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Clinical observation | Kliničko zapažanje

Achalasia complicated with bilateral pneumonia and sepsis

Ahalazija kompliciranа obostranom pneumonijom i sepsom

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Descriptors
ESOPHAGEAL ACHALASIA – complications; PNEUMONIA, ASPIRATION – etiology; SEPSIS – etiology; ESOPHAGEAL FISTULA; RESPIRATORY TRACT FISTULA; PLEURAL DISEASES; CRITICAL CARE

SUMMARY. Achalasia is a rare esophageal motility disorder that is mostly manifested by the basic triad of symptoms: dysphagia, regurgitation, and retrosternal pain. Patients often disregard the symptoms for years or are treated for overlapping conditions with similar symptoms, such as GERD, gastritis, or various lung diseases from asthma to obstructive pulmonary disease. A common complication is aspiration leading to pneumonia, and these patients often go from pulmonologists to gastroenterologists in search of a diagnosis and cure. This study presents the case of a patient treated for severe, rare complication of achalasia, megaesophagus and esophagopleural fistula. The case study highlights the importance of a multidisciplinary approach, choosing the right therapeutic approach, and objective assessment of the situation, when we decide on one option while another option arises as the only one that is sustainable. In this case it is a complex intensive care approach.

Deskriptori
AHALAZIJA JEDNJAKA – komplikacije; ASPIRACIJSKA PNEUMONIJA – etiologija; SEPSA – etiologija; FISTULA JEDNJAKA; FISTULA DIŠNOG SUSTAVA; PLEURALNE BOLESTI; INTENZIVNO LIJEČENJE

SAŽETAK. Ahalazija je rijedak poremećaj pokretljivosti jednjaka koji se najčešće manifestira osnovnom trijadom simptoma: disfagijom, regurgitacijom i retrosternalnom boli. Pacijenti često zanemaruju simptome godinama ili se liječe zbog preklapajućih stanja sa sličnim simptomima, kao što su GERB, gastritis ili različite plućne bolesti, od astme do opstruktivne plućne bolesti. Česta komplikacija je aspiracija koja vodi do upale pluća, a ovi pacijenti često prelaze od pulmologa do gastroenterologa u potrazi za dijagnozom i liječenjem. Ova studija predstavlja slučaj pacijenta liječenog zbog teške i rijetke komplikacije ahalazije, megaezofagusa i ezofagopleuralne fistule. Studija slučaja ističe važnost multidisciplinarnog pristupa, odabira pravog terapijskog pristupa te objektivnog vrednovanja situacije, kada se odlučujemo za jednu opciju dok druga opcija postaje jedina koja je održiva. U ovom slučaju riječ je o kompleksnom pristupu intenzivnoj skrbi.

Achalasia is a disorder characterized by inadequate relaxation of the lower esophageal sphincter and the absence of peristalsis. The etiology is usually primary (idiopathic), but it can also be secondary in conditions including esophageal dysfunction. In idiopathic achalasia, enteric neurons that control the lower esophageal sphincter and the esophageal body musculature are most likely affected by an inflammatory agent.[1] The disease progresses over the years, and in untreated cases there are complications such as regurgitation, aspiration, consequent pneumonia, progressive esophageal dilation with loss of functionality that may lead to the development of a sigmoid-shaped dolichomegaesophagus.[2] Esophagopleural fistula is an extremely severe and rare complication that is observed in individual cases.

Case report

This study presents the case of a 57-year-old female patient hospitalized due to worsening dyspnea in the context of chronic obstructive pulmonary disease, for which she has been treated for ten years. She also has elevated blood pressure, congestive cardiomyopathy, class 3 obesity with BMI of 40.2 kg/m2, and, recently, she has had multiple episodes of pneumonia. Regarding the past surgeries, she has mentioned a complete thyroidectomy, the reason for which was unknown to her, and that she is receiving hormone replacement therapy. She denies any harmful habits and she does not take medications regularly. She has brought the previous CT scan report from six months ago, showing bilateral interstitial changes and patchy areas of GGO (ground-glass opacity), along with the pathological finding of a dilated esophagus, with laterolateral (LL) diameter of up to 60 mm, thinned wall, and completely filled with heterodense content possibly corresponding to the previously ingested meal. The megaesophagus finding was not further monitored. At the time of admission, the patient was afebrile, cyanotic, dyspneic, with tachycardia (150 beats/min),

