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ПРИКАЗ БОЛЕСНИКА / CASE REPORT
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Inflammatory Myofibroblastic Tumours of the Respiratory Tract: A Series of Three Cases with Varying Clinical Presentations and Treatment

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SUMMARY

Introduction Inflammatory myofibroblastic tumor in the respiratory system is a rare and controversial disease. It is macroscopically well-circumscribed, non-encapsulated, firm and usually a yellowish-white mass. Histologically it is composed of the following spindled and inflammatory cells: lymphocytes, plasma cells, and histiocytes, including Touton type multinucleated giant cells.

Case Outline The series included a 49-year-old man with a tracheal inflammatory myofibroblastic tumor who complained of hoarseness; a 42-year-old man who was coughing and had a blood-stained sputum, and inflammatory myofibroblastic tumor was in the right main and intermediate bronchus; and a 32-year-old man with chest pain and inflammatory myofibroblastic tumor as a solitary peripheral nodule in the left lower lobe. In all the cases, the tumor was resected bronchoscopically and surgically.

Conclusion Inflammatory myofibroblastic tumor of the lung and the trachea is rare. Complete resection, when possible, should be the choice of treatment. After the complete removal, prognosis is generally excellent and recurrences are rare.

Keywords: inflammatory myofibroblastic tumor; lung; trachea

INTRODUCTION

Inflammatory myofibroblastic tumor (IMT) is a rare and controversial disease that is known under various names in literature, such as plasma cell granuloma, myofibroblastic tumor, inflammatory pseudotumor etc. [1-4].

Etiology and pathogenesis are insufficiently elucidated [5]. It is more often diagnosed in younger patients. Over 50% of patients with the respiratory localization of the tumor have non-specific respiratory symptoms [6, 7]. IMT is mainly localized in the lung as a peripheral node. Multiple nodes, intraluminal polyp and mass are rare [2, 7]. It is macroscopically well-circumscribed, with rare calcification and hemorrhage. Histologically it is composed of the following spindled and inflammatory cells: lymphocytes, plasma cells, and histiocytes, including Touton type multinucleated giant cells [8]. Differential diagnosis considers a number of pathological conditions (plasmacytoma, lymphoma, lymphocytic interstitial pneumonia, malignant fibrous histiocytoma, sarcomatoid carcinoma, primary sarcomas of the lung) and correct pathological diagnosis involves the application of immunohistochemistry [8, 9].

Although spontaneous regression of IMT is possible, complete surgical or endoscopic resection is the choice of treatment for these patients. Corticosteroid monotherapy, radiation therapy or chemotherapy are used in inoperable patients [10]. Recurrences of this disease are rare and occur as a consequence of incomplete primary resection [3, 11]. Prognosis of the disease is good [12].

The objective of this paper was to present various clinical presentations and treatment of IMT in the respiratory system.

CASE REPORTS

Case no. 1

A 49-year-old man, former smoker, reported to a doctor because of cough, difficulty in breathing, hoarseness, poor appetite and weight loss.

Upon admission to our hospital, the patient was poorly nourished, afebrile, with audible inspiratory stridor. Computerized tomography (CT) of the thorax showed a sessile polyp (20 mm) on the left lateral side of the initial portion of the trachea which infiltrated mucosa and submucosa (Figure 1). The patient underwent three bronchoscopies during the hospitalization. A lobular tumor, which obstructed the lumen of the trachea by 85%, was seen 5 mm

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from the vocal cords during the first bronchoscopy (Figure 2). The bioptic sample on hematoxylin and eosin stained preparations was a mixture of spindle cells which showed storiform architecture. The spindle cells have oval nuclei, fine chromatin, inconspicuous nucleoli, and abundant lightly eosinophilic cytoplasm and obscuring inflammatory infiltrate containing lymphocytes, plasma cells and histiocytes around it. We diagnosed IMT (Figure 3). The second bronchoscopy and tracheal recanalization were performed five days later. The distal portion of the trachea was normal, but 5 mm from the vocal cords there was a part of the polyp that engaged the lumen of the trachea by 30%. Detached polyp had been located in the distal portion of the left main bronchus, and was removed bronchoscopically. The third bronchoscopy was performed the following day. The remainder of the polyp was noted on the right vocal cord, and complete mechanical obstruction removal and bronchial biopsy were performed when IMT diagnosis was confirmed by immunohistochemical staining. Spindled cells were the following: vimentin and CD117 positive and SMA, desmin, ALK, CD34 and panCK negative. The patient hasn't had any recurrences 26 months after the endoscopic resection.

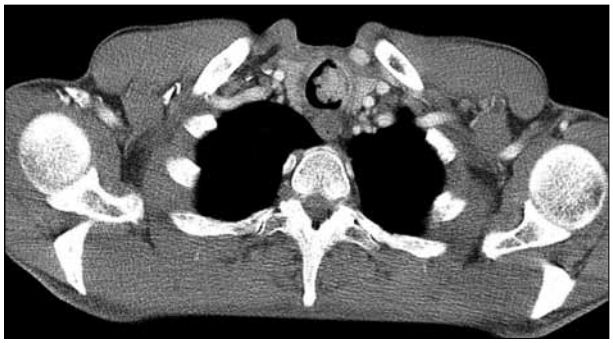

Figure 1. A computed tomographic scan of the chest shows the tumor, which occupies approximately 90% of the tracheal lumen

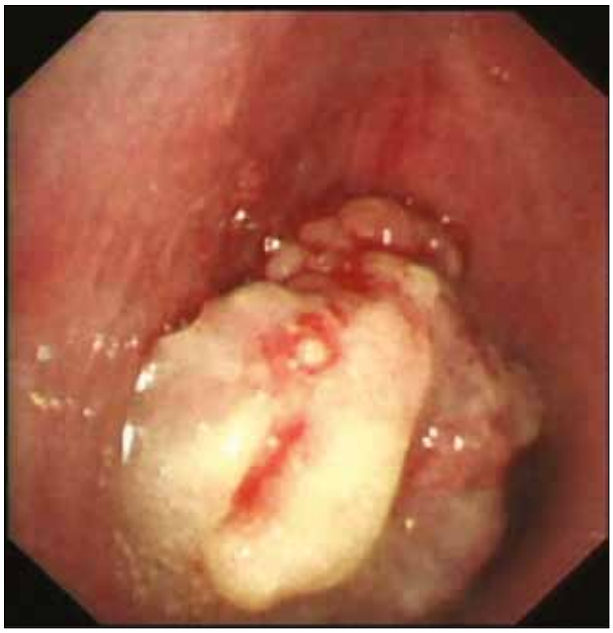

Figure 2. Bronchoscopy shows a polypoid lesion, which almost completely closes the trachea

