CASE REPORT
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A rare case of inflammatory myofibroblastic tumor presenting with pneumothorax

Redak slučaj inflamatornog miofibroblastnog tumora udruženog sa pneumotoraksom

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Abstract

Introduction. An inflammatory myofibroblastic tumor (IMT) is a rare mesenchymal tumor of unclear etiology, which demonstrates myofibroblastic differentiation accompanied by inflammatory cells. IMT is a frequent primary lung tumor in children and is of nonspecific symptomatology and imaging methods. Its definitive diagnosis requires histopathology and immunohistochemistry of the tissue sample obtained after a rigid bronchoscopy or after complete surgical resection. **Case report.** A 16-year-old male patient was admitted to our clinic for further treatment of IMT verified by rigid bronchoscopy. He had previously been treated at another institution for left-sided pneumothorax with thoracic drainage. Since it had not resulted in lung reexpansion, a chest computed tomography was performed followed by rigid bronchoscopy that eventually established IMT diagnosis in the distal part of the left main bronchus. Since the tumor surrounded the left lobar carina and infiltrated the pulmonary artery, pneumonectomy was undertaken. Its morphology and immunoprofile determined the IMT diagnosis. Four years after surgical resection, the patient showed no recidivism of the illness. **Conclusion.** IMT is one of the most frequent primary lung tumors in children and needs to always be suspected upon. Pneumothorax can appear as an IMT manifestation. Its occurrence could be the consequence of either a visceral pleura lesion in case of peripheral tumors or a ball valve mechanism in case of endobronchial tumors. Definitive diagnosis of IMT requires not only histopathology but also immunohistochemical analysis. Complete surgical resection results in the best survival rates. Further monitoring of patients is necessary due to the risk of recurrence.

Key words:
adolescent; diagnosis; lung neoplasms; pneumothorax; pneumonectomy; treatment outcome.

Apstrakt

Uvod. Inflamatorni miofibroblastni tumor (IMT) je redak mezenhimalni tumor, nejasne etiologije, koji pokazuje miofibroblastnu diferencijaciju udruženu sa inflamatornim ćelijama. IMT je čest primarni tumor pluća kod dece i nespecifične je simptomatologije kao i radiološkog nalaza. Za definitivnu dijagnozu potrebna je histopatološka i imunohistohemijska obrada materijala dobijenog nakon rigidne bronhoskopije ili nakon kompletne resekcije tumora. **Prikaz bolesnika.** Bolesnik, star 16 godina, primljen je u našu ustanovu radi nastavka lečenja IMT dokazanog rigidnom bronhoskopijom. Prethodno je bio lečen torakalnom drenažom zbog levostranog pneumotoraksa u drugoj ustanovi. Pošto reekspanzija pluća nije bila ostvarena, učinjena je kompjuterizovana tomografija grudnog koša, a potom i rigidna bronhoskopija kojom je postavljena dijagnoza IMT u distalnom delu levog glavnog bronha. Zbog zahvatanja leve lobarne karine i plućne arterije, učinjena je leva pneumonektomija. Morfološkom i imunohistohemijskom analizom dokazan je IMT. Bolesnik je bio bez recidiva četiri godine nakon operacije. **Zaključak.** Na IMT treba uvek posumnjati u dečijem dobu jer je jedan od najčešćih primarnih tumora pluća kod dece. Pneumotoraks se može javiti kao manifestacija IMT. Njegova pojava mogla bi biti posledica lezije visceralne pleure u slučaju perifernih tumora ili posledica valvularnog mehanizma kod endobronhijalnih tumora. U cilju postavljanja definitivne dijagnoze, osim histopatološke, neophodna je i imunohistohemijska analiza. Kompletna hirurška resekcija daje najbolju mogućnost za preživljavanje. Zbog mogućnosti recidiva neophodne su dalje kontrole ovih bolesnika.

Ključne reči:
adolescenti; dijagnoza; pluća, neoplazme; pneumotoraks; pneumonektomija; lečenje, ishod.

