Book (2005), 6th ZIMS Abstract book (2006), 7th ZIMS Abstract Book (2007), 8th ZIMS Abstract Book (2008), 9th ZIMS Abstract Book (2009), 10th ZIMS Abstract Book (2010), 11th ZIMS Abstract Book (2011), 12th ZIMS Abstract book (2012), 13th ZIMS Abstract book (2013), 14th ZIMS Abstract book (2014), 15th ZIMS Abstract book (2015), 16th ZIMS Abstract book (2016) with ISSN 0024-3477, 17th ZIMS Abstract book (2017), 18th ZIMS Abstract book (2018), 19th ZIMS Abstract book (2019), 20th ZIMS Abstract book (2020) and 21st ZIMS Abstract book (2021).

ZIMS is an independent annual student congress organized by medical students from Zagreb University School of Medicine who are members of Croatian Medical Association – Student Section (SSCMA) and European Medical Students' Association Zagreb (EMSA Zagreb). Contributors from all fields of medicine and adjacent sciences are welcome to apply and post their Abstract, and Full-text articles for publishing.
All participants in ZIMS must be students or young doctors graduated within five years.

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1. CASE REPORTS

Liječnički vjesnik, 144; 2022; suplement 7; 7
https://doi.org/10.26800/LV-144-supl7-7

A developing Fournier gangrene in an obstipated patient – a case report

Authors: Karla Lužaić[1], Viktoria Knežević[1], Jure Brkić, MD[2] (mentor), Kristina Šemanjski, MD, PhD[2]

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Background:

Fournier's gangrene is a rare acute necrotic infection of the scrotum, penis or perineum. It is associated with high mortality, therefore, emergency surgical debridement of necrotic tissues is crucial. This case report shows that when it comes to complex cases, it is important to do a thorough examination and to have differential diagnoses in mind with possible multidisciplinary treatments.

Case report:

A 71-year-old male patient presented to the emergency department due to severe constipation and lower abdominal pain of eight-day duration. The day before admission, he started vomiting intestinal substances. Previous medical history noted diabetes. Moreover, one month before, a solid cystic formation, located between the bladder and rectum, was verified by multislice computed tomography-urography. Physical examination revealed a distended abdomen with diffuse tenderness to palpation and abnormal peristalsis. Since inflammatory markers were elevated (C-reactive protein 141 mg/L, leukocytes 15 x 10^9/L), and air-fluid levels with colon meteorism were present on the x-ray, an indication for surgical management was established. A bipolar colostomy was formed because no organic cause of obstruction was found. However, the patient's condition worsens. He became febrile, and inflammatory markers continued to increase. The abdomen was still distended. He also developed edema, hyperemia, and tenderness of the testis, scrotum, and penis. Within one day, the skin of the perineum and perineal region became necrotic. Emergent exploration and extensive necrectomy were performed. Intraoperatively, there were no visible communications with the colon. After several necrectomy procedures, inflammatory markers returned to normal, and the patient was afebrile with no pain. The patient, in good general condition, with symptom relief, was discharged to home care after twenty-nine days of hospital treatment.

Conclusion:

Since the perineal region is often overlooked and the inflammation is difficult to notice, any clinical signs of developing infection and perineal pain require the exclusion of possible gangrene.

Keywords:

Debridement, Fournier gangrene, Necrosis

Liječnički vjesnik, 144; 2022; suplement 7; 8
https://doi.org/10.26800/LV-144-supl7-8

An immune system gone away: Ulcerative colitis accompanied by multiple autoimmune diseases – case report

Authors: Sandro Kukić[1], Marjan Kulaš[1], Matej Krišto[1], Lucija Virović Jukić[1,2] (mentor)

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[2] Department of Gastroenterology and Hepatology, Sisters of Charity University Hospital Centre, Zagreb, Croatia

Background:

Ulcerative colitis (UC) is a relapsing and remitting inflammatory disorder of the colonic mucosa. In 5% of UC cases, patients also develop primary sclerosing cholangitis (PSC). Both of the diseases are essentially autoimmune disorders and it is not uncommon to find other autoimmune diseases in affected patients.

Case presentation:

A 35-year-old female patient presented to the Department of Gastroenterology and Hepatology in 2014 with bloody diarrhea, weight loss, and fatigue. A colonoscopy was performed and the diagnosis of extensive, moderately severe ulcerative colitis was established. Her medical history was remarkable for type I diabetes mellitus diagnosed in 2001 and psoriasis diagnosed in 2010. The patient started treatment with mesalazine and corticosteroids, which resulted in clinical and endoscopic remission. During a follow-up, the elevation of cholestatic liver enzymes required further work-up, including MR cholangiopancreatography, which revealed changes consistent with PSC. The patient started treatment with ursodeoxycholic acid. In 2018, she discontinued corticosteroids, which resulted in a relapse of UC with exacerbation of psoriatic skin plaques and multiple-joint pain. A rheumatologist found no signs of spondyloarthritis at that moment. Treatment with an anti-TNF agent, adalimumab, was started in 2018, but had to be discontinued due to an episode of fever and hilar lymphadenopathy of unknown cause, which was resolved with steroid therapy. The trial of other biological agents, including vedolizumab and ustekinumab, showed no effect on UC symptoms. Finally, in 2021 the patient started treatment with tofacitinib, which showed great progress in reducing gastrointestinal symptoms, joint pain, and skin lesions.

Conclusion:

Treating patients with multiple autoimmune disorders is often complex and requires a multidisciplinary and individual approach. Frequent and thorough follow-up visits should be made to adjust medications and identify new symptoms that are possible indicators of underlying autoimmune diseases or complications related to the disease or treatment.

Keywords:

arthritis, autoimmune diseases, primary sclerosing cholangitis, psoriasis, ulcerative colitis

29Liječnički vjesnik, 144; 2022; suplement 7; 9
https://doi.org/10.26800/LV-144-supl7-9

Capillary leak syndrome following COVID-19 vaccination

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Background:

Capillary leak syndrome (CLS), also known as Clarkson's disease emerged as a new adverse event after immunization associated to COVID-19 vaccination. CLS is a rare condition characterized by increased capillary permeability, resulting in hypoalbuminemia, hypotension and oedema mainly in the upper and lower limbs.

Case presentation:

A 60-year-old woman presented to the emergency department due to onset of dyspnea on exertion, palpitations and weight gain of 10 kg in the last few weeks. She reported receiving Johnson & Johnson vaccine against COVID-19 three weeks prior. Physical examination findings included symmetrical oedema of legs and abdomen above the chest wall level, with positive fluid wave test. Laboratory tests showed significantly elevated urea (23.6 mmol/L) and creatinine (184 mmol/L). After further diagnostics proteinuria 5 g/dU with significantly reduced glomerular filtration (eGFR 24 ml/min/1.73 m2) and hypoalbuminemia were determined. She was diagnosed with an acute kidney injury as part of the capillary leak syndrome that occurred as a result of the vaccine against COVID-19. Ultrasound and kidney biopsy were performed to exclude other causes of kidney failure. Patient refused corticosteroid therapy, so she was treated empirically with furosemide, fluid and salt restriction, thromboprophylaxis with low molecular weight heparin and antibiotic therapy with ceftriaxone. The patient responded to the treatment with a gradual recovery of kidney function, but with the persistence of mild to moderate oedema.

Conclusion:

Although capillary leak syndrome is a rare side effect of the Johnson & Johnson vaccine against COVID-19, it should be considered in patients who present with oedema, haemoconcentration and hypotension. There are no specific diagnostic criteria for CLS, so it may be challenging to recognise this disease. Since the causal relationship between COVID-19 vaccine and CLS has not yet been established, more research is needed.

Keywords:

capillary leak syndrome, COVID-19 vaccination, side effect

Liječnički vjesnik, 144; 2022; suplement 7; 10
https://doi.org/10.26800/LV-144-supl7-10

Case report: Pitt-Hopkins like syndrome with CNTNAP2 mutation in three siblings

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Background:

Pitt-Hopkins like syndrome with CNTNAP2 mutation or Pitt-Hopkins like syndrome 1 (PTHSL1) is a very rare autosomal recessive neurodevelopmental disorder, with less than 30 affected individuals reported in literature worldwide.

Case presentation:

The patient is a seven-year-old female who presented with multiple epileptic seizures at the age of 9 months. Initial examination revealed only a minor delay in motor development. Family history included two older sisters (six and four years old), one older brother (died at three) and an aunt (died young) with epilepsy and severe intellectual disability of unknown cause. Initial diagnostic work-up, including EEG, was within normal limits, and the child was successfully treated with valproate. However, due to the burdensome family history, additional tests were performed, including a gene panel for epilepsy, which detected a homozygous deletion of the CNTNAP2 gene, probably of pathogenic significance, which was also later confirmed in two of the patient's older sisters. Seizures began to reappear at the age of three and were more severe, even requiring treatment in the ICU on one occasion. Delay in psychomotor and speech development also became more pronounced.

The patient's epilepsy is currently under control with levetiracetam, oxcarbazepine and phenobarbitone. Despite occupational and physical therapy, she is severely intellectually disabled and exhibits bizarre behaviour (coprophagia), similarly to her older sisters. Recently, at the age of seven, she developed signs of precocious puberty, which was also the case in one of the sisters, and as far as we know, is not yet described as part of Pitt-Hopkins like syndrome 1.

Conclusion:

Here we present a typical case of a very rare neurodevelopmental disorder with early-onset epilepsy, delayed psychomotor development, intellectual disability, severe speech impairment, behavioural abnormalities and precocious puberty as a possible addition to phenotypic spectrum of the syndrome.

Keywords:

CNTNAP2, developmental delay, epilepsy, paediatrics, Pitt Hopkins-like syndrome 1

Liječnički vjesnik, 144; 2022; suplement 7; 11
https://doi.org/10.26800/LV-144-supl7-11

Cecum perforation of unknown etiology in early postpartum period – a case report

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Background:

Among serious early complications in postpartum patients, colonic perforation is extremely rare. It can be seen more commonly following a caesarean section (C-section) than a normal vaginal delivery. This case report shows an infrequent complication in the postpartum period in a previously healthy patient.

