MINIMALNO INVAZIVNA TORAKOSKOPSKA HIRURGIJA KAO DIJAGNOSTIČKI I TERAPIJSKI PRISTUP KOD BILATERALNOG PNEUMOTORAKSA U TRUDNOĆI UZROKOVANOG LIMFANGIOLEIOMIOMATOZOM – PRIKAZ SLUČAJA

PRIKAZ SLUČAJA

CASE REPORT

MINIMALLY INVASIVE THORACOSCOPIC SURGERY AS A DIAGNOSTIC AND THERAPEUTIC APPROACH IN BILATERAL PNEUMOTHORAX IN PREGNANCY CAUSED BY LYMPHANGIOLEIOMYOMATOSIS – A CASE REPORT

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SAŽETAK

Uvod: Limfangioleiomiomatoza (LAM) je retka bolest i uglavnom se javlja kod žena u generativnom periodu, kao i tokom trudnoće, dok je kod muškaraca opisano samo nekoliko pojedinačnih slučajeva. Javlja se u vidu sporadičnog oblika ili je povezana sa kompleksom tuberozne skleroze. Dijagnoza se može postaviti na osnovu nalaza kompjuterizovane tomografije grudnog koša visoke rezolucije (*HRCT*), ili je potrebna histopatološka analiza. U kliničke manifestacije bolesti spadaju: progresivna dispneja pri naporu, recidivantni pneumotoraks, hilotoraks, angiomiolipomi i limfangiomiomi.

Prikaz slučaja: Pacijentkinja stara 32 godine, u trećem tromesečju trudnoće, primljena je na našu kliniku nakon levostranog pneumotoraksa, verifikovanog na rendgenu grudnog koša. Početni tretman je uključivao eksuflaciju, a potom torakalnu drenažu levog pleuralnog kavuma. Zbog produženog gubitka vazduha kroz torakalni dren i poodmakle trudnoće, urađen je carski rez. Nakon porođaja, rendgenom grudnog koša, utvrđen je kompletni desnostrani pneumotoraks, koji je zahtevao torakalnu drenažu, kao i nedovoljno reekspandirano levo plućno krilo. Na učinjenom *HRCT* snimku zabeležene su cistično-bulozne promene u plućima, te je najpre sa leve, a potom i sa desne strane, torakohirurškim minimalno invazivnim pristupom, histopatološki verifikovana LAM, uz hirurško lečenje obostranog pneumotoraksa.

Zaključak: Pneumotoraks je česta komplikacija limfangioleiomiomatoze. Zbog visoke stope recidiva, treba izvršiti definitivnu ranu hirurško intervenciju. Trenutne smernice preporučuju hemijsku pleurodezu i operaciju, za prvu epizodu pneumotoraksa. Prilikom lečenja pneumotoraksa u trudnoći treba primeniti adekvatnu terapijska proceduru, vodeći računa o bezbednosti trudnoće i porođaja.

Ključne reči: pneumotoraks, trudnoća, limfangioleiomiomatoza

ABSTRACT

Introduction: Lymphangioleiomyomatosis (LAM) is a rare disease which mainly occurs in women in the generative period, as well as during pregnancy, while only a few individual cases have been described in men. It occurs in sporadic form or is associated with tuberous sclerosis complex. The diagnosis can be made on the basis of high-resolution computed tomography (HRCT) findings, or histopathological analysis is required. Clinical manifestations of the disease include the following: progressive dyspnea on exertion, recurrent pneumothorax, chylothorax, angiomyolipomas and lymphangiomyomas.

Case report: A 32-year-old female patient was admitted to our clinic, in her third trimester of pregnancy, after a left-sided pneumothorax was verified on chest X-ray. Initial treatment included needle aspiration, followed by thoracic drainage of the left pleural cavity. Due to the prolonged air leak through the thoracic drain and the advanced stage of the pregnancy, a caesarean section was performed. After delivery, chest X-ray revealed complete right-sided pneumothorax, which required thoracic drainage, as well as an insufficiently reexpanded left lung. HRCT was performed and cystic bullous changes in the lungs were noted; LAM was histopathologically verified through a minimally invasive thoraco-surgical approach, first on the left and then on the right side, while bilateral pneumothorax was surgically treated.

Conclusion: Pneumothorax is a common complication of LAM. Due to the high recurrence rate, definitive early surgical intervention should be performed. Current guidelines recommend chemical pleurodesis and surgery for the first pneumothorax. When treating pneumothorax in pregnancy, the appropriate therapeutic procedure should be applied, taking into account the safety of the pregnancy and of the delivery.