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Introduction

An inflammatory myofibroblastic tumor (IMT) is a rare tumor. Its occurrence is more frequently documented in children than in adults [1, 2]. It usually manifests as peripheral nodes, less so endobronchially [3–5]. The etiology of IMT is uncertain. According to the classification of the World Health Organization (WHO), IMT is defined as an intermediate soft tissue tumor that demonstrates myofibroblastic differentiation accompanied by inflammatory cells, plasma cells, and lymphocytes [6]. It presents with nonspecific symptomatology, including cough, high fever, dyspnea, pneumonia, and chest pain [3–5]. Chest X-ray and computed tomography (CT) scan are not sufficient to determine it. Definitive diagnosis requires histopathology and immunochemical analysis of the adequate tissue obtained after rigid bronchoscopy and surgical procedure. Surgical resection is the method of choice in IMT treatment [2, 4]. We report a 16-year-old male patient with IMT in the lung manifested as a left-sided pneumothorax.

Case report

A 16-year-old male patient was admitted to our clinic for further diagnostics and treatment of IMT previously verified by rigid bronchoscopy.

The patient was originally hospitalized at another institution because of the left-sided spontaneous tension pneumothorax accompanied by pain, weakness, and cough. Thoracic drainage was performed, and because it did not result in lung reexpansion within a day, further tests were undertaken (Figure 1). Prior to hospitalization, the patient was experiencing weakness, chest pain, and cough to a smaller degree for a month. He had no history of lung diseases, thoracic trauma, or medical intervention that could have caused pneumothorax.

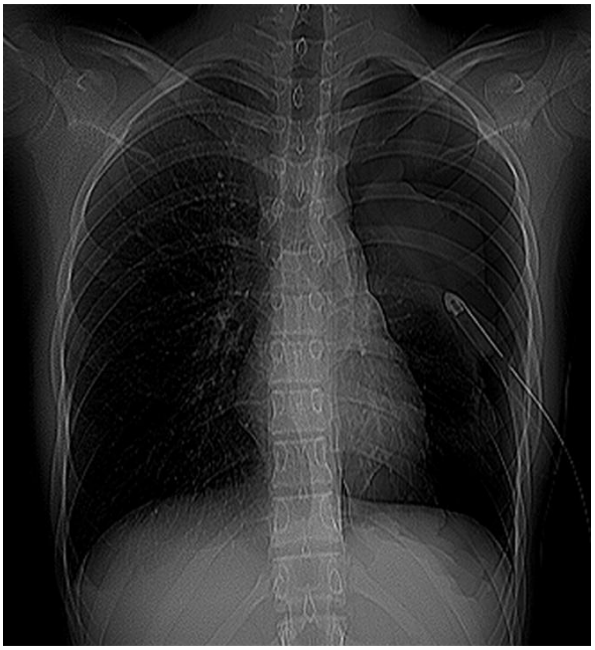

Fig. 1 – Chest X-ray showing left-sided pneumothorax and thoracic drain.

Thorax CT scan showed almost complete obstruction of the left main bronchus in its distal part by a hypodense soft-tissue tumor with dimensions 28 × 25 × 22 mm. On the neoplasm periphery, three amorphous calcified formations were detected, with the largest being 8 mm in diameter. The upper left lobe was atelectatic, while the lower was compressed with present pneumothorax (Figure 2).

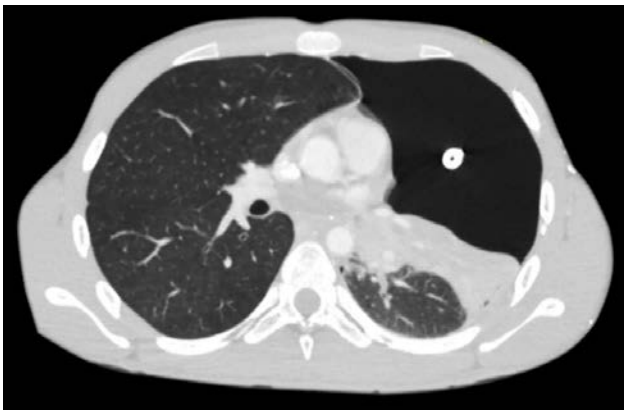

Fig. 2 – Computed tomography showing tumor almost completely obstructing left main bronchus and pneumothorax with atelectasis of the left upper lobe.