Case presentation:

A 31-year-old female patient presented to the emergency department due to severe abdominal pain and fever, two days after a successful C-section was performed without reported intraoperative complications. The patient complained of crampy pain in the upper abdomen, weakness, and belching. Physical examination showed a distended abdomen with diffuse pain and guarding. Peristaltic sounds were not heard on auscultation. Additionally, a gynaecological examination was conducted which showed no gynaecological pathology other than a small volume of free fluid in the Douglas pouch. Laboratory parameters were within normal limits, except for slightly lower haemoglobin (93 g/dl) and elevated markers of inflammation (C-reactive protein 365 mg/l, procalcitonin 1,38 μg/L). Emergency multislice computed tomography (MSCT) of the abdomen and pelvis was performed and found signs of significant pneumoperitoneum and air-fluid levels. Immediately, surgery was performed, and exploration revealed excessive amounts of free fluid and multiple perforations of the cecum. A right hemicolectomy was carried out. The postoperative period was uneventful, and the patient in good clinical condition was discharged to home care with the recommended control referral.

Conclusion:

Colon perforation is an extremely rare complication in postpartum patients and rapid diagnosis with immediate treatment is required.

Keywords:

Caeserian section, Cecum perforation; Pneumoperitoneum; Postpartum complications

Liječnički vjesnik, 144; 2022; suplement 7; 12
https://doi.org/10.26800/LV-144-supl7-12

Chondrosarcoma of the jugular foramen

Authors: Josip Prnjak[1], Lorena Dolački[1], Jakov Ajduk, MD, PHD[1,2] (mentor)

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Background:

Chondrosaromas of the skull are locally agressive malignant tumors that account for 0.15% of all intracranial neoplasms. Around three fourths of these lesions are located at the skull base. Primary chondrosarcomas of the jugular foramen are exceptionally rare, with only 11 documented cases in the medical literature.

Case presentation:

A 65-year-old male presented with the pain and congestion in the right ear and a facial nerve paresis along with decreased hearing and pulsations on the left side. His physical exam showed a perforation of the right eardrum in the lower quadrants, and on the left side, protrusion of the posterior quadrants along with dried blood. Left facial nerve paresis (HB III/VI) was also present. Otomicroscopy was done on the left side with myringotomy and placement of the ventilation tube. MSCT of the middle ear and the temporal bone revealed a lobulated mass on the left side that has filled out the jugular fossa, invaded the mastoid and the hypotympanum. Lesion has also destroyed the petrous part of the temporal bone and eroded the wall of the carotid canal. Left facial nerve canal was infiltrated and there was an absence of blood flow in the left sigmoid sinus and the internal jugular vein

Since the tumor araised primarily from the jugular foramen, the treatment plan centered on surgery through an Fisch infratemporal fossa approach type A.

Pathology report was consistent with a moderately well differentiated chondrosarcoma. Patient recovered well. Interstingly, as opposed to the other cases of the primary jugular foramen CSA, our patient first presented with a facial nerve paresis even before having any symptoms of conductive hearing loss.

Conclusion:

The goal of treatment for well differentiated jugular foramen CSAs is total surgical removal that can be achieved through an infratemporal fossa approach type A.

Keywords:

Chondrosarcoma, jugular foramen

Liječnički vjesnik, 144; 2022; suplement 7; 13
https://doi.org/10.26800/LV-144-supl7-13

Clinically recognizable disease with negative result of routine gene panel — in search of genetic background with innovative whole genome sequencing

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Background:

Spinal muscular atrophy with respiratory distress type 1 (SMARD1) is an autosomal recessive disease with early presentation and unfavorable clinical course. Pseudohypoparathyroidism type 1A (PHP1A) is an autosomal dominant disease characterized by end-organ resistance to PTH, a hormone responsible for the control of calcium, phosphorus, and vitamin D levels in blood. People with PHP1A likewise have resistance to other hormones, such as TSH and gonadotropins. In addition, it is also associated with an array of clinical features referred to as Albright hereditary osteodystrophy (AHO).

Case Presentation:

We present a 6-year-old girl on a mechanical ventilator due to respiratory insufficiency, with symmetrically diminished growth, multiple skeletal defects (cervicothoracic kyphosis, abnormally fused arches of the cervical vertebrae, equinus feet), liver lesion, dystonia, and delayed motor development. She developed necrotizing enterocolitis and was diagnosed with intraventricular hemorrhage grade 1, two weeks after birth. She has deviation in neurological status, dystonia, hypertonia, lags in acquisition of postural mechanisms, secondary osteoporosis due to malnutrition, chronic atelectasis of the left lung lobe, recurrent urinary bladder infections, and bilateral ureterolithiasis. Muscle biopsy excluded primary muscle disorder, while electromyoneurography indicated nerve disorder. Panel gene testing for the most frequent variants for SMA was negative, leaving the patient undiagnosed. A whole genome joint analysis was done under the "CroSeq-GenomeBank" project, yielding two causal variants in IGHMBP2 gene and one in GNAS gene. The patient was finally diagnosed with spinal muscular atrophy with respiratory distress type 1 and pseudohypoparathyroidism type 1A.

Conclusion:

Whole genome joint analysis provided new diagnostic findings, detected variants not previously identified on panel testing and allowed interrogation of newly found variants. Whole genome sequencing is superior to other gene testing tools currently in use. It is both cost- and time-effective due to its elimination of the steps in-between, leading to faster diagnosis and reducing complications.

Keywords:

CroSeq-GenomeBank, Personalized Medicine, Whole Genome Sequencing

Liječnički vjesnik, 144; 2022; suplement 7; 14
https://doi.org/10.26800/LV-144-supl7-14

Congenital Glaucoma Diagnosed in Late Childhood: A Case Report

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Background:

Primary congenital glaucoma (PCG) is the most common childhood glaucoma. It is caused by a defective development of the trabecular meshwork and the anterior chamber angle, which is believed to be inherited as an autosomal recessive disorder. The disease is characterised by high intraocular pressure (IOP), buphthalmos with corneal enlargement, and tears in Descemet's membrane. Although rare, it is a significant cause of blindness in children worldwide.

Case presentation:

A 12-year-old Romani girl came to the department of ophthalmology complaining of epiphora and right eye enlargement. In her medical history, recurrent eye redness, lacrimation, and photosensitivity were noted, with symptoms lasting 7-9 years, which had been treated as conjunctivitis. Upon examination, enlargement of the right eye (axial length 25.63 mm) and divergent strabismus could be seen. Visual acuity in the enlarged eye was reduced to hand movement and slit lamp showed corneal clouding and Haab's striae. Applanation tonometry measured IOP of 34 mmHg in the right eye. Fundus examination of the affected eye revealed a pale optic disc with a cup-to-disc ratio of 0.9 and visual field test showed residual temporal island of vision. The left eye had a complete normal finding. Based on clinical examination and imaging, PCG was diagnosed and trabeculectomy with mitomycin-C was performed on the right eye. Reassessment after four weeks showed a formed filtration bubble with IOP of 10 mmHg in the operated eye, but severe amblyopia persisted. After 12 months, visual acuity, IOP values, and visual field remained unchanged.

Conclusion:

Atrophy of the optic nerve caused by congenital glaucoma leads to a severe visual impairment in early years of life. This case illustrates the importance of early recognition and appropriate management of PCG to improve prognosis and to avoid irreversible damage to the visual function.

Keywords:

Haab's striae, intraocular pressure, optic nerve, primary congenital glaucoma

Liječnički vjesnik, 144; 2022; suplement 7; 15
https://doi.org/10.26800/LV-144-supl7-15

Diabetes insipidus secondary to craniopharyngioma

Authors: Jana Bebek[1], Drago Baković[1], Božena Bradarić[2], Tomislav Bulum[1,2] (mentor)

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Background:

Craniopharyngiomas are rare embryonic malformations of the sellar and parasellar area. There is a bimodal age distribution, with peak incidence rates for childhood-onset craniopharyngiomas occurring between the ages of 5 and 14, and for adult-onset cases between ages 50 to 74. Most common clinical manifestations include pituitary deficiencies, visual impairment and increased intracranial pressure. It is rare for diabetes insipidus to be an initial symptom of craniopharyngioma.

Case presentation:

We present a 20-year-old male patient who visited the emergency room because of polydipsia and polyuria. He drank approximately 10 liters of fluids per day; every 20 minutes including the night. Further, his vision was blurred, and he was vomiting twice per week. Central diabetes insipidus was diagnosed by a water deprivation test. Urine osmolality was around 120 mOsm/kg at the beginning. After desmopressin was administered, urine osmolality increased up to 700 mOsm/kg. Moreover, laboratory findings showed decreased levels of ACTH, TSH, LH and increased levels of prolactin. Because of panhypopituitarism, brain CT was indicated. CT and MRI showed expansive suprasellar lesion that infiltrated the infundibulum and compressed the optic chiasm. The patient underwent neurosurgery and pathohistological analysis confirmed craniopharyngioma. The patient was then discharged in good general condition. He requires endocrine substitution of all hypothalamic–pituitary axes. Hormonal substitution includes hydrocortisone, levothyroxine, desmopressin, and testosterone. After a year, there were no relapses or new tumors seen on the follow-up MRI.

Conclusion:

Diabetes insipidus is described as the inability to conserve water and maintain an optimum free water level. The water deprivation test is used to distinguish central diabetes insipidus from nephrogenic diabetes insipidus. Central diabetes insipidus is caused by injury to the central nervous system and in this case, it was craniopharyngioma.