Key words: pneumothorax, pregnancy, lymphangioleiomyomatosis

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UVOD

Limfangioleiomiomatoza (LAM) je progresivna, retka, multisistemska bolest nepoznate etiologije, koja se pretežno javlja kod žena, pri čemu uzrokuje oštećenje plućne funkcije [1]. Epidemiološka studija, sprovedena u sedam zemalja, pokazala je da je incidencija limfangioleiomiomatoze 3,4 – 7,8 slučajeva na milion žena [2]. LAM se uglavnom manifestuje u vidu cistične destrukcije plućnog parenhima, kao i ekstrapulmonalne bolesti, koja se sastoji od angiomiolipoma, limfnih tumora (limfangioleiomioma) i hiloznih izliva [3]. Limfangioleiomiomatoza je retka u opštoj populaciji, ali je česta kod žena sa kompleksom tuberozne skleroze (engl. *tuberous sclerosis complex – TSC*). Javlja se u 30 – 40% slučajeva (*TSC*-LAM) [4]. Prisutna je kod žena između menarhe i menopauze, prosečne starosti od 34 godine [5].

Značajan broj pacijentkinja sa LAM-om razvija svoje početne simptome tokom trudnoće. Zabeleženo je da je trudnoća kod limfangioleiomiomatoze povezana sa povećanom incidencijom pneumotoraksa, iako neke pacijentkinje imaju nekomplikovanu trudnoću [6]. Najčešće, pacijenti imaju kratak dah, kašalj i pneumotoraks. Ređe su prisutni hilozni pleuralni izlivi i hemoptizije [7,8].

Cilj ovog rada jeste da se prikaže slučaj trudnice koja je razvila spontani bilateralni pneumotoraks tokom trećeg tromesečja trudnoće i odmah nakon porođaja, ali i da se ukaže na značaj minimalno invazivnog video-asistiranog torakohirurškog pristupa (engl. *video-assisted thoracoscopic surgery – VATS*) u dijagnostici limfangioleiomiomatoze i lečenju pneumotoraksa izazvanog limfangioleiomiomatozom.

PRIKAZ SLUČAJA

Tridesetdvogodišnja pacijentkinja je primljena na našu kliniku, u 36. nedelji gestacije druge trudnoće, dva dana nakon pojave iznenadnog bola u levom hemitoraksu, praćenog akutnom kratkoćom daha. Pacijentkinja nije imala istoriju ranijih hroničnih plućnih bolesti ili drugih komorbiditeta. Njena prethodna trudnoća je protekla bez komplikacija. Prilikom fizikalnog pregleda, imala je tahipneju, tahikardiju i hiperrezonantni perkusioni zvuk, sa smanjenim disajnim pokretima levog hemitoraksa. Pregledima kardiovaskularnog sistema nije zabeležen patološki nalaz niti je verifikovana organomegalija. Rezultati krvne slike, kao i testovi funkcije jetre i bubrega bili su normalni. Radiografski snimak grudnog koša potvrdio je prisustvo kompletnog levostranog pneumotoraksa (Slika 1).

Početni tretman je podrazumevao eksuflaciju levog pleuralnog kavuma, a nakon učinjene navedene intervencije i nalaza bez poboljšanja, učinjena je tora-

INTRODUCTION

Lymphangioleiomyomatosis (LAM) is a progressive and rare multisystem disease of unknown etiology, which predominantly affects women, causing damage to the function of the lungs [1]. An epidemiological study, carried out in seven countries, showed the incidence of LAM to be 3.4 – 7.8 cases per one million women [2]. LAM mainly manifests in the form of cystic destruction of the lung parenchyma, as well as in the form of extrapulmonary disease, consisting of angiomyolipoma, lymph tumors (lymphangioleiomyoma) and chylous effusions [3]. Lymphangioleiomyomatosis is rare in the general population but is frequent in women with tuberous sclerosis complex (TSC). It occurs in 30 – 40% of cases (*TSC*-LAM) [4]. It is present in women between menarche and menopause, of the average age of 34 years [5].