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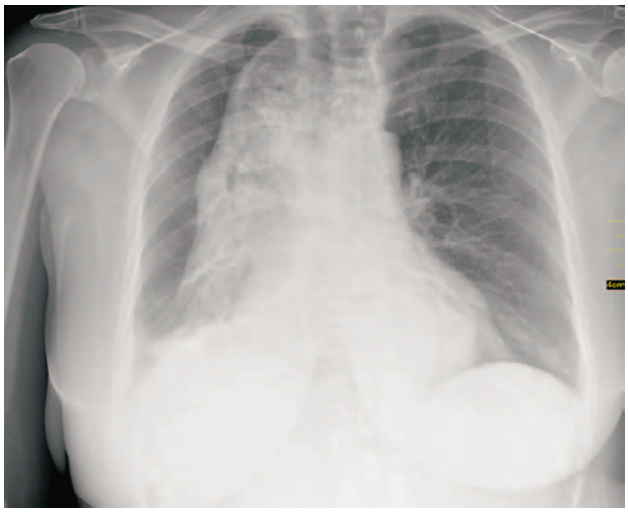

Figure 1. Chest X-ray at the time of admission
Slika 1. Rendgenska snimka prsnog koša pri prijmu

normotensive, with cardiac decompensation, swollen feet, and highly reduced mobility due to obesity. Chest X-ray showed an enlarged mediastinal shadow on the right and a narrowed right hemithorax (Figure 1).

In the laboratory analyses there was a manifest partial respiratory insufficiency, leukocytosis with neutrophilia, elevated proinflammatory parameters, and worsening of kidney and liver parameters (Table 1).

CT scan of the chest showed an extremely dilated esophagus throughout its length, with LL diameter of 87 mm, haustral appearance, and thinned wall, completely filled with gas-liquid content. The dilated esophagus compressed the posterior wall of the trachea, narrowing the tracheal lumen with anteroposterior (AP) diameter of approximately 3 mm, and compressing and narrowing the right primary bronchus, compressing cardiovascular structures to anterior position, with smaller areas of atelectasis of periesophageal lung parenchyma. There was a minor fistula on the left side, AP diameter 2 mm (measured at the level of the T9 vertebra). Retroesophageal air inclusions were visible on the left side. Pleural effusion was present on the right side. Cardiomegaly was detected. Pericardial effusion was not detected (Figure 2).

Due to the progression of respiratory insufficiency and hemodynamic instability, the patient was intubated following the RSI protocol, and mechanical ventilation was initiated following the protective protocol. A central venous catheter was placed, and invasive arterial pressure monitoring was initiated with minimal inotropic support due to hypotension. Esophagogastroduodenoscopy showed that the esophagus was dilated throughout its length, with large amount of putrid content and food remains. The esophageal mucosa was eroded, covered with fibrinous granulations and purulent accumulations, with contact bleeding. In the distal part of the esophagus on the left side, at 38 cm from incisors, there was a suspicious wall perforation with a diameter of 8 mm, the base of which could not be distinguished. The walls of the defect were covered with fibrin and necrotic detritrus without infiltrative changes. The gastroscope could not pass through the region of esophagogastric junction due to the esophageal aperistalsis.

Echocardiography showed reduced global systolic function, ejection fraction (EF) of 45%, and apical akinesia. Ultrasound examination of the right pleura confirmed the separation of the pleural layers by approximately 3 cm. Therefore, a chest tube was placed in the right pleural space, from which serous fluid was drained in the following days. Enteral nutrition via nasogastric tube was contraindicated. Accordingly, total parenteral nutrition with adjusted formulas was initiated. Surgical treatment of the diagnosed esophagopleural fistula was planned, but the patient developed worsening multiple organ dysfunction syndrome (MODS), with fever up to 38°C, hemodynamic instability, worsening gas exchange, and oliguria.

Laboratory findings showed a very large increase in inflammatory markers (Table 1), and from a radiological perspective, there were pneumonic infiltrates in the left basal segments, and in the basal and middle lung fields on the right side. Serous secretion was further drained from the chest tube.