Keywords:

craniopharyngioma, diabetes insipidus, polyuria-polydipsia syndrome

Liječnički vjesnik, 144; 2022; suplement 7; 16
https://doi.org/10.26800/LV-144-supl7-16

Early-onset Alzheimer's disease due to novel LDLR gene mutation

Authors: Manuela Frančić[1], Romana Perković[2], Ratimir Petrović[3], David Ozretić[4], Stipe Škara[5], Ivan Pećin[6], Fran Borovečki[2] (mentor)

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Background:

Early-onset Alzheimer's disease (EOAD), with onset in individuals younger than 65 years, comprises approximately 5% of AD. It is associated with delays in diagnosis and an aggressive course. Mutation in LDLR is a well-known cause of familial hypercholesterolemia, but genetic variants in LDLR make no significant contribution to AD risk in the general population. This is the first known case of EOAD caused by the rs140241383 variant of the LDLR gene.

Case presentation:

A patient is a 44-year-old male who presented with spatial disorientation, short-term memory loss, and alteration in handwriting. He was also misplacing objects. MRI T2 and FLAIR sequence showed a chronic vascular lesion of the superior frontal gyrus on the left and initial atrophic changes of the cortex. Three years later, dyscalculia, constructional apraxia, clear attention deficits, and clear impairments of short-term verbal memory were noted. A score of 25 was noted on MMSE. He was diagnosed with unspecified dementia. Atorvastatin was introduced due to high LDL-cholesterol levels. Six months later significant deficits of organic type were present in terms of non-verbal functions, memory, attention, and executive functions. Decreased beta-amyloid levels and increased levels of tau and ptau were detected in CSF. PET scanning showed pathological deposition of extracellular amyloid diffusely in the cerebrum parenchyma and donepezil was introduced. Clinical exome sequencing detected a heterozygous mutation of LDLR variant rs140241383 on chromosome 19p13, also known as p.Ser265Arg. The patient was diagnosed with early-onset Alzheimer's disease. Increased levels of LDL-cholesterol were detected in the serum of the patient's two sons. They were diagnosed with familial hypercholesterolemia and were prescribed statins.

Conclusion:

Considering that hypercholesterolemia may be an early risk factor for AD, it is necessary to keep in mind the possible development of cognitive impairment in patients with ineffective lipid metabolism. In young patients with hypercholesterolemia and dementia, LDLR mutation should be taken into consideration.

Keywords:

Dementia; Early-onset Alzheimer's disease; Familial hypercholesterolemia; Genetics; LDLR

Liječnički vjesnik, 144; 2022; suplement 7; 17
https://doi.org/10.26800/LV-144-supl7-17

Infarction of three spleens due to torsion in a patient with incomplete situs inversus – a case report

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Background:

Splenic infarction is considered a rare cause of abdominal pain. Incomplete situs inversus is an infrequent condition in which the organs of the abdomen are arranged in a mirror image reversal of the normal positioning with the heart on the normal left side of the thorax. In 95% of cases, congenital heart disease is present. It is associated with asplenia or, less commonly, polysplenia.

Case presentation:

A 12-year-old female patient was admitted to the Department of Pediatric Surgery due to abdominal pain and multiple vomiting with gastric content since the morning. In the abdominal ultrasound, several oval areas of intermediate echogenicity were detected on the right side of the lower abdomen and between the right kidney and liver. Due to the atypical image on ultrasound and abdominal x-ray, it was decided to expand the diagnostics. The CT scan of the abdomen with contrast revealed: incomplete situs inversus with 13 spleens, of which three were not enhanced after administration of contrast (image of the splenic infarction). Three spleens measuring 41x30x62 mm, 65x33x60 mm, and 14x11x10 mm were located laterally to the right kidney. A cardiologist consulted the patient and no relevant abnormalities were found. The patient was qualified for laparoscopic surgery.

Conclusion:

CT scan with contrast is the primary modality in the diagnosis of abdominal organs infarctions. Splenic torsion is a rare but clinically important cause of acute abdomen, that should be recognized as fast as possible by the physician. Incomplete situs inversus may be the reason for delayed diagnosis of emergencies and may require the use of extended diagnostics.

Keywords:

acute abdomen, radiology, situs inversus, spleen infarction

Liječnički vjesnik, 144; 2022; suplement 7; 18
https://doi.org/10.26800/LV-144-supl7-18

Interdisciplinary care of the patient in demanding socioeconomic circumstances: a Case Report from general physician point of view

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Background:

General physicians commonly face legal and ethical issues when dealing with patients in demanding socioeconomic circumstances. Interdisciplinary approach is often needed in order to achieve satisfactory treatment results.

Case presentation:

A 78-year-old patient was discharged home after arthroplasty performed due to hip fracture. He lives with his son and wife in poor socioeconomic circumstances. His 46-year-old son, whom he is the legal guardian of, has been treated for schizophrenia since the age of 23. Patient's wife has untreated schizoaffective disorder and is not capable of caretaking. Post-surgery home health care was recommended and provided by our health center, however his wife refused caregivers help due to her untreated psychiatric condition. During the general physician's home visit shortly after the procedure, the patient was found undermedicated, immobile and in unsanitary conditions, which seriously endangered his recovery. After issuing a referral to stationary rehabilitation, social welfare was contacted, in order to transfer patient's guardianship to social welfare or another family member.

Conclusion:

Socioeconomic circumstances can determine a patient's recovery process, despite all the efforts of health institutions and services. Interdisciplinary approach is essential when dealing with psychiatric patients, especially undiagnosed and untreated ones. Social welfare is often involved in these situations in order to regulate legal difficulties that medical workers face in contact with patients. Ideal patient recovery can be achieved by immediate admission to to stationary rehabilitation after hospital discharge.

Keywords:

family medicine, interdisciplinary care, schizophrenia, social welfare

Liječnički vjesnik, 144; 2022; suplement 7; 19
https://doi.org/10.26800/LV-144-supl7-19

Kaposiform hemangioendothelioma with Kasabach-Meritt syndrome: life-threatening tumor treated with sirolimus

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Background:

Kaposiform hemangioendothelioma (KHE) is a rare and aggressive, potentially life-threatening vascular tumor typically occurring in infancy. It is frequently associated with the Kasabach-Meritt syndrome (KMS), a serious consumptive coagulopathy with thrombocytopenia and hypofibrinogenemia. Because of this, morbidity rates are high. As of yet, no standardized guidelines exist for the treatment of KHE.

Case presentation:

In January 2019 a male full-term newborn presented to the neonatal intensive care unit (NICU) with a 14x10 cm tumor on the left side of the neck. The pregnancy itself was well-controlled and the male newborn was delivered by an elective C-section, with an Apgar score of 9/9. The tumor, purple in color and covered in petechiae and ecchymoses, was extending from the base of the neck towards the mandibula. Upon the transfer to the NICU, laboratory findings (platelets 9,000/μL, fibrinogen 0.8 g/L, D-dimer >10 mg/L, aPTT 37.1 s) showed significant thrombocytopenia and hypofibrinogenemia. Initial assessment (MRI and TOF angiography) showed a hypervascular, heterogeneous structure suggestive of hemangioma. The initial treatment strategy consisted of administering blood derivatives, DSA embolization of the tumor, propranolol, antifibrinolytics, and corticosteroids – but no clinical or laboratory improvement was noted. The MRI, laboratory findings, and the clinical course of the disease were all indicative of KHE, hence treatment with peroral sirolimus (an mTOR inhibitor) in combination with parenteral corticosteroids was started. In the following two months, complete resolution of KMS was noted with a progressive reduction in tumor size. The coagulation parameters turned normal. The patient is still on sirolimus and demonstrates nearly complete involution of the lesion with no apparent side effects.

Conclusion:

As there are no standardized guidelines for the treatment of KHE, this case strongly suggests the effectiveness of sirolimus treatment in severe KHE/KMS.

Keywords:

Kaposiform hemangioendothelioma, Kasabach-Meritt syndrome, Sirolimus

Liječnički vjesnik, 144; 2022; suplement 7; 20
https://doi.org/10.26800/LV-144-supl7-20

Massive hemoptysis caused by pseudoaneurysm in a patient with pulmonary tuberculosis

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Background:

Hemoptysis represents an alarming symptom that can potentially be a first sign of pulmonary tuberculosis. In the presence of tuberculosis, hemoptysis might be caused by various etiopathologies. Pseudoaneurysm, even though a rare one, can be a cause of this life-threatening emergency. This case describes a pseudoaneurysm causing massive hemoptysis in a patient with pulmonary tuberculosis.

Case presentation:

We present a 51-year-old male patient experiencing chronic productive cough lasting for months, with severe hemoptysis that had occurred 7 days before hospitalization, as well as shortness of breath, recent night sweats and weight loss. Laboratory workup showed microcytic anemia, leukocytosis, elevated C-reactive protein, hypokalemia, hyponatremia and hypoalbuminemia. The classic chest X-ray showed inhomogeneous shading of the upper lung lobe on the right, with a large round soft tissue shadow located in the middle lobe, with bilateral spotted infiltrates. Flexible bronchoscopy was interrupted before bronchoscopic sampling was done, due to the patient's intolerance. A CT scan showed a completely morphologically altered upper lung lobe on the right and a large consolidation in the anterior segment of the lower lung lobe with foci of destruction containing a pseudoaneurysm. A positive culture for *Mycobacterium tuberculosis* confirmed a finding, given by direct microscopy, and a diagnosis of extensive pulmonary tuberculosis, with pseudoaneurysm within the inflammatory consolidation of the right lower lobe, was established. The patient was treated with conservative therapy that included rest, cough suppressant, tranexamic acid, blood transfusion and the first line of antituberculous therapy. His clinical condition was gradually improved and there was no need for bronchial artery embolisation (BAE) or urgent surgical procedures.

Conclusion:

Pseudoaneurysm is an extremely rare complication of tuberculosis, but it might cause a life-threatening condition. This case emphasizes the importance of comprehensive knowledge of atypical tuberculosis manifestations and complications since prompt diagnosis and early interventions are essential.