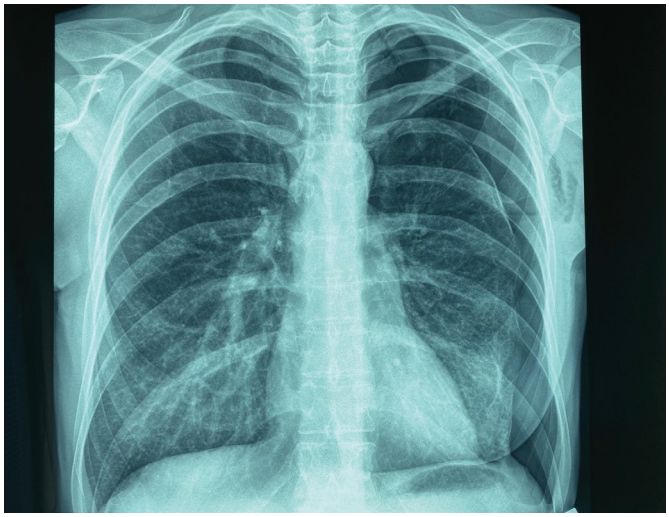
A significant number of patients with LAM develops initial symptoms during pregnancy. It has been recorded that pregnancy in cases of lymphangioleiomyomatosis is linked to an increased incidence of pneumothorax, although some of the patients have an uncomplicated pregnancy [6]. Most frequently, patients have shortness of breath, coughing, and pneumothorax. Less frequently, there are chylous pleural effusions and hemoptysis are present [7,8].

The aim of this paper is to present the case of a pregnant woman who developed spontaneous bilateral pneumothorax during the third trimester of her pregnancy and immediately after childbirth, as well as to point out the importance of minimally invasive video-assisted thoracoscopic surgery (VATS) in the diagnosis of LAM and in treating pneumothorax caused by LAM.

CASE REPORT

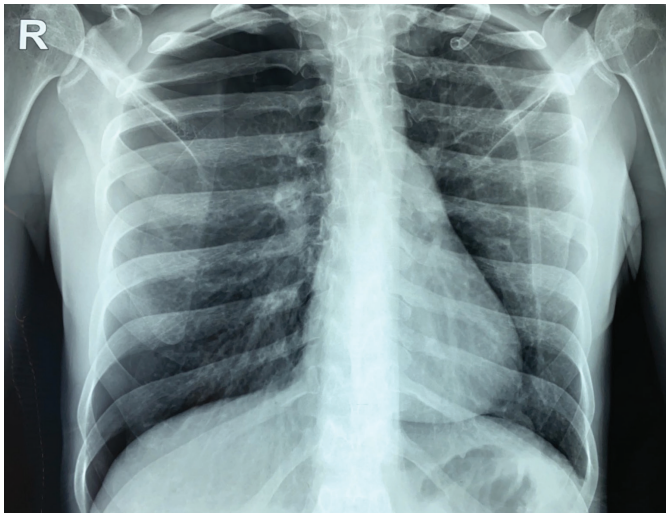
A thirty-two-year-old female patient was admitted to our hospital in the 36th week of gestation of her second pregnancy, two days after experiencing sudden pain in the left hemithorax, which was followed by acute shortness of breath. The patient had no previous history of chronic pulmonary disease or other comorbidities. Her first pregnancy was without complications. On physical examination, she displayed tachypnea, tachycardia, and hyperresonance with percussion of the chest, with reduced breathing movements of the left hemithorax. Examination of the cardiovascular system did not yield a pathological finding nor was organomegaly verified. The blood count results, as well as the test of liver function and kidney function were normal. The radiographic image of the thorax confirmed the presence of complete left-sided pneumothorax (Figure 1).

Initial treatment included exsufflation of the left pleural cavity, and after this procedure yielded no improvement, thoracic drainage of the left pleural cavity



Slika 1. Radiografija grudnog koša na prijemu na kliniku na kojoj se verifikuje levostrani pneumotoraks

Figure 1. Chest X-ray at hospital admission verifying left-sided pneumothorax



Slika 2. Radiografija grudnog koša nakon porođaja na kojoj se verifikuje desnostrani pneumotoraks, uz prethodno plasirani torakalni dren – levo

Figure 2. Chest X-ray after delivery verifying right-sided pneumothorax, with a previously placed thoracic drain – left ax

kalna drenaža levog pleuralnog kavuma, sa torakalnim drenom povezanim na podvodnu aspiraciju. S obzirom da nije došlo do reekspanzije levog plućnog krila, torakalni dren je naknadno priključen na aktivnu aspiraciju. Zbog produženog gubitka vazduha kroz torakalni dren i poodmakle trudnoće (37. nedelja gestacije), urađen je carski rez. Rođena je devojčica od 3.130 grama sa dobrim Apgar skorom (9).

Nakon porođaja, radiografijom grudnog koša, utvrđen je kompletni desnostrani pneumotoraks, koji je zahtevao torakalnu drenažu, uz prethodno plasirani torakalni dren, zbog levostranog pneumotoraksa (Slika 2).