During rigid bronchoscopy, the tumor was seen as an off-white endobronchial mass in the left main bronchus located 4 cm from the carina of the trachea. Microscopically, according to its morphology and immunoprofile, the detected tumor was consistent with IMT with the understanding that its biological characteristics will be determined by surgical resection.

Laboratory analysis values fell within their respective reference intervals.

The patient was then referred to our clinic, where left pneumonectomy was performed by posterolateral thoracotomy after a completed preoperative procedure. Macroscopically, we noticed atelectasis of the upper left lobe that was unexpandable under positive airway pressure while the lower lobe was expandable. Visceral and parietal pleura were with no significant changes. A small amount of serous pleural effusion was present. Tumor location indicated pneumonectomy because it surrounded the left lobar carina and infiltrated the pulmonary artery. Neoplasm characteristics were consistent with endoluminal and intrapulmonary growth patterns. A solid off-white tumor was well separated from the surrounding lung tissue and was of dimensions 28 × 20 × 20 mm. The tumor did not spread to the visceral pleura. Microscopically, the tumor nodule was covered by regular respiratory epithelial cells (Figure 3a). The unencapsulated tumor consisted of a mixture of spindle cells in fascicles and those in storiform patterns. As expected, tumor cells had abundant light eosinophilic cytoplasm, oval nuclei, and inconspicuous nucleoli. Mitosis and cytologic atypia were not noticed. An inflammatory infiltrate containing numerous lymphocytes and a prominent number of plasma cells was between spindle mesenchymal cells. Histiocytes were also obtained, including some Touton-type giant cells (Figure 3b). Immunohisto-

chemically, all tumor cells expressed vimentin (Figure 3c), and most of them smooth-muscle-actin (SMA) (Figure 3d). Anaplastic lymphoma kinase (ALK) expression was detected in some tumor cells (Figure 3e). Ki67 was expressed in less than 10% nuclei of spindle tumor cells (Figure 3f).

The postoperative course of a surgical treatment proceeded with no complications. The patient was released from the hospital on the eighth postoperative day. In regular follow-up visits, four years after the procedure, the patient showed no recidivism of the illness.

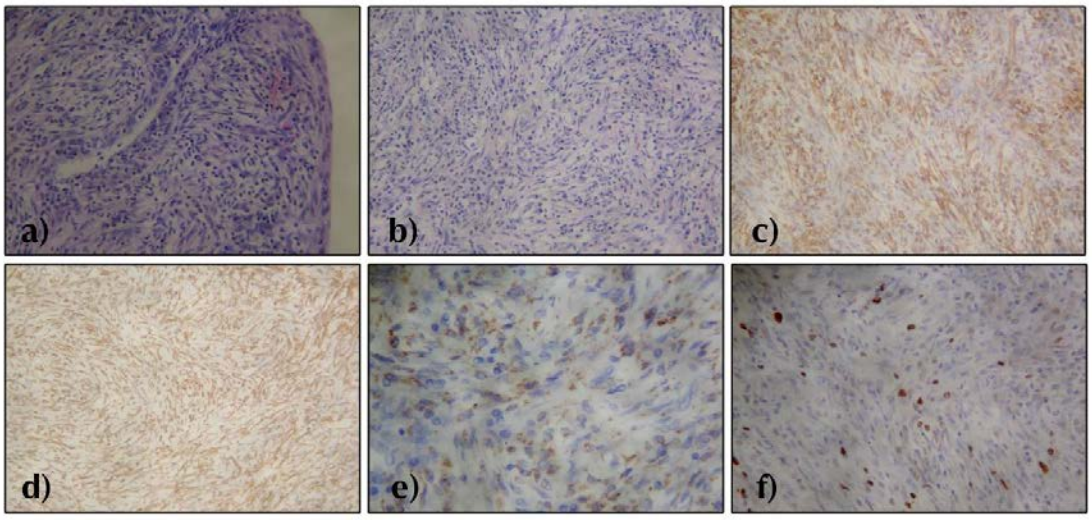

Fig. 3 – a) Endoluminal growth pattern of tumor, covered by respiratory epithelia [hematoxylin & eosin (HE), x10]; b) Mixed cellularity of pseudotumor, spindle, and inflammatory cells (HE, x40); c) The mesenchymal origin of the tumor was confirmed by vimentin (x20); d) Tumor cells originate from myofibroblasts [smooth-muscle-actin (SMA), x20]; e) Some tumor cells express anaplastic lymphoma kinase (ALK, x40); f) Ki67 is expressed in less than 10% nuclei of tumor cells (x40).