Keywords:

hemoptysis, pseudoaneurysm, tuberculosis

Liječnički vjesnik, 144; 2022; suplement 7; 21
https://doi.org/10.26800/LV-144-supl7-21

Moyamoya disease

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Background:

Moyamoya disease (MMD) is a chronic, occlusive cerebrovascular disease characterized by progressive stenosis at the terminal portion of the internal carotid artery and an abnormal vascular network at the base of the brain. The clinical presentation is variable. Children mainly present with ischemia-related neurologic episodes whereas MMD in adults can manifest as either an ischemic event or an intracranial hemorrhage (ICH).

Case presentation:

We present a 35-year-old man presented with recurrent paresthesias of the left side of the face, left hand, left foot and dysarthria in the emergency department. Initial CT angiography verified steno-occlusive changes in cerebral blood vessels typical of Moyamoya syndrome. Further processing on the performed MR excluded the existence of acute ischemia with multiple chronic changes. Cerebral panangiography confirmed changes in cerebral vessels that morphologically correspond to MMD. The patient underwent direct revascularization, creating an anastomosis between the superficial temporal artery and the middle cerebral artery (STA-MCA) without any complications. Following surgery, he was prescribed 100 mg aspirin and discharged home with a follow-up visit 6 months later.

Conclusion:

MMD has become a more established cause of stroke for children and adults.To obtain the best result in patients, it is crucial to identify the disease at an early stage. In adult patients with Moyamoya disease, careful neurologic and radiologic long-term follow-up is vital to avoid further stroke and improve performance.

Keywords:

Moyamoya, Ischemia, Revascularization

Liječnički vjesnik, 144; 2022; suplement 7; 22
https://doi.org/10.26800/LV-144-supl7-22

Multiple endocrine neoplasia type 2B – the role of the ophthalmologist

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Background:

Multiple endocrine neoplasia type 2B (MEN2B) is rare (estimated prevalence between 1 in 600,000 to 1 in 4 million) but often fatal cancer syndrome. This hereditary autosomal-dominant condition is caused by activating germline mutations in the *RET* proto-oncogene. MEN2B syndrome can cause thyroid and parathyroid gland carcinoma, pheochromocytoma, and benign lesions such as multiple submucosal neuromas. Distinctive physical features are often seen in affected individuals, including marfanoid habitus, full lips and thickened eyelids. We aim to present patients with MEN2B diagnosed by ophthalmologists based on characteristic ocular findings.

Case presentation:

Between 2012 and 2022 at University Hospital Centre Zagreb MEN2B syndrome was suspected in two patients (aged 7 and 12 years) and confirmed by genetic testing. Molecular genetic analysis detected a mutation at codon 918 of the *RET* proto-oncogene present in 95% cases of MEN2B. Both patients were clinically examined, a detailed record of symptoms was made and a family history was taken, the necessary tests and procedures were performed. The patients had prominent corneal nerves and nodules located on eyelids, conjunctiva, lips and tongue so as characteristic facies. Serum calcitonin and intraocular pressure were elevated in both patients. Surgical treatment and histologic analysis confirmed medullary thyroid carcinoma. In one patient metastasis in the lymph nodes of the neck were found. There were no signs of pheochromocytoma.

Conclusion:

Characteristic findings of MEN2B include prominent corneal nerves in a clear stroma and multiple submucosal neuromas of the conjunctiva, eyelids, lips, and tongue. Ophthalmologists have a critical role to play in recognizing these signs, because the early diagnosis may be lifesaving. Higher awareness regarding the early non-endocrine signs of MEN2B could lead to earlier diagnosis, prevention of medullary thyroid cancer development and thus better prognosis.

Keywords:

medullary thyroid cancer, multiple endocrine neoplasia type 2B, ophthalmology, prominent corneal nerves, submucosal neuromas

Liječnički vjesnik, 144; 2022; suplement 7; 23
https://doi.org/10.26800/LV-144-supl7-23

Never underestimate the importance of surveillance – a case report of a patient with post-EVAR endoleaks

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Background:
Endovascular aneurysm repair (EVAR) has become a well-established approach in the elective treatment of abdominal aortic aneurysms (AAA). It represents a treatment of choice for high-risk patients ineligible for open surgery due to the increased risk of perioperative morbidity and mortality. However, it requires lifelong surveillance with CT aortography (CTA) or contrast-enhanced ultrasound due to more long-term complications compared to open surgery. Endoleak is the most common graft-related complication with type II endoleak being the most common type. Type I and III endoleaks (T1E, T3E) are the most dangerous type of endoleaks, both leading to pressurization of the aneurysm sac and rupture. We report the case of a 72-year-old male patient with various types of endoleaks after EVAR.

Case presentation:
In 2015 ASA IV patient with known asymptomatic infrarenal 6.6x6cm AAA underwent elective EVAR with main device and bilateral iliac limbs (Medtronic, Endurant II). His past medical history revealed myocardial infarction, ischemic cardiomyopathy, hypertension, pancreatitis, and cholecystectomy. He was on regular stent-graft surveillance. Until 2021 he had been free of any EVAR-related complications when he presented to the emergency department with cramping abdominal pain. CTA demonstrated the presence of T1aE and T1bE. ChEVAR with Aortic Extension 32mm (Medtronic, Endurant II) and BeGraft Peripheral 5x59mm for T1Ea, stent grafting with two additional main device extensions, 28x28mm and 13x13mm, for T1Eb followed by ballooning, was successfully performed. Follow-up CTA in 2022 revealed the presence of a T3E that was immediately managed with an additional 16x10x199 mm endograft extension and by repeat ballooning at areas of component overlap.

Conclusions:
Endoleak is an important complication for EVAR which is often asymptomatic hence regular follow-up is needed and immediate management is crucial to prevent future aneurysm rupture. Nevertheless, this case demonstrates the importance of lifelong attentive surveillance to promptly diagnose and treat complications.

Keywords:
Endoleak, endovascular aneurysm repair, surveillance

Liječnički vjesnik, 144; 2022; suplement 7; 24
https://doi.org/10.26800/LV-144-supl7-24

Primary Ewing sarcoma of lungs with mediastinal metastasis, a rare type of metastatic lung neoplasm

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Background:

The Ewing sarcoma family of neoplasms comprises different types of tumors which share mutual neuroectodermal histology and pathogenesis. Although skeletal Ewing sarcoma is the second most common primary bone tumor, extraosseous Ewing sarcoma remains extremely rare. In this case report, we presented a young female patient with metastatic Ewing sarcoma of the lungs.

Case presentation:

A young female patient was diagnosed with primary Ewing sarcoma of the left lung at the age of 12. Initial therapy included a left-sided lobectomy followed by adjuvant chemoradiotherapy. Further PET CT investigations showed signs of disease in remission. One year after the last chemotherapy treatment by Euro Ewing protocol, MRI and PET CT investigations showed the disease in progression. PET CT showed increased metabolic activity in the right upper lobe of the lungs. Mediastinal lymphadenopathy of the left hilus was confirmed and metastatic disease was suspected. Accordingly, an endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was performed. The results of cytological analysis of 3 samples obtained from left hilar lymph nodes (region 10L) confirmed metastasis of the Ewing sarcoma. Additional chemoradiotherapy was performed, but with limited effect. A year and a half after the metastatic disease was confirmed, the disease progressed and oral metastases were found.

Conclusion:

Since there have been very few or no studies on the treatment of metastatic primary extraskeletal Ewing sarcoma, there has been no international consensus on how to treat Ewing sarcoma family neoplasms. Some studies claim a similar treatment for almost all types of Ewing sarcomas. Furthermore, there are studies which showed a more significant role of surgery in the extraskeletal group of Ewing sarcomas. Lastly, metastatic and inoperable Ewing sarcomas have a limited spectrum of action since most patients have already taken up all treatment possibilities.

Keywords:

endoscopic ultrasound-guided fine needle aspiration; extraosseus Ewing sarcoma; lung cancer

Liječnički vjesnik, 144; 2022; suplement 7; 25
https://doi.org/10.26800/LV-144-supl7-25

Psychogenic Nonepileptic Seizure Disorder – A Drop in the Ocean of Seizures

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Background:
According to ICD-11 Psychogenic Nonepileptic Seizures (PNES) are defined as paroxysmic and episodic events associated with motor, sensory, mental, or autonomic manifestations, which resemble epileptic seizures (ES), but are not caused by epileptogenic activity. PNES mostly differ from ES by longer duration, hip, and head movements, and closed eyes. This case report will show the effect of stressful events causing seizures without organic etiology.

Case presentation:
A 22-year-old female was hospitalized at the Department of Neurology due to a history of frequent seizures. Day after the hospitalization the patient underwent video EEG monitoring. It showed no abnormalities although she suffered a seizure. During the 7 minutes of the seizure, she had closed eyes and was uncontactable with both head and hip movements and grimaces being present. Furthermore, the patient has been receiving psychiatric treatment for depression and anxiety attacks since 2017. They were triggered by the suicide attempt of her sister, father's alcoholism, and bad family relations which all together led to the development of the seizures. The patient had a neuropsychiatric multidisciplinary examination which showed lower cognitive function with emotional instability and disorganized thoughts. Therefore, the neurologists and psychiatrists diagnosed the patient with PNES. She was transferred to the Department of Psychiatry where she was treated with appropriate psychopharmacotherapy with the support of psychotherapy. Clonazepam, Sertraline, Flufenazine, Quetiapine and Biperiden were introduced as therapy. Although the diagnosis and treatment proved to be successful, the patient regularly quits the therapy due to the weakening of the symptoms which leads to a recurrence of the seizures

Conclusion:
The difference in the clinical presentation of PNES and ES must be recognized to avoid mistreatment with antiepileptics. Finally, it is crucial to highlight the importance of the patient being consistent with the therapy to see the long-term effects.

Keywords:

psychogenic nonepileptic seizure disorder, psychological trauma, seizures

Liječnički vjesnik, 144; 2022; suplement 7; 26
https://doi.org/10.26800/LV-144-supl7-26

Respiratory distress in a pregnant woman caused by COVID-19

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Background:

Pregnant women are more prone to respiratory diseases, including the novel coronavirus disease (COVID-19). Research shows that COVID-19 increases the chance of preterm birth, intrauterine growth retardation, and miscarriage. In pregnant women, extremely rarely, a possibly fatal respiratory distress can occur that demands mechanical ventilation.