Nalaz kompjuterizovane tomografije grudnog koša visoke rezolucije (engl. *high-resolution computed tomography HRCT*) je pokazao bilateralne višestruke difuzne cistične promene tankih zidova, rasute po plućnom parenhimu, veličine do 22 milimetra (Slika 3). Kompjuterizovana tomografija abdomena i male karlice nije pokazala abnormalnosti.

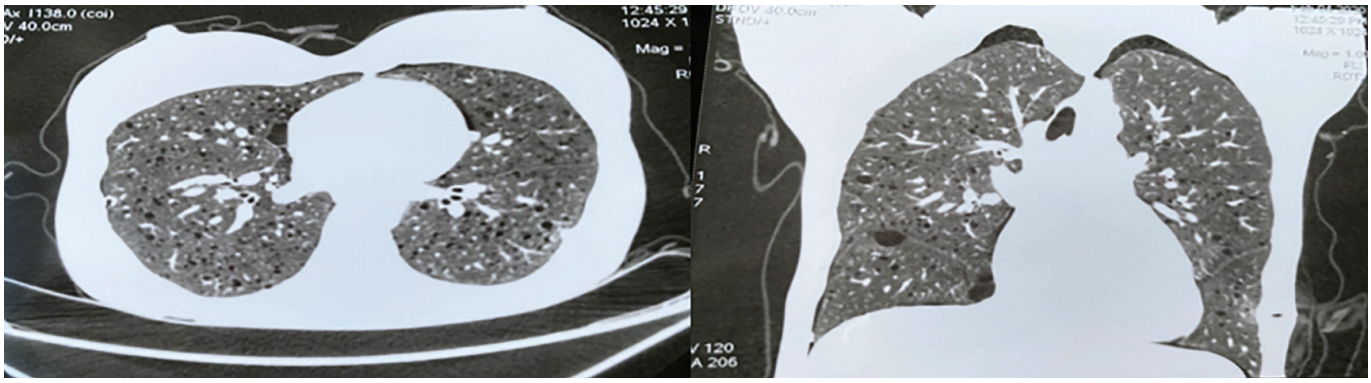
U ovim okolnostima odlučili smo se za hirurško lečenje pneumotoraksa.

using under water sealed drainage (UWSD). Since re-expansion of the left lung did not occur, the thoracic drain was subsequently connected to active aspiration. Due to prolonged air loss via the thoracic drain and the advanced stage of pregnancy (37th week of gestation), a C-section was performed and a girl weighing 3,130 grams with a good Apgar score (9) was born.

After the delivery, an X-ray of the patient's chest revealed complete right-sided pneumothorax, which required thoracic drainage, in addition to the thoracic drain previously placed due to left-sided pneumothorax (Figure 2).

The high-resolution computed tomography (HRCT) chest scan showed bilateral multiple diffuse thin-walled cystic lesions, scattered throughout the lung parenchyma, which measured up to 22 mm in diameter (Figure 3). Computed tomography (CT) of the abdomen and the lesser pelvis showed no abnormalities.

In such circumstances, we decided on surgical treatment of the pneumothorax.



Slika 3. Aksijalni i koronalni preseci *HRCT* snimaka grudnog koša na kojima se verifikuju cistične difuzne bilateralne promene u plućnom parenhimu

Figure 3. Axial and coronal sections of the HRCT images of the thorax verifying cystic diffuse bilateral lesions in the lung parenchyma

Inicijalno, sedmog dana nakon porođaja, izveli smo levostrani *VATS* pristup. Intraoperativno su otkrivene pleuralne adhezije u predelu levog gornjeg režnja. Nakon razdvajanja pleuralnih adhezija, u gornjem i donjem režnju je nađeno više mehurića i bula, predominantno u lingularnom segmentu gornjeg režnja i apikalnom segmentu donjeg režnja (Slika 4). Endostaplerom smo učinili klinastu resekciju apikalnog segmenta donjeg režnja i lingularnog segmenta gornjeg režnja. Urađena je hemijska pleurodeza sa 30 ml pedesetoprocentnog rastvora glukoze i mehanička pleurodeza sa abrazijom kostalne parijetalne pleure.

Histopatološki nalaz je pokazao proširenu alveolarni prostor sa glatkim mišićnim tkivom u njegovim zidovima, perivaskularnu proliferaciju glatkih mišića, agregate limfoidnih ćelija i proširene limfne prostore. Nije primećen granulom ili malignitet. Utvrđeno je da su kultivisane ćelije glatkih mišića pozitivne na humani melanomski blok-45 (HMB-45). Dakle, dijagnoza limfangioleiomiomatoze je potvrđena.