Discussion

IMT is a rare tumor of the mesenchymal original that more frequently occurs in children than in adults [1]. Of all reported IMTs, 35% were recorded in children under the age of 15 [2]. It is most commonly manifested as peripheral nodes in the lungs while much less so endobronchially [3–5]. In reported child cases, IMT accounts for around 20% of all primary lung tumors [7]. There are no gender differences in its incidence [7]. It gets detected most typically in the second decade of life [3].

The etiology of IMT is uncertain. According to the WHO classification from 2013, IMT is defined as an intermediate soft tissue tumor that demonstrates myofibroblastic differentiation accompanied by inflammatory cells, plasma cells, and lymphocytes [6].

It is considered that several genes and chromosomal abnormalities are linked to IMT occurrence. It is shown that chromosome translocation of ALK genes is present in around 50% of the reported IMT cases [1].

Recent studies have described fusions involving the ROS1 and PDGFRβ genes in a subset of ALK-negative cases [1]. Change in HMGIK (HMGA2) gene is also documented [8]. Aneuploidy is present in around half of the IMT patients and points to a tumor with aggressive behavior [9].

Various autoimmune diseases, trauma, as well as infections caused by *Mycobacterium tuberculosis* and other mycobacteraa, *Mycoplasma* spp., *Pseudomonas aeruginosa*, *Actinomycetes*, *Nocardia* spp., Epstein-Barr virus, and human herpesvirus are also believed to be linked to IMT occurrence [2, 3].

The clinical report is nonspecific. Around 40–50% of IMT patients are asymptomatic [2, 5] when it is accidentally discovered, while in other patients, it is manifested through cough, pain, hemoptysis, weakness, difficulty breathing, pneumonia, weight loss, and arthralgia [3–5]. Endobronchial tumor location is associated with the earlier manifestation of mentioned symptoms and a smaller percentage of asymptomatic cases, only around 21%, as opposed to the peripheral one [5].

In the literature, we were able to find only two cases of reported IMT associated with pneumothorax. In the first case, regarding peripheral tumor location, persistent pneumothorax existed, and its occurrence was explained by chronic visceral pleura lesion that was the result of repeated lung reexpansion and collapse accompanied by inflammation [10]. The significance of IMT on that lesion and pneumothorax development is unclear. We think that the peripheral IMT location could bring about chronic visceral pleura lesion and consequent pneumothorax. In the other reported case, the tumor was developed endobronchially in the presence of subcutaneous emphysema. It was hypothesized that, in this case, pneumothorax is a consequence of ball valve mechanism with subsequent air obstruction and alveolar rupture [5]. We consider this to be a pneumothorax development mechanism in the case of our patient, as well as subsequent complete upper lobe bronchus obstruction that could explain lung reexpansion inability after thoracic drainage and applied positive airway pressure during surgery. The existence of subcutaneous emphysema in the mentioned case could be explained by peribronchial air expansion further across medias-

tinum towards the neck and subcutaneous tissue, which did not happen in the case of our patient.

Chest radiographs are nonspecific as well. IMT is usually seen as a peripheral, solitary, lobulated, sharply circumscribed mass predisposed towards lower lobes [3].

Thorax CT scan is significant in determining the precise location of the lesion and its scope. The tumor manifests itself as a nonspecific heterogeneous mass with different contrast enhancement. Notable calcifications are infrequent, reported in only 15% of the cases [11], and more common in children than adults [3]. Lymphadenopathy is rarely documented [3, 11]. Multiple lesions are observed in 5% of the reported cases, and endobronchial involvement exists in 10% of the noted cases [3]. In the case of our patient, both endobronchial and intrapulmonary components of the tumor with peripheral calcifications were discerned.