Case presentation:

We present a 34-year-old COVID positive female in the 32nd week of pregnancy who was transferred to Intensive Care Unit (ICU) from another hospital because of rapid deterioration in general health and pregnancy monitoring. Bilateral pneumonia was confirmed, and the urine analysis showed bacteriuria. Ceftriaxone was introduced. Clexane 0.6mL s.c. and an intravenous Dexamethasone dose of 12mg were continued from the therapy used in the previous facility. The patient's nasal mask with a flow of 15 L/min was replaced with high-flow nasal oxygen (55 L/min with 70% oxygen). In the next two days, the patient's condition improved, only to deteriorate severely on the third day of the treatment. Cardiotocography showed pathological findings that suggested possible fetal hypoxia. An emergency cesarean section was made, and the baby was successfully delivered. After the delivery, the patient was transferred again to the ICU, intubated and mechanical ventilation was started. Prone positioning and adequate ventilation modalities led to the improvement of respiratory function, which led to the extubation on the 9th day of the treatment.

Conclusion:

Respiratory distress caused by COVID-19 in pregnant women demands a prompt reaction and special treatment of both patients- the mother and the baby. Such a reaction could only be done by an experienced team in a well-equipped facility.

Keywords:

COVID-19, Intensive Care Unit, Pregnancy, Respiratory Distress Syndrome

Liječnički vjesnik, 144; 2022; suplement 7; 27
https://doi.org/10.26800/LV-144-supl7-27

Severe metabolic acidosis as initial manifestation of a neuroendocrine pancreatic tumor

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Background:

Neuroendocrine tumors (NETs) are a heterogeneous group of tumors that usually arise in the gastrointestinal tract, lungs, adrenal glands or thyroid gland, with the pancreas being the most common site. NETs of the pancreas are usually nonfunctional, present with nonspecific symptoms, and thus can be difficult to detect.

Case presentation:

A 58-year-old male patient, with a history of type 2 diabetes mellitus, presented in the emergency department with fatigue and widespread pain. One week prior, the patient began experiencing stomach cramps, nausea and abdominal pain that radiates to the back. During this time, he lost his appetite. Upon arrival, laboratory tests showed an acid-base disturbance, with a blood pH of 6.8 and lactate levels above 15 mmol/l. Creatinine levels were 954 µmol/l and urea was 38.9 mmol/l. Because the patient was being treated with metformin therapy, he was initially admitted to the intensive care unit for possible metformin lactic acidosis and acute renal failure. Suspecting mesenteric ischemia, a CT scan was performed revealing an expansive mass, 4.5x3.5 cm in size, located at the pancreatic tail and infiltrating the splenic hilus and the gastric wall. Initial treatment included renal dialysis, intravenous bicarbonate, norepinephrine and antibiotics with gradual improvement. The patient was transferred to the Chronic Liver Disease Center for further evaluation of the abdominal mass. Multiple biopsies were obtained during the esophagogastroduodenoscopy and histopathological findings showed a G3 neuroendocrine tumor (NET). He underwent surgery followed by adjuvant chemotherapy with etoposide and cisplatin, and has no evidence of recurrence after 18 months.

Conclusion:

We report the first case, to our knowledge, of metastatic pancreatic NET presenting with severe lactic acidosis. This report emphasises the importance of a thorough diagnostic workup and intensive treatment, enabling a long-term positive outcome for the patient.

Keywords:

lactic acidosis; metformin; neuroendocrine tumors

Liječnički vjesnik, 144; 2022; suplement 7; 28
https://doi.org/10.26800/LV-144-supl7-28

Splenic flexure volvulus in adult patient with cerebral palsy

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Background:

Colonic volvulus is a clinical entity characterized by abnormal torsion of the large bowel intestine loop around the axis of its mesentery leading to bowel obstruction. Colonic volvulus constitutes only 15% of all large bowel obstructions, with the sigmoid colon and cecum as the most commonly affected sites. On the contrary, splenic flexure volvulus (SFV) represents the rarest subtype of all colonic volvulus that cause less than 1% of all of them. To date, only a few cases of SFV have been reported in the literature, of which very few are in adult patients with cerebral palsy.

Case presentation:

A 42-year-old female with a previous history of cerebral palsy, mental retardation, epilepsy, and tetraplegia presented to the emergency department with complaints of abdominal pain and vomiting that had been going on for a day. There was also a history of chronic constipation, laxative use, psychotropic drugs, and no previous abdominal surgeries. Her vital signs were within normal limits. Physical examination revealed a distended and tympanic abdomen with mild generalized tenderness but without signs of peritoneal irritation. Laboratory tests showed mild leukocytosis (12.5 x 10^9/L) and neutrophilia (10.8 x 10^9/L). An abdominal plain X-ray film demonstrated distension of the cecum and ascending colon. Computed tomography revealed mesentery torsion with a whirl sign in the splenic flexure area leading to a diagnosis of SFV. The patient underwent an emergency decompressive colonoscopy with successful devolvulation of the colon and complete regression of symptoms.

Conclusion:

Splenic flexure volvulus is an extremely rare cause of intestinal obstruction with possible severe complications. This case report shows that SFV, despite its infrequency, should be considered a possible cause of acute abdomen in patients with cerebral palsy due to irregular bowel habits, immobility, and drugs.

Keywords:

Cerebral palsy, intestinal obstruction, splenic flexure volvulus

Liječnički vjesnik, 144; 2022; suplement 7; 29
https://doi.org/10.26800/LV-144-supl7-29

Successful treatment of dumping syndrome in infant with Haddad syndrome

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Background:

Haddad syndrome (HS) is a rare neurocristopathy caused by mutations in the PHOX2b gene. Two main symptoms include congenital central hypoventilation syndrome (CCHS) and Hirschsprung disease (HD). Impaired glucose tolerance is one of the rarely reported and possibly overlooked symptoms of HS.

Case presentation:

Our patient is a 4-month-old boy born at term from a second uncomplicated pregnancy from healthy, young, and unrelated parents. He was transferred to the newborn intensive care unit on the first day of birth due to frequent apnoea. Multiple unsuccessful attempts of extubation and signs of hypoventilation during sleep lead to diagnosis of CCHS. The boy also developed signs of HD in first weeks of life. Diagnosis of HS was confirmed by genetic testing. At the age of four months frequent asymptomatic hypoglycaemias were observed despite adequate peroral intake. The lowest measured blood glucose (BG) was 2.1 mmol/L, with insulin levels of 2.6 mU/L. Readings from continuous subcutaneous glucose monitoring revealed dumping syndrome pattern with hyperglycaemia in first hour, followed by hypoglycaemia in a second hour postprandially. Various combinations of milks and frequency of feedings were attempted to prevent dumping syndrome but none of the were successful. Finally, at the age of 6 months, to retard the digestion of carbohydrates in the small intestine, an alpha-glucosidase inhibitor (Acarbose) was introduced in treatment which led to normal glucose tolerance without side effects.

Conclusions:

Haddad syndrome is a rare condition that needs lifetime care of a multidisciplinary team. Given its rarity, it is usually diagnosed late. Impaired glucose tolerance is an overlooked symptom of unexplained aetiology that can easily be missed. Acarbose is safe, tolerable, and efficient in treatment of impaired glucose tolerance in patients with HS.

Keywords:

Alpha-glucosidase inhibitor, Congenital central hypoventilation syndrome, Haddad syndrome, Hirschsprung disease

Liječnički vjesnik, 144; 2022; suplement 7; 30
https://doi.org/10.26800/LV-144-supl7-30

Supracricoid partial laryngectomy

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Background:

Supracricoid partial laryngectomy (SCPL) is a procedure invented in 1959, since then it hasn't been used very often. SCPL is an organ preservation surgical technique alternative to total laryngectomy for selected laryngeal malignant neoplasms. It has the advantage of preserving larynx phonatory function, lung-powered speech and swallowing function, without a permanent stoma. Our question is: What is the quality of life after SCPL and does it provide more benefits than total laryngectomy?

Case presentation:

In our case report we present a 56-year-old male patient, who had dysphonia for the last six months. He had no respiratory or swallowing problems. Due to these symptoms, an extensive diagnosis was made with fiber optic endoscopy, laryngomicroscopy and biopsy. The patient was diagnosed with planocellular (PCC) laryngeal carcinoma, located in the anterior half of the right vocal cord, anterior commissure and anterior third of the left vocal cords at stage T2N0. He was a smoker for about 20 years and has 30 pack years. He stopped smoking 3 months ago. The chosen surgical procedure was SCPL. An unilateral dissection of the neck was performed in the II-IV regions on the right side. Tracheotomy was also performed and a temporary tracheostoma was placed. After rehabilitation, the patient showed a remarkable recovery of speech and swallowing.

Conclusion:

SCPL achieves the functional goals of speech and swallowing rehabilitation. The speech recovery process is quite natural, and tracheostomy is temporary, which is the main detriment to the quality of life. On the other hand, swallowing rehabilitation requires more work. In conclusion, SCLP shows many benefits in the rehabilitation process and should be considered as a treatment alternative to non-surgical treatment or total laryngectomy.

Keywords:

Laryngeal carcinoma, partial laryngectomy, supracricoid

Liječnički vjesnik, 144; 2022; suplement 7; 31
https://doi.org/10.26800/LV-144-supl7-31

The Human Parechovirus as a rare cause of the encephalitis in neonate

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Background:

In the era of PCR analysis of the cerebrospinal fluid (CSF), the human parechovirus (HPeV) is an increasingly recognized cause of central nervous system (CNS) infections in infants younger than 3 months. HPeV encephalitis is a rare infection in term-born children and mainly affects premature neonates. The symptoms of HPeV infection include fever, rash, irritability, lethargy, seizures, cough, diarrhea and feeding difficulties. HPeV can also cause sepsis and even death. Parechovirus encephalitis in neonates and infants can lead to neurological sequelae or neurodevelopmental delay.