Hirurško lečenje desnostranog pneumotoraksa *VATS* pristupom izvedeno je 15. dana nakon porođaja. Intraoperativno smo primetili više mehurića i bula, predominantno u srednjem režnju. Učinjena je klinasta resekcija srednjeg režnja endostaplerom, a zatim hemijska i mehanička pleurodeza, kao u prethodnoj operaciji. Histopatološki nalaz odgovarao je nalazu prethodne operacije.

Postoperativni tok, nakon oba hirurška zahvata, protekao je uredno, uz potpunu reekspanziju desnog i levog plućnog krila, koja se održavala nakon uklanjanja torakalnih drenova.

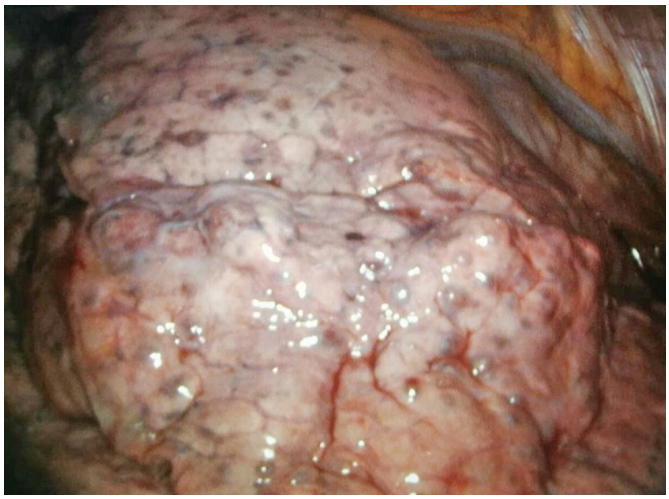
Pacijentkinja je otpuštena iz bolnice 20. dana nakon porođaja. Na dan otpusta iz bolnice, rendgenski snimak grudnog koša je pokazao potpuno reekspandirano levo i desno plućno krilo.

Testiranje plućne funkcije tri, šest i dvanaest meseci nakon porođaja pokazalo je referentne vrednosti.

Ponovljeni *HRCT* snimci abdomena i karlice, šest meseci i godinu dana nakon porođaja, nisu pokazali abnormalnosti. Rendgen snimci grudnog koša, mesec dana, tri meseca, šest meseci i godinu dana nakon porođaja, pokazali su potpuno reekspandirano levo i desno plućno krilo. Ponovljeni *HRCT* snimci grudnog koša, šest meseci i godinu dana nakon porođaja, nisu pokazali progresiju bolesti. I pacijentkinja i njeno dete ostali su zdravi nakon godinu dana praćenja.

DISKUSIJA

Limfangioleiomiomatoza je progresivna, cistična bolest pluća, koja se javlja pretežno kod žena u tridesetim godinama života [1,5]. LAM se retko javlja u opštoj populaciji. Obično se javlja kod žena sa *TSC*-om (30 – 40% slu-



Slika 4. Intraoperativni nalaz difuznih cističnih promena u plućnom parenhimu

Figure 4. Intraoperative finding of diffuse cystic lesions in the lung parenchyma

Initially, on the seventh day after delivery, we performed left-sided VATS. Intraoperatively, pleural adhesions were discovered in the region of the left superior lobe. After the separation of the pleural adhesions, a number of blisters and bullae were found in the superior and inferior lobe, predominantly in the lingular segment of the superior lobe and the apical segment of the inferior lobe (Figure 4). Using an endostapler, we performed wedge resection of the apical segment of the inferior lobe and the lingular segment of the superior lobe. Chemical pleurodesis was performed with 30 ml of 50% glucose solution, as well as mechanical pleurodesis with abrasion of the costal parietal pleura.

The histopathological finding revealed enlarged alveolar space with smooth muscle tissue in its walls, perivascular proliferation of smooth muscles, aggregates of lymphoid cells, and enlarged lymph spaces. Granuloma or malignancy was not found. The cultivated cells of smooth muscle tissue proved positive to human melanoma block-45 (HMB-45). Thereby, the diagnosis of lymphangioleiomyomatosis was confirmed.

Surgical treatment of the right-sided pneumothorax with the VATS approach was performed on the 15th day after delivery. Intraoperatively, we detected a number of blisters and bullae, predominantly in the middle lobe. Wedge resection of the middle lobe was performed with the use of the endostapler, followed by chemical and mechanical pleurodesis, in the same way as in the previous operation. The histopathological finding was in keeping with the one from the previous surgery.

Postoperative recovery, after both surgeries, was uneventful and full reexpansion of both the right and the left lung was achieved, with the reexpansion persisting after the removal of the thoracic drains.