Due to its nonspecific symptomatology and thus late diagnosis and treatment, its spreading towards mediastinum [3] is possible as was observed in our patient.

Radiographs, CT scans, fiberoptic bronchoscopy, and fine needle aspiration biopsy are usually not sufficient for definitive diagnosis. However, rigid bronchoscopy is advised when dealing with endobronchial tumors. It produces adequate tissue samples and facilitates definitive IMT diagnosis in over 80% of those cases [4]. In the case of our patient, rigid bronchoscopy was undertaken at the institution he was treated at before transferring to ours, and the obtained results supported IMT diagnosis, which was confirmed after surgical resection.

The established diagnosis of IMT was concluded upon surgical tumor specimen according to its growth pattern, morphology, and immunoprofile.

The characteristic morphology of this mostly unencapsulated tumor is a mixture of spindle cells with fascicular and storiform patterns and collagen, accompanied by lymphocytes, plasma cells, and histiocytes. We confirmed mesenchymal proliferation by vimentin expression and its myofibroblastic origin by focal SMA expression [12]. ALK was expressed in some tumor cells. It was reported that ALK was expressed in some tumor cells in 40% of the IMT cases [13]. No expression of S-100 protein excluded its neuroectodermal origin. The absence of cytokeratin-AE1/AE3 excluded lung spindle cell carcinoma, while its focal expression could be found in some cases of IMT. Its focal immunopositivity is potentially explained by alveolar entrapment. Ki67 was expressed in less than 10% of tumor cells, and that was a reason for 3–6-month follow-up visits due to the risk of IMT recurrence. The guidelines for IMT diagnosis followed the 2004 and 2015 WHO classification of lung tumors [12, 14].

The method of choice in IMT treatment is complete surgical resection. The 5-year postoperative survival rate is 91.3%, while recidivism rates are between 4% and 13% and are associated with incomplete surgical resection [4, 15].

When the complete resection is not doable or in the case of tumor recurrence or comorbidities, medical therapy alone or in combination with radiation needs to be considered.

Effects of nonsurgical IMT treatments are based upon single case reports and a small number of patients. Therefore, it is hard to talk about their contribution to future recommendations.

Carboplatin and paclitaxel chemotherapy could be used in certain cases, but generally, it did not provide satisfactory results. It is implemented in the treatment of recidivism and unresectable cases [16]. The application of vinorelbine and methotrexate has also shown success in certain IMT cases [17].

The use of corticosteroids is controversial because it resulted in complete tumor regression in certain cases [18] while, in other cases, it resulted in further tumor progression [19].

Nonsteroidal anti-inflammatory drugs (NSAID), such as celecoxib, due to its antiangiogenic effects, were implemented in some ALK and ROS-1 negative patients [20]. In ALK and ROS-1 positive patients, the use of tyrosine kinase inhibitor crizotinib produces certain positive effects [1].

Radiotherapy is used in patients when surgical treatment is not applicable, when recidivism is detected, or in the case of metastatic tumor [4].

IMT could be of different malignant potential, but it could generally be said that it has a benign course. Rare cases of distant metastases and spontaneous remission have been documented [3, 4]. The possibility of recidivism calls for further monitoring of these patients.

Conclusion

The inflammatory myofibroblastic tumor is one of the most frequent primary lung tumors in children, and it always needs to be suspected upon. Patients could be asymptomatic or manifest nonspecific symptomatology, such as cough, dyspnea, chest pain, exertion, and respiratory infections. Pneumothorax could be one of the IMT manifestations. Its occurrence could be the consequence of either a visceral pleura lesion in the case of peripheral tumors or a ball valve mechanism in the case of endobronchial tumors. Definitive diagnosis of IMT and treatment methods require not only histopathology but also immunohistochemical analysis. Complete surgical resection as a treatment of choice has, as a result, the best survival rates. Medical and radiation therapy are documented to be less effective and are used in selective cases. Further monitoring of patients is necessary due to the risk of recurrence.

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