The treatment was initiated according to the sepsis treatment protocol, with antibiotic de-escalation therapy and volume replacement by crystalloids, along with vasoactive support. After that, our patient faced additional complications, including hematemesis, with fresh bleeding seen in the nasogastric tube; continuous proton pump inhibitor therapy was administered, leading to cessation of bleeding. ECG showed ischemic changes, with newly present negative T-wave distribution in the lateral wall, indicative of myocardial dysfunction in the context of septic deterioration. Therefore, dobutamine was introduced as the first choice to improve hemodynamic status. *Acinetobacter baumannii* was isolated from tracheal aspirate; it was sensitive to Colistin that was introduced into the therapy. β-D-glucan was positive, and since *Candida albicans* was isolated from blood culture, antifungal therapy was added. Due to the patient's very severe general condition, surgical intervention was abandoned. Improvement was achieved in the following days with the prescribed therapy. Due to the need for prolonged mechanical ventilation and better airway hygiene, a tracheostomy was created. Nutrition was provided exclusively in the form of total parenteral nutrition. On the fifteenth day of admission a nasojejunal tube was placed under gastroscopic guidance, and postpyloric feeding was introduced; the feeding volume was grad-

Table 1. Laboratory findings at the time of admission to the hospital, at the time of deterioration, and at the time of discharge

Tablica 1. Laboratorijski nalazi prilikom prijma u bolnicu, u trenutku pogoršanja i prilikom otpusta

Laboratory parameters / Laboratorijski parametri	At the time of admission / U trenutku prijma	At the time of deterioration / U trenutku pogoršanja	At the time of discharge / U trenutku otpusta	Unit / Jedinica	Reference interval / Referentni interval
pH	7.457	7.40			7.35–7.45
pCO2	4.44	5.46		kPa	4.7–6.0
pO2	6.03	9.55		kPa	8.8–13.3
BE	–0,3	0,6		mmol/L	+/–3
P/F		88,93			>300
Bicarbonates / Bikarbonati	22.8	25,0		mmol/L	22–26
SaO2	84.0	90,3		%	>95
Leukocytes / Leukociti	23.3	30,8	8,5	$x10^9$/L	4.0–11.0
Neutrophils / Neutrofili	89	92	57	%	20.0–46.0
Lymphocytes / Limfociti	5	3	28	%	44.0–75.0
Erythrocytes / Eritrociti	5.17	3,00	3.69	$x10^{12}$/L	3.8–5.0
Haemoglobin / Hemoglobin	144	83	110	g/L	119.0–157.0
Hematocrit / Hematokrit	0.439	0,27	0.32	L/L	0.35–0.47
Thrombocytes / Krvne pločice	266	267	210	$x10^9$/L	150.0–450.0
Blood Glucose / Glukoza	8.9	7,5	6.2	mmolL	4.1–6.1
Urea	10.9	15,8	3.3	mmol/L	2.8–8.1
Creatinin / Kreatinin	182	147	45	µmol/L	44.0–80.0
LDH	9.49	15,8		µkat/L	4.5–7.13
GGT	4.10	8,6	2.40	µkat/L	0.1–0.7
CRP	663	430	37.5	mg/L	<5
Procalcitonin / Prokalcitonin	5.32	10,3	0,42	ng/mL	<0.05

ually increased until caloric needs were met. After the follow-up imaging with the contrast agent applied through the tube, minimal contrast extravasation into the mediastinum was observed, along with gas inclusion at the level of the T9 vertebra. Consolidation areas and pleural effusion on the right side were regressing. Clinical and laboratory signs of the patient's recovery were observed on a daily basis, so the patient was transitioned to weaning, with gradual transition to spontaneous mode, decrease of support and PEEP, decrease of the fraction of inspired oxygen, and transition to a hydrotrachea after 22 days of mechanical ventilation. Physiotherapy was continued, with active-passive exercises in bed, well-tolerated by the patient, along with gradual verticalization. The nasojejunal tube was removed, and a metal cannula was placed. The patient coughed sufficiently, she was trained in using and maintaining the hygiene of the cannula, and, after 35 days of intensive therapy, she was transferred to a ward. The follow-up chest X-ray was satisfactory, without signs of enlarged mediastinal shadow, parenchymal condensation, and intrapleural complications. Follow-up laboratory findings were satisfactory (Table 1). The patient was feeding well. The patient was