The patient was discharged form hospital on the 20th day after delivery. On the day of discharge, the

čajeva), ili se javlja kao sporadični oblik. Postoje specifični kriterijumi za dijagnostikovanje *TSC*-a [9]. U slučaju naše pacijentkinje, kriterijumi za *TSC* nisu ispunjeni.

Pneumotoraks je čest kod pacijenata sa limfangioleiomiomatozom. Studija registra Nacionalnog instituta za srce, pluća i krv (engl. *National Heart, Lung, and Blood Institute - NHLBI*) u Sjedinjenim Američkim Državama, koja je obuhvatila 230 pacijenata sa limfangioleiomiomatozom, zabeležila je pneumotoraks u 55,5% slučajeva [10]. Druge studije su pokazale da je incidencija pneumotoraksa kod limfangioleiomiomatoze 1.000 puta veća nego u opštoj ženskoj populaciji [11]. Štaviše, 50 – 80% pacijenata će razviti pneumotoraks tokom bolesti. Pojava recidiva pneumotoraksa je česta, sa prosečnim brojem pneumotoraksa od oko četiri [10–14].

Nespecifične kliničke karakteristike sa neupadljivim rendgenskim snimcima grudnog koša na prezentaciji dovode do kašnjenja u dijagnozi ili netačne dijagnoze [7,8].

Komplikacije povezane sa limfangioleiomiomatozom, uključujući pneumotoraks i hilotoraks, mogu se javiti tokom trudnoće, a izražena je zabrinutost zbog moguće povezanosti trudnoće sa progresijom limfangioleiomiomatoze. Takođe je zabeleženo da žene sa LAM-om imaju lošiji ishod trudnoće, uključujući i više prevremenih porođaja i abortusa [6,15,16].

U literaturi je opisan pneumotoraks izazvan LAM-om, u poslednjem tromesečju trudnoće i ubrzo nakon porođaja. Ovaj fenomen se objašnjava činjenicom da hormonska stimulacija tokom trudnoće dovodi do povećanja cističnih struktura u plućima, te potom, na kraju trudnoće ili ubrzo nakon porođaja, dolazi do opadanja hormonske stimulacije i posledično do rupture neke od tankozidnih cističnih struktura i pojave pneumotoraksa. Ovo takođe objašnjava činjenicu da je LAM, skoro tipično, ženska bolest [17,18].

Ranije se pokazalo da je dispneja pri naporu, kao prisutni simptom, povezana sa povećanim mortalitetom kod limfangioleiomiomatoze [19]. Nasuprot tome, prethodno se smatralo da pacijenti sa pneumotoraksom imaju povoljniju prognozu [1]. Kasnije studije nisu pokazale vezu između pneumotoraksa i dugoročnog ishoda [20,21].

Ako pacijent sa potvrđenom LAM-om ima pneumotoraks, treba ga lečiti u skladu sa standardnim smernicama za lečenje sekundarnog pneumotoraksa [22]. Lečenje pneumotoraksa u trudnoći zavisi od stepena i faze progresije. Obično se koristi torakalna drenaža, sa ili bez aktivne aspiracije [16]. U slučaju naše pacijentkinje, dijagnoza limfangioleiomiomatoze nije bila poznata prilikom donošenja odluke o inicijalnom zbrinjavanju pneumotoraksa, pa smo koristili preporuke zvaničnih smernica za lečenje pneumotoraksa u trudnoći [23].

chest X-ray showed a completely reexpanded left and right lung.

Pulmonary function tests performed three, six, and twelve months upon delivery, showed results that were within the reference range.

Repeated HRCT scans of the abdomen and pelvis, six and twelve months after delivery, showed no abnormalities. X-rays of the chest made one, three, six, and twelve months after delivery, showed a completely reexpanded left and right lung. Repeated HRCT scans of the chest, six and twelve months after delivery, showed no progression of the disease. Both the patient and her child remained healthy after a year of follow-up.

DISCUSSION

Lymphangioleiomyomatosis is a progressive cystic pulmonary disease, occurring mainly in women in their thirties [1,5]. LAM rarely occurs in the general population. It usually develops in women with TSC (30 – 40% of cases), or it may occur as a sporadic form. There are specific criteria for diagnosing TSC [9]. In the case of our patient, the TSC criteria were not met.

Pneumothorax is frequent in patients with lymphangioleiomyomatosis. The study of the National Heart, Lung, and Blood Institute(NHLBI) registry (USA), involving 230 patients with LAM, registered pneumothorax in 55.5% of cases [10]. Other studies have shown that the incidence of pneumothorax in LAM is 1,000 greater than in the general female population [11]. Moreover, 50 – 80% of patients will develop pneumothorax during the illness. The recurrence of pneumothorax is frequent, with the average number of pneumothorax episodes being around four [10–14].