Case presentation:

A seven-day-old neonate (birth at 39 weeks gestation) was admitted to the Department of Neonatal Pathology due to otitis externa. The boy was noted to be reluctant to eat and severely anxious. The neonate presented insufficient weight gain, features of dehydration, erythematous-papular rash on the surface of the trunk and limbs, and a tense abdomen. The fever (38°C) with tachycardia appeared a few hours after the admission. There were two episodes of clonic hemiplegic seizures on the next day of hospitalization. The presence of HPeV was detected in the PCR test of CSF. The MRI of the CNS showed symmetrical, diffuse inflammatory lesions located in the white matter and periventricular. The boy was diagnosed with parechovirus encephalitis and received immunoglobulin treatment. After a month, a follow-up MRI showed the evolution of inflammatory lesions in the brain.

Conclusion:

Parechovirus encephalitis in term-born neonatea is an uncommon infection. MRI is the primary modality for imaging inflammatory lesions of the CNS especially in children. Early detection of the HPeV through the combination of the PCR--based assays for CSF and MRI scans allows the diagnosis and early application of appropriate treatment. Children after HPeV encephalitis require long-term follow-up due to possible neurological complications, such as impairment in auditory or visual functions, or gross motor function delay.

Keywords:

encephalitis, neonate, the human parechovirus

Liječnički vjesnik, 144; 2022; suplement 7; 32
https://doi.org/10.26800/LV-144-supl7-32

Unusual Non-ST-Elevation myocardial infarction presentation in a 75-year-old male with diabetes

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Background:

Acute myocardial infarction is a common emergency condition split into myocardial infarction with ST elevation (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina. NSTEMI patients usually present with classic symptoms of myocardial infarction: chest pain that may radiate to either arm, neck, or jaw, associated dyspnea or nausea. Elderly patients, females or patients with diabetes can present with rare/uncommon symptoms.

Case presentation:

We report a 75-year-old male that was examined by his family medicine physician for left shoulder pain. The patient had a long-term history of hypertension and diabetes, and reported he had fallen the previous day. Physical examination did not provide any signs of traumatic damage and were all negative for rotator cuff injury. The patient was instructed to ice and rest his shoulder with analgesics as needed and to make an X-ray imaging of the shoulder. The patient returned in a week with a non-deviating x-ray and unmitigated pain in the shoulder. A further anamnesis revealed that the patient had been experiencing dyspnea and shortness of breath in the last few days alongside being unable to handle more laboring activities. An ECG revealed ST-elevations in leads V1-V4, indicative of NSTEMI. The patient was hospitalized through the emergency department and an invasive coronarography was indicated the next morning. The coronarography revealed a near-total stenosis of the LCx and a 50% stenosis of the LAD artery, in the same procedure the LCx was stented. The patient was released after one more day of hospitalization with a new diabetic and hypertension therapy as well as a new diet and other cardiovascular disease recommendations.

Conclusion:

NSTEMI is a life-threatening condition which can be easily missed due to non-specific symptoms that can be seen in long-term diabetics with advanced neuropathy and the elderly.

Keywords:

myocardial infarction, NSTEMI, shoulder pain, diabetic neuropathy

2. ORIGINAL RESEARCHES

Liječnički vjesnik, 144; 2022; suplement 7; 34
https://doi.org/10.26800/LV-144-supl7-34

Automated ImageJ/FIJI plug-in for morphological study of neurons and biological objects (LUSCA)

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Introduction: The plasticity of the mammalian brain is achieved through fine-tuning of the number of contacts among cells. This means that the cell's length, shape, and the quantity of its projections are not static parameters. As such, any image analysis is faced with the quantification of thousands of cells of various sizes, shapes, and dimensions, requiring specialized, often proprietary programs.

Aim: The main goal was to develop a new plug-in for ImageJ/Fiji that can perform automatic morphological analysis of neurons.

Materials & methods: Neural stem cells, isolated from the telencephalic wall of 14.5 days old mouse embryos, were cultivated in differentiation medium for ten days, and labelled with MAP2 and SMI312. Images were analysed with Lusca, validated against the golden standard (manual analysis), and compared to similar scripts: NeuronJ, NeuriteTracer, NeurphologyJ, CellProfiler and Imaris. The unpaired t-test was used for the statistical analysis of width, while all the other analysis was done using the one-way ANOVA with the Tukey Kramer multiple comparisons post-hoc test.

Results: Lusca performs image segmentation using a machine learning process - Trainable Weka Segmentation, followed by fine tuning with respect to intensity and size thresholds. Particle analysis is used for determination of area/volume, number, and intensity of the objects, while the length and width analysis are performed using one-pixel lines and Local Thickness. The colocalization analysis is based on the JaCoP plug-in. Comparison with similar programs revealed that Lusca offers more options for analysis, with faster and more accurate quantifications, including better noise elimination and recognition of barely visible details.

Conclusion: Lusca is a useful tool for automatic, fast, and accurate analysis of images of neurons, representing a viable and time-saving alternative to current open-source software. Since it utilizes machine learning, it also facilitates analysis of other biological objects such as mitochondria and blood vessels.

Keywords: automated quantification, image analysis, ImageJ, machine learning, neuronal morphology

Liječnički vjesnik, 144; 2022; suplement 7; 35
https://doi.org/10.26800/LV-144-supl7-35

Expression of NOTCH1 intracellular domain in intracranial meningioma

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Introduction: Intracranial meningioma count for one of the most common primary brain tumors. Although mostly benign, small portion of meningioma can develop malignant characteristics. Aberrant cellular signalling can lead to tumorigenesis, but the underlying mechanism of meningioma progression is still unknown. Notch signalling pathway has a role in maintaining neural progenitor cells during embryogenesis. In tumorigenesis, activation of this signalling pathway can lead to proliferation, invasion and progression. One of the main molecular actors of the pathway is NOTCH1. Translocation of Notch intracellular domain (NICD) to the nucleus can commence transcription of oncogenes. Information on the role of NICD in meningioma is still scarce.

Aim: The aim of this study was to investigate expression and localization of NOTCH1 intracellular domain in different grades of meningioma.

Materials & Methods: Formalin-fixed paraffin-embedded sections were collected from 56 patients diagnosed with meningioma tumors of different grades. In order to study expression and localization of NICD in meningioma sections, we used DAB-labelled immunohistochemical reaction with Anti-Notch1 intracellular domain antibody (ab8287, Abcam, Cambridge, UK). Healthy brain tissue from cortex was also analysed, and results were compared to the ones of tumor samples.

Results: In healthy brain tissue we observed high cytoplasmic expression of NCID (IRS=12). However, the translocation of NICD into nuclei was absent. Contrary, in meningioma only 10.71% samples lacked nuclear expression of NICD, while 71.43% had strong expression in more than half of nuclei in the field of view. The cytoplasmic expression of NICD was observed in all meningioma samples with strong expression in 69.64%, medium in 25% and low in 5.36%. The higher nuclear expression was accompanied with higher cytoplasmic expression (p=0,002).

Conclusion: Nuclear translocation of NICD in meningioma, which was absent in healthy brain tissue, suggests aberrant Notch signalling in intracranial meningioma.

Key words: Intracranial meningioma, NOTCH1 intracellular domain, Notch signalling pathway

Liječnički vjesnik, 144; 2022; suplement 7; 36
https://doi.org/10.26800/LV-144-supl7-36

Non-invasive ventilation in COVID-19 patients – high vs low PEEP

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Introduction: Positive end-expiratory pressure (PEEP) is a positive pressure that remains in the airway at the end of expiration, decreasing atelectasis and improving ventilation-perfusion (VQ) mismatch. Ideal PEEP value is one that enables the preponderance of potential benefits over potential complications. Use of non-invasive ventilation (NIV) in COVID-19 patients with acute respiratory distress syndrome (ARDS), although still debatable, is associated with decreased mortality. Recent studies suggest that high PEEP ventilation decreases atelectrauma, pulmonary oedema, reduces the risk of patient self-inflicted lung injury and helps patients to breathe easier.

Aim: Assessment of respiratory response to high PEEP NIV in COVID-19 patients.

Materials & Methods: A retrospective cohort study was conducted in the COVID-19 intensive care unit (ICU) of University Hospital Centre Zagreb. Study included 93 patients treated with NIV from October 2021 to February 2022. PEEP values and respiratory frequencies (RF) were observed and HACOR score was calculated on 1st, 3rd and 7th day of hospitalization. The definite outcome was objective and subjective assessment of work of breathing.

Results: Out of 93 patients treated with NIV, 40 (43.0%) patients required a switch to invasive mechanical ventilation. For 53 (57.0%) patients, NIV was the only ventilation method for their entire stay in ICU. There was a statistically significant difference between 1st and 3rd ($p=0.005$), and 1st and 7th day ($p=0.010$) in RF. A statistically significant difference was found for HACOR scores ($p<0.001$) between 1st and 3rd day of hospitalization. Patients requiring intubation had higher HACOR scores. Additionally, it was found that for each point of the 7th-day HACOR score, the risk of NIV failure was 66% higher ($p=0.003$).

Conclusion: Treatment of COVID-19 ARDS with high PEEP NIV reduces the work of breathing, improves oxygenation, and helps patients feel comfortable and breathe easier.

Keywords: COVID-19, Non-Invasive Ventilation, PEEP

Liječnički vjesnik, 144; 2022; suplement 7; 37
https://doi.org/10.26800/LV-144-supl7-37

Preoperative volumetry analysis is associated with higher efficacy of stereotactic evacuation of cystic brain lesions or abscess: retrospective comparison in a single center

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Introduction: Preoperative volumetry is used to assess the volume of fluid in different brain cystic lesions in patients undergoing stereotactic cyst evacuation. We hypothesize that preoperative volumetry might aid in optimizing the extent of cyst volume reduction by providing a benchmark.

Aim: We aimed to compare cyst evacuation efficacy with regards to (non) performance of preoperative volumetric analysis.

Materials & Methods: Clinical Hospital Center Zagreb digital archive was screened for patients who underwent stereotactic brain cyst aspiration between January 2013 and December 2019. Data were collected on patient age, sex, and pre- and postoperative cysts volumes. Patient data were compared between volumetry and non-volumetry group, also pre- vs. postoperative cyst volumes were compared intragroup.

Results: We identified eleven patients, eight were operated for a brain abscess and three for a tumor cyst. Median age was 31 years (range 6-64), three were women and eight men. Median preoperative cyst volume was 21.0 cm^3 (range 1.0-38.2 cm^3), median postoperative volume 5.4 cm^3 (0.8-16.1 cm^3), median change in volume 9.7 cm^3 (range 0.8-27.4 cm^3). Five patients had a preprocedural volumetry (volumetry group) and six patients did not (non-volumetry group); there were no significant differences in age, sex, preoperative volume, postoperative volume, and volume change across groups. There was a lower median residual cystic volume in the volumetry group. The pre- vs. postoperative difference in cyst volume was significant in the volumetry group (10.8 cm^3 to 2.7 cm^3, $P = 0.012$) and not significant in the non-volumetry group.

Conclusion: Our results suggest an association between volumetric assessment and extent of brain cyst evacuation. Notwithstanding limitations due to sample size, we hold that the data are indicative and warrant further research. Volumetric analysis should be considered a standard diagnostic adjunct in all patients undergoing a brain cyst evacuation procedure.

Key words: brain abscess, stereotaxy, volumetry

Liječnički vjesnik, 144; 2022; suplement 7; 38
https://doi.org/10.26800/LV-144-supl7-38

Transcriptional activity of *PTX3* gene in diffuse gastric carcinoma subtype

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Introduction: Gastric cancer (GC) is the fifth most commonly diagnosed malignancy and the third leading cause of cancer-associated mortality worldwide. Based on its histological characteristics GC has been historically divided into three major subtypes: intestinal-, diffuse- and mixed-type GC. Among them, patients with diffuse-type gastric cancer (DGC) have a particularly poor prognosis that only marginally improved over the last decades, as conventional chemotherapies are frequently ineffective and specific therapies are unavailable. Up to now, the molecular mechanisms underlying the pathohistogenesis of DGC have not been fully elucidated.

Aim: This study aimed to explore the mRNA expression pattern of long pentraxin 3 (PTX3), an acute-phase protein, and a newly clarified mediator for innate immunity and inflammation in DGC tumor tissue samples and non-tumor gastric tissue controls.

Materials & Methods: *PTX3* mRNA expression levels were measured in 62 DGC tumor tissues and 62 normal gastric mucosal samples obtained from patients with non-malignant disease using quantitative real-time PCR (RT-qPCR). *In silico* analysis of *PTX3* mRNA levels in GC tissues and normal control samples based on publicly available RNA-sequencing data (UALCAN database) derived from the TCGA-STAD project was performed as well.

Results: qRT-PCR-results revealed no difference in *PTX3* mRNA expression between the DGC tumor tissues and normal non-malignant gastric mucosal samples. The obtained qRT-PCR results were further confirmed by in silico analysis of TCGA-STAD RNA-sequencing data. However, the data obtained by *in silico* analysis revealed a statistically significant difference in *PTX3* mRNA expression between the normal tissue samples and the intestinal-GC type and between the DGC and intestinal-GC subtype.

Conclusion: The present study's findings indicate the possible role of the *PTX3* gene in the pathogenesis of histologically different GC subtypes. However, elucidation of its role, if any, in DGC histological subtype requires further analysis.

Keywords: diffuse gastric carcinoma, PTX3, RNA-sequencing data, UALCAN database

3. REVIEWS

Liječnički vjesnik, 144; 2022; suplement 7; 40
https://doi.org/10.26800/LV-144-supl7-40

Breastfeeding and childhood leukemia incidence in developed countries

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Introduction: The prevalence of breastfeeding decreased in modern countries due to the social changes that happened in the last century. It is thought that breastfeeding for six months or longer (which is suggested by WHO) may reduce the risk of numerous childhood diseases. In modern countries, cancer is one of the leading causes of death among children. One of the most common cancer types is leukemia, accounting for around 30% of all childhood malignancies.

Aim: The purpose of this review was to summarize the current evidence on the relation of breastfeeding with the risk of childhood leukemia in developed countries.

Materials & Methods: We analyzed various studies on PubMed and JAMA, published after 1995, using the keywords “breastfeeding”, “childhood leukemia“ and “protective effect”, and found 11 of them strongly related to the topic. To be included in the review, studies had to be case-control and to be conducted in developed countries.

Results: 8 of the 11 reviewed studies suggest that breastfeeding is associated with a decreased risk of childhood leukemia. The largest conducted study showed that any breastfeeding compared with never breastfeeding is associated with a 9% lower risk for childhood leukemia while being breastfed for 6 months or longer reduces the risk of the disease by 21%. Moreover, 5 studies suggest that prolonged breastfeeding significantly reduces the risk for leukemia. Additionally, one study found that being breastfed for 7-9 months has the best protective effect against leukemia.

Conclusion: While results have shown the positive effect of breastfeeding, greater and more recent studies are needed to suggest firm conclusions on the connection between lack of breastfeeding and the occurrence of childhood leukemia. In addition to all the previously known benefits, these findings provide additional reasons for health professionals to promote breastfeeding, a low-cost public health measure.

Keywords: breastfeeding, childhood leukemia, protective effect

Liječnički vjesnik, 144; 2022; suplement 7; 41
https://doi.org/10.26800/LV-144-supl7-41

Medicinal Properties Of Dwarf Mountain Pine (*Pinus mugo Turra*): A Literature Overview

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Introduction: Dwarf mountain pine (*Pinus mugo*), was historically used as a medicinal herb. We present here a brief overview of its possible therapeutic effects and applications in today's medicine.

Aim: We aim to assess and quantify the historically recognised medicinal qualities of *Pinus mugo* by identifying and reviewing its biologically active substances and their possible application in modern medicine.

Materials & Methods: We reviewed articles issued by the European Forest Institute, the European Atlas of Forest Tree Species and the PubMed database using Pinus mugo as keywords. Results: α-pinene and β-pinene are some of the biologically active molecules found in the Pinus mugo species. Several studies proved their anti-inflammatory, analgesic, bronchodilatory, cardioprotective, neuroprotective as well as anxiolytic and anticarcinogenic effects. α-pinene provides antioxidant activity through several mechanisms: reduction of lipid peroxidation induced by H 2 O 2 , ROS formation and NO release. Its cardioprotective effects are due to prevention of low-density-lipoprotein (LDL)-oxidation. Also, by blocking efflux pumps of *S. aureus*, α-pinene has a synergistic effect with several antibiotics..

Conclusion: Our results provide an overview of the so far identified medicinal properties *of Pinus mugo*. There is clearly an insufficient understanding of many of the historically used medicinal herbs and their underlying mechanisms of action, which presents significant opportunities for investigation of potentially effective treatments. Increasingly health-conscious members of the public often use herbal supplements as “aid” in therapy of their conditions; however, family physicians are usually unfamiliar with potential interactions between prescribed drugs and herbal supplements. It is necessary to broaden the understanding of traditional herbal supplements in order to provide better advice to patients about their safe and effective use, thereby improving patient care and health related outcomes.

Keywords: alfa-pinene, essential oils, herbal medicine, monoterpene, Pinus mugo

Liječnički vjesnik, 144; 2022; suplement 7; 42
https://doi.org/10.26800/LV-144-supl7-42

Steven-Johnson Syndrome and Toxic Epidermal Necrolysis Following COVID-19 Vaccination: An Analysis of the EMA EudraVigilance Database

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Introduction: Steven-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare, potentially life-threatening mucocutaneous disorders arising as drug hypersensitivity reactions, most commonly following treatment with antibiotics or anticonvulsants. However, rare cases developing after vaccination were also described.

Aim: SJS/TEN clinical presentation is impressive and anti-vaxxers' misinformation regarding COVID-19 vaccination campaign was focused on SJS/TEN to increase vaccine hesitancy. We conducted an analysis of the European Medicine Agency's EudraVigilance database of suspected adverse drug reaction reports (SADRR) to provide a more data-based outlook on the potential link between COVID-19 vaccination and SJS/TEN.

Materials and Methods: Data reported up to 9th July 2022, regarding the total number of SADRR, and the number of SADRR reporting on SJS/TEN were retrieved for seven vaccines. This included five COVID-19 vaccines: Moderna and Pfizer-BioNTech (mRNA), AstraZeneca and Janssen (adenovector) and Novavax (protein), as well as two influenza vaccines (control group). The odds ratios (OR) and 95% confidence intervals (CI) for SADRR reporting on SJS/TEN were calculated for each vaccine and compared to the control group, and to every other COVID-19 vaccine.

Results: Our analysis suggests that the odds that a SADRR reports on SJS/TEN are significantly lower for COVID-19 vaccines than for the control group, apart from SJS and the Moderna vaccine (OR=0.47; 95%CI [0.22 -1.00]). Furthermore, the odds that a SADRR reports on SJS are significantly higher for the Moderna vaccine when compared with the Pfizer-BioNTech (OR=2.30; 95%CI [1.57 - 3.38]) or AstraZeneca (OR=2.38; 95%CI [1.43 -3.95]) vaccines.

Conclusion: SJS/TEN after COVID-19 vaccination seems to be a possible, but exceedingly rare adverse drug reaction. The potential signal identified in our short analysis, regarding the Moderna vaccine, deserves further in-depth analysis and could be due to the substantially higher dose used by the Moderna vaccine (100 µg) compared to the Pfizer-BioNTech vaccine (30 µg).

Keywords: COVID-19 Vaccines, Pharmacovigilance, Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis

Liječnički vjesnik, 144; 2022; suplement 7; 43
https://doi.org/10.26800/LV-144-supl7-43

The effect of vegetarian diet on chronic kidney disease (CKD) progression – systematic review

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Introduction: Vegetarian diet is more and more popular around the world as the alternative to the casual omnivore diet. It is considered not only a healthy way of consuming but also a sustainable way of living. Chronic Kidney Disease (CKD) is a rising problem for the global population. It is the main cause of death for 1.5% of the global population and it is projected to increase in the future. One of the nutritional strategies to tackle the problem of CKD is a protein-restricted diet (<0.8 grams of protein per day). It helps to decrease the proteinuria, uremic toxins, oxidative stress and improves renal function.

Aim: This systematic review is meant to examine the potential benefits of changing the diet to vegetarian to delay the progression of CKD.

Materials & Methods: Cochrane and Pubmed engines were used to search for the results. The investigation was carried out with the help of PRISMA 2020 Checklist and PRISMA 2020 flow diagram. Two investigators were involved in the selection. Selected terms for this research were: 'vegetarian diet' AND 'nephropathy', 'eGFR', 'albuminuria', 'chronic kidney disease'.

Results: According to studies from the last 6 years vegetarian diet improves eGFR and reduces proteinuria. It also decreases the serum urea and acidosis. Compared to the omnivore group, vegetarians have 16% and vegans have 13% less chance of CKD development. For diabetic patients' odds for CKD occurrence are 0.68 for both vegetarian and vegan diets indicating their protective aspect.

Conclusions: The vegetarian diet could be an alternative for low protein conventional diet not only improving the renal results but also the overall health of the patients. Vegetarians tend to have lower: BMI, LDL, blood pressure, oxidative stress. Although some studies emphasize the positive effect of plant-based diet on CKD, there is a need for big cohort studies with a larger population to deeply examine this aspect.

Keywords: albuminuria, chronic kidney disease, diabetes mellitus, vegetarian diet, vegetarianism

4. WORKSHOPS

Abused child: Was it just a fall?

Students' section for pediatrics

During their career, every doctor will doubtlessly have an encounter with a child as their patient, even if they don't specialize in pediatrics. Since children are a very vulnerable, yet very active group prone to accidents it is very important for every doctor to recognize abused child and to know the difference between abuse and accident. This workshop's goal is to review the most important physical and psychological signs of abuse and to teach participants how to recognize all types of abuse, but also differentiate accidents from abuse through an interactive lecture and a number of interesting case reports.

Drug interactions

Prof. Robert Likić, MD, PHD

It is crucial for every doctor to be familiar with pharmacokinetics and pharmacodynamics of every drug they have prescribed, and that includes the possible drug interactions. Anytime our patient is taking more than one medication, or even mixes it with certain food, a drug interaction can occur. For instance, patients taking atorvastatin should avoid drinking grapefruit juice, as it inhibits the activity of CYP3A4 enzymes and decreases the metabolism of the drug, resulting in the increase of the drug in the bloodstream. That way, therapeutic doses of affected medications could lead to serious adverse reactions. Through this engaging workshop, students will learn about the most common drug interactions and where to check for them.

ECG interpretation

Students' section for cardiology

During his or her education, every medical student will come across an ECG interpretation course (or probably even more than just one) but as it is one of the most ordered tests in medicine you can never have too much practice. Every young doctor should be able to recognize the most common heart conditions (such as atrial fibrillation) and the most urgent ones (e.g., myocardial infarction). That is the purpose of this workshop: to remind everyone of the basic ECG pathologies so that they can feel confident one day in diagnosing them, and also to give basics to those who may have not yet had the chance to encounter an ECG interpretation course.

ENT examination

Borna Miličić, MD

Students' section for otorhinolaryngology, head and neck surgery

Nowadays, ENT examination is performed to diagnose and treat diseases and disorders of the ear, nose, throat and related structures of the head and neck. This workshop was designed to focus on this physical examination. Due to that, participants had the opportunity to inspect the external ear before using an otoscope/auriscope with whom they had a good look on the tympanic membrane, eardrum and ear canal. In the second phase of the workshop, they examined the nose and its function, airway resistance and sense of smell. At last, the workshop was concluded with a throat examination. Those who are interested in otorhinolaryngology could learn something new which can help them later in their work.

FAST ultrasound

Vjekoslav Štambuk, MD

Students' section for radiology

The Focused Assessment with Sonography in Trauma (FAST) is an ultrasound protocol that was developed as a ''screening test'' for hemoperitoneum and hemopericardium. Four classic areas are examined for free fluid (usually blood in traumatic injury): perihepatic space (including Morison's pouch or the hepatorenal recess), perisplenic space, pericardium, and the pelvis. This fast procedure can be a lifesaving one for patients with internal bleeding. During this workshop students can practice their ultrasound skills on live models, ensuring the best learning experience.

Hypertension: the silent killer

Students' section for hypertension

The hypertension section workshop consisted of two parts. In the first part, we discussed the importance of hypertension today, risk factors and therapeutic options. Emphasis is placed on preventive options that can prevent the occurrence of high blood pressure, and later other cardiovascular, cerebrovascular and kidney diseases. The name silent killer emphasizes the main problem of high blood pressure, which is that it lasts for a long time and often does not cause any symptoms. In the second part of the workshop, the participants had the opportunity to practice the skill of correct pressure measurement, and the most common mistakes made were explained. Furthermore, all those interested could learn about the body composition monitor and the values it measures. The third practical skill that was shown to the participants was the measurement of central arterial pressure with the assessment of the age of blood vessels.

Lab interpretation

Maja Pavlović, MD

Laboratory tests are one of the most common methods of medical testing and billions of these tests are performed each year. They help us diagnose a wide rage of diseases and condition, so it is important to navigate the sea of numbers and measuring units presented on the laboratory reports. Through presentation of a dozen cases with specific laboratory images (but not necessarily obvious diagnoses) the exact diagnosis and clinical presentation of the same are determined interactively.

Neurology 101

Students' section for neurology

A neurological examination is an evaluation of a person's nervous system. It includes assessment of motor and sensory skills, reflexes, balance, coordination and mental status. This examination is very important because early diagnosis of a neurological disease can decrease long-term complications. During examination all parts of the nervous system will be tested: brain (mental status), peripheral nerves (motor and sensory function) 12 cranial nerves (motor and sensory function, vision, smell, taste, hearing) and reflexes using a reflex hammer. After this workshop everyone will be able to perform a full neurological examination.

Primary wound care

Students' section for surgery

There are a few things that every good and resourceful doctor should know (just in case he is the only doctor in an isolated village in the middle of nowhere) and primary wound treatment is one of them. Treating a cut or some other smaller physical trauma is a very useful skill, as they are fairly frequent injuries and every doctor will probably encounter them during his career. Since we can't practice these skills on real-life patients, they will be simulated in this workshop by piggy legs. Each participant will get his or her very own injured "patient" and will be presented with the chance to treat this injury.

Trauma examination

Adis Keranović, MD

All people who have experienced trauma should be systematically assessed and taken care of according to guidelines. In the Pre-hospital trauma examination, guidelines such as ITLS, ATLS, and PHTLS are used. These guidelines are based on basic procedures regarding the traumatic event and both primary and secondary examination of the patient. The basic procedures include the mechanism of injury, security (of the area, ourselves and injured persons), as well as a quick assessment of the site of accident. In the primary examination it is essential to evaluate and detect possible problems, and here time is of the essence. The examination begins with an assessment of the general impression of the patient, and then focuses on A (airway), B (breathing), C (circulation), D (disability) and E (exposure). The secondary examination includes structured examining of the injured person from head to toe. During the transport to the hospital certain protocols are also applied. It is absolutely essential to appropriately document all of the actions medical professionals have undertaken.

Traumatic brain injury

Ante Sekulić, MD, PHD

Marijana Matas, MD

Traumatic brain injury is medical, public health and social problem. Entire workshop is devoted to these problems. Treatment of traumatic brain injury has two phases: preclinical and clinical (hospital). Each of these has simple rules according to actual guidelines developed by Brain Trauma Foundation (USA). In the first phase correction of hypotension and hypoxemia is a primary goal. In the second phase mechanical ventilation of the lungs, capnography and measurement of intracranial pressure are essential procedures. Very important step is daily measurement of Glasgow Coma Scale Score. At the end of treatment Glasgow outcome Scale is use for evaluation of the treatment success. Capnography and airway management will be presented during workshop.

Venous ultrasound

Prof. Ivan Gornik, MD, PHD

Students' section for emergency medicine

Venous ultrasound is an important, but also simple, diagnostic test that can detect deep vein thrombosis. Ultrasound uses sound waves and the piezoelectric effect to produce images, most often in the search for blood clots in the veins of the legs.

5. LECTURES

Croatian Medical Chamber and Medical Law

Mijo Karaula, JD

- Head of Legal Department at Croatian Medical Chamber

Medical Law and Ethics

Associate prof. Sunčana Roksandić, LLD, dr. dr.hc.

- Lecturer of criminal law, economic criminal law, transitional justice, EU substantive criminal law and the protection of victims (Jean Monnet Module co-Leader) and bioethics and human rights (UNESCO Model Course) at Faculty of Law, University of Zagreb
- Lecturer of Medical ethics at the Medical School, University of Zagreb
- Head of the Croatian Unit for the International Network of the UNESCO Chair in Bioethics
- member of the Executive Board of Croatian Association for Criminal Law Sciences and Practice

Disciplinary Procedure in Croatian Medical Chamber

Dino Salihagić, LLM

- Legal Counsel, Legal Department at Croatian Medical Chamber

The Right to a Diagnosis

Ivana Hrastar, MSW

- Social Worker at National organization for Rare Diseases Croatia

Unvoluntary Treatment in Psychiatry: Models and Issues

Marko Ćurković, MD, PhD

- Specialist of psychiatry
- Lecturer of Medical ethics at the Medical School, University of Zagreb
- Medical doctor court expert

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