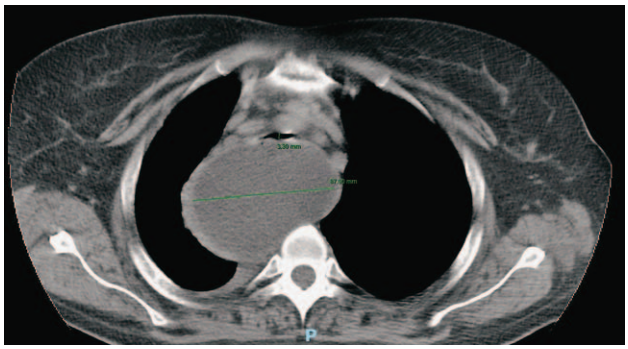

Figure 2. CT finding at the time of admission
Slika 2. CT nalaz prsnog koša pri prijmu

transferred to a regional hospital in improved general condition for further conservative treatment.

Discussion

Achalasia is a primary esophageal motility disorder, where, due to degeneration of the myenteric plexus, the lower esophageal sphincter is inadequately relaxed, and the peristaltic wave of the esophagus is lost.[3] There is a lack of exactness in detecting the etiology, but in the study conducted by Kraichelyet al. it was found that the patients with primary achalasia had an extremely high level of neuronal autoantibodies compared to the healthy population, suggesting that plexus degeneration is a consequence of autoimmune and neurodegenerative conditions.[4] Achalasia can be primary, when it is idiopathic, secondary as seen in Chagas disease, or pseudoachalasia in 2–4% of the cases when it results from tumors, neuromuscular or metabolic conditions.[2] The incidence is 2.92 per 100,000 adult patients, with nearly equal male-to-female ratio, making it a relatively rare esophageal motility disorder. It has a bimodal age distribution, with most patients aged 20–40, and/or 60–70, while the incidence increases with age.[3] In a multicenter study conducted in Japan with over 1,000 patients it was concluded that male sex and positive family history may be risk factors for achalasia.[5] On the other hand, socioeconomic status, lifestyle, and occupations with low income have also turned out to be possible contributing factors to the development of achalasia. The most common symptoms of this disease are: difficulty swallowing solid or liquid food that becomes more pronounced over time, regurgitation accompanied by respiratory symptoms such as cough, dyspnea and hoarseness, and chest pain. These three main symptoms of achalasia develop gradually, patients get used to them, and often many years can pass before the disease is diagnosed. There are various scoring systems for quantifying the severity of the clinical picture, with the Eckardt scoring system being the most commonly used for the assessment of symptoms, stage of disease, and efficacy of achalasia treatment. This system scores four main symptoms, and depending on the total score the clinical stage is determined (Table 2). The score of 0–1 corresponds to stage 0, 2–3 points correspond to stage I, 4–6 points correspond to stage II, and the total score >6 corresponds to the most advanced stage III.[6]

Table 2. Eckardt score for symptomatic evaluation of achalasia[7]
Tablica 2. Eckardtova skala za simptomatsku procjenu ahalazije[7]

Score / Skala	Weight loss / Gubitak težine (kg)	Dysphagia / Disfagija	Retrosternal pain / Retrosternalna bol	Regurgitation / Regurgitacija
0	None / Bez promjene	None / Bez promjene	None / Bez promjene	None / Bez promjene
1	<5	Occasional / Povremeno	Occasional / Povremeno	Occasional / Povremeno
2	5–10	Daily / Dnevno	Daily / Dnevno	Daily / Dnevno
3	>10	Each meal / Svaki obrok	Each meal / Svaki obrok	Each meal / Svaki obrok

However, based solely on symptoms, it is difficult to say that achalasia is the cause, as it often overlaps with other gastrointestinal or respiratory diseases. Moreover, sometimes there is no positive correlation between manometry, the degree of esophageal dilation, or prognosis. Therefore, when there is a suspicion of achalasia a complete examination is necessary, not only for the diagnosis but also for planning further therapeutic measures.[6] Among the diagnostic measures for determining achalasia there are several options for the assessment of esophageal motor function. Barium esophagography, where pathognomonic bird's beak sign is found, and endoscopy are complementary tests that can be added to manometry, but they are not sensitive enough.[8] A significant diagnostic tool is also a CT scan of the chest with oral contrast, where the typical sign of a narrowed lower sphincter with proximal esophageal dilation is found.[9] According to the maximum esophageal diameter, there are four stages of achalasia (Table 3).[14]

Table 3. Radiological stages of achalasia[14]
Tablica 3. Radiološke faze ahalazije

Radiological stage / Radiološka faza	Esophageal diameter / Promjer jednjaka	Esophageal shape / Oblik jednjaka
I	≤4 cm	–
II	4–6 cm	–
III	≥6 cm	–
IV End-stage disease / Terminalna faza bolesti	≥6 cm	Sigmoid / Sigmoidan

High-resolution manometry is considered the gold standard for diagnosing esophageal achalasia, because it reveals both esophageal aperistalsis and the lack of relaxation of the lower esophageal sphincter. Based on pressure and contraction patterns obtained from manometry, achalasia is classified into three subtypes according to the Chicago Classification Version 3.0.[1] Our patient's symptoms had been present for many years before the occurrence of the complication described in this case report. The patient reported being treated multiple times for pneumonia, both in outpatient and inpatient settings, with the latest episode being two months before the admission to our institution. In an interesting study Sinan et al. analyzed a sample of 110 patients with achalasia, showing that cough develops in as many as 40% of the patients as one of the leading symptoms, occurring daily, and followed by aspiration and dysphonia. These symptoms occur due to both the regurgitation of food retained in the esophagus and the mass effect of the dilated esophagus.[11] In her documentation she presents a CT scan of the chest showing the mass effect of the dilated esophagus; however, the patient was not further examined in that direction, and she presented to us when the enlarged esophageal mass caused the compression of the airway and esophageal perforation. The literature contains the description of a small number of cases where tracheal compression occurs as a complication of a dilated esophagus. In a similar case study Kathz et al. explained the causal relationship between the dilated esophagus and airway obstruction and possible perforation, based on the principle of a one-way valve that forms in such a dilated esophagus, trapping air, with the inability of relaxation of the upper sphincter during swallowing. There is also a theory of loss of the belch reflex, that under normal conditions causes simultaneous relaxation of the upper and lower esophageal sphincters.[9] As our patient was in a state of sepsis, with vasoactive support, the measures of intensive treatment were continued, and she responded well to those measures. According to ESPEN guidelines early parenteral nutrition was started due to contraindications for the enteral route, until the route for postpyloric nutrition was enabled.[12] The treatment of achalasia should be guided by the current guidelines of the European Society of Gastroenterology, European Society of Neurogastroenterology and Motility, European Society of Gastrointestinal and Abdominal Radiology, and European Association for Endoscopic Surgery issued in 2020, aiming to reduce symptoms, improve quality of life, and prevent disease progression and development of late complications, such as aspiration, progressive dilation, and carcinogenesis.[1] The end stage of achalasia is characterized by massive dilation and food retention with severe mucosal damage despite previous treatment measures. The literature shows that less than 5% of patients reach this stage, where treatment is directed towards esophagectomy as the only solution, an intervention that is associated with high risk of complications and mortality.[13]

Conclusion

According to the definition of the end stage of the disease, that involves the esophagus dilated for more than 6 centimeters, our patient was a candidate for surgical intervention. However, no other criterion was met for proceeding with the surgical procedure. General condition, sepsis, and multiple organ dysfunction were present at the time of making the decision regarding further treatment. Through this study our goal was to show that timely selection of appropriate antibiotic therapy, lung protection using mechanical ventilation, prevention of VAP, choice and route of nutrition, rehabilitation program, and all other measures of intensive care treatment led to complete recovery, while the decision towards a major surgical procedure would have been a path to a fatal outcome. Adherence to guidelines and protocols related to the intensive care of septic patient, followed by a consultative approach to treatment, daily consultation, and the availability of thoracic and abdominal surgeons are of invaluable importance when it comes to treating pathological conditions of the esophagus.

INFORMATION ON CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest relevant to this work

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AUTHOR'S CONTRIBUTION

Conception or design of the manuscript: JI, IS
Data acquisition, analysis or interpretation: JI, SP, IE
Drafting of manuscript: JI, BJ
Critically revising for important intellectual content: JI

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