Nonspecific clinical characteristics with unremarkable chest X-rays on presentation lead to delayed diagnosis or misdiagnosis [7,8].

Complications connected to LAM, including pneumothorax and chylothorax, may occur in pregnancy, and the possible connection between pregnancy and the progression of LAM is cause for serious concern. Also, it has been recorded that women with LAM have a poorer outcome of pregnancy, including a greater number of premature births and miscarriages [6,15,16].

Pneumothorax caused by LAM in the third trimester of pregnancy and shortly after delivery has been described in literature. This phenomenon is explained by the fact that hormone stimulation during pregnancy leads to the increase in cystic structures in the lungs, and subsequently, at the end of pregnancy or soon after delivery, hormone stimulation drops, and consequently, some of the thin-walled cystic structures rupture, leading to pneumothorax. This also explains the fact that LAM is, almost typically, a female disease [17,18].

Smernice Američkog torakalnog društva/Japanskog respiratornog društva (engl. *American Thoracic Society/Japanese Respiratory Society Clinical Practice Guidelines*) podržavaju kliničku dijagnozu limfangioleiomiomatoze zasnovanu na *HRCT* nalazima tipičnim za limfangioleiomiomatozu (npr. ciste/mehurići difuzni, tankih zidova, okrugli) koji su praćeni bilo kojom od sledećih kliničkih karakteristika: *TSC*, angiomiolipom bubrega, cistični limfangioleiomiom, ili hilozni izliv u grudnom košu i/ili abdomenu. Smernice daju snažnu preporuku za korišćenje testa *VEGF-D* (vaskularni endotelni faktor rasta D; engl. *vascular endothelial growth factor D test*) za postavljanje dijagnoze limfangioleiomiomatoze, pre razmatranja biopsije pluća, kod pacijenata sa cističnim abnormalnostima na *HRCT* nalazu, karakterističnim za LAM, ali bez drugih potvrdnih kliničkih karakteristika [24].

Histopatološka potvrda limfangioleiomiomatoze može se dobiti na različite načine, uključujući transbronhijalnu, perkutanu ili *VATS* biopsiju. Rizik od pneumotoraksa nakon transbronhijalne biopsije je 1 – 6 %, a čak je i veći nakon perkutane biopsije. Prednost *VATS*-a je minimalna hirurška trauma, kao i odgovarajući uzorak za patološku potvrdu, kada se radi bulektomija i pleurodeza ili pleurektomija [25]. Neke retrospektivne serije sugerišu da transbronhijalna biopsija pluća može biti bezbedna i efikasna u delu pacijenata sa sumnjom na limfangioleiomiomatozu. U studiji koju su objavili Meraj i saradnici, među 63 pacijenta koji su bili podvrgnuti transbronhijalnoj biopsiji pluća, kada se prvobitno sumnjalo na limfangioleiomiomatozu, kod 35 pacijenata (56%) je ovim postupkom potvrđena LAM. Stopa prijavljenih komplikacija prilikom transbronhijalne biopsije bila je približno 14% (6% sa pneumotoraksom, 4% sa krvarenjem, 2% sa bolom u grudima i 2% sa pneumonijom) [26].

Međutim, hirurška biopsija pluća primenom *VATS* pristupa se smatra zlatnim standardom za dobijanje histopatološke potvrde limfangioleiomiomatoze. Kada je potrebna definitivna dijagnoza kod pacijenata sa parenhimskim cistama specifičnim za limfangioleiomiomatozu prisutnim na *HRCT* nalazu, ali bez dodatnih potvrdnih karakteristika limfangioleiomiomatoze, Smernice Američkog torakalnog društva/Japanskog respiratornog društva predlažu dijagnostički pristup koji uključuje transbronhijalnu biopsiju pluća, pre hirurške biopsije pluća [27]. U slučaju naše pacijentkinje, dijagnoza limfangioleiomiomatoze je postavljena *VATS* pristupom, koji je ujedno predstavljao i terapijski postupak za rešavanje pneumotoraksa.

Pošto je stopa recidiva visoka, trenutne smernice preporučuju pleurodezu u vreme prve epizode pneumotoraksa, kod pacijenata sa potvrđenom LAM-om

It has been found earlier that dyspnea on exertion, as a symptom, is connected with increased mortality in LAM [19]. Conversely, it used to be believed that patients with pneumothorax had a more favorable prognosis [1]. More recent studies have not shown a link between pneumothorax and the long-term outcome [20,21].

If a patient with confirmed LAM has pneumothorax, this patient should be treated in keeping with the standard guidelines for treating secondary pneumothorax [22]. Treatment of pneumothorax in pregnancy depends on the degree and phase of progression. Usually, thoracic drainage is used, but without active aspiration [16]. In the case of our patient, the diagnosis of LAM was not known at the time when the decision was made on initial pneumothorax treatment, which is why we applied the recommendations of the official guidelines for treating pneumothorax in pregnancy [23].

The American Thoracic Society/Japanese Respiratory Society Clinical Practice Guidelines support the clinical diagnosis of LAM based on HRCT findings that are typical for lymphangioleiomyomatosis (e.g., diffuse, thin-walled, spheric cysts/blisters) accompanied by any of the following characteristics: TSC, renal angiomyolipoma, cystic lymphangioleiomyoma, or chylous effusion in the thorax and/or abdomen. The guidelines strongly recommend the use of the VEGF-D test (vascular endothelial growth factor D test) for establishing the diagnosis of LAM, before considering lung biopsy in patients with cystic abnormalities characteristic of LAM present on the HRCT scan, but without other positive clinical characteristics [24].

Histopathological confirmation of LAM may be obtained in different ways, including transbronchial, percutaneous or VATS biopsy. The risk from pneumothorax after transbronchial biopsy is 1 – 6 %, and it is even higher after percutaneous biopsy. The advantages of VATS are reflected in minimal surgical trauma, as well as in the fact that it enables the obtaining of an adequate sample for pathological confirmation, when bullectomy and pleurodesis or pleurectomy are performed [25]. Some retrospective studies suggest that transbronchial lung biopsy may be safe and efficient in some of the patients with suspected LAM. In a study by Meraj et al., amongst 63 patients who underwent transbronchial lung biopsy at the time when LAM was initially suspected, in 35 (56%) patients LAM was confirmed in this way. The rate of reported complications of transbronchial biopsy was approximately 14% (6% with pneumothorax, 4% with bleeding, 2% with chest pain, and 2% with pneumonia) [26].

However, surgical biopsy of the lungs with the application of VATS is believed to be the golden standard for obtaining histopathological confirmation of LAM.

[22,27]. Međutim, pleurodeza kod pacijenata sa LAM-om ima ograničenu efikasnost, a zabeleženo je da se stope recidiva pneumotoraksa kreću između 18% i 32% [27,28]. Nedostaju jasne smernice o tome da li je hemijska ili hirurška pleurodeza optimalna, ali je važno rano uključiti grudne hirurge, jer će nekim pacijentima biti potrebna transplantacija pluća, u dužem vremenskom roku. Smernice za dijagonzu i lečenje limfangioleiomiomatoze (*LAM*) Evropskog respiratornog društva (engl. *European Respiratory Society Guidelines for the Diagnosis and Management of Lymphangioleiomyomatosis – LAM*) i Smernice Američkog torakalnog društva/Japanskog respiratornog društva preporučuju hemijsku pleurodezu i operaciju, za prvi pneumotoraks [22,26]. U slučaju naše pacijentkinje, učinili smo hemijsku i mehaničku pleurodezu. Prethodne pleuralne procedure nisu kontraindikacija za buduću transplantaciju pluća [29].

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When a definitive diagnosis is necessary in patients with parenchymal cysts characteristic of LAM present on the HRCT finding, but without additional positive characteristics of LAM, the American Thoracic Society/Japanese Respiratory Society Clinical Practice Guidelines suggest a diagnostic approach which includes transbronchial lung biopsy, before surgical lung biopsy [27]. In our patient, the diagnosis of LAM was established with the VATS approach, which was also the treatment procedure for pneumothorax.

Since the recurrence rate is high, current guidelines recommend pleurodesis at the time of the first episode of pneumothorax, in patients with confirmed LAM [22,27]. However, pleurodesis in patients with LAM has limited efficiency, and it has been recorded that recurrence rates for pneumothorax range from 18% to 32% [27,28]. Clear guidelines are lacking as to whether chemical or mechanical pleurodesis is optimal, but it is definitively important to include thoracic surgeons into the process early on, as some of the patients will need a lung transplant, in the long-term. European Respiratory Society Guidelines for the Diagnosis and Management of Lymphangioleiomyomatosis (LAM) and the American Thoracic Society/Japanese Respiratory Society Clinical Practice Guidelines recommend chemical pleurodesis and surgery, for the first pneumothorax [22,26]. In the case of our patient, we performed chemical and mechanical pleurodesis. Previous pleural procedures are not a contraindication for a future lung transplant [29].

Conflict of interest: None declared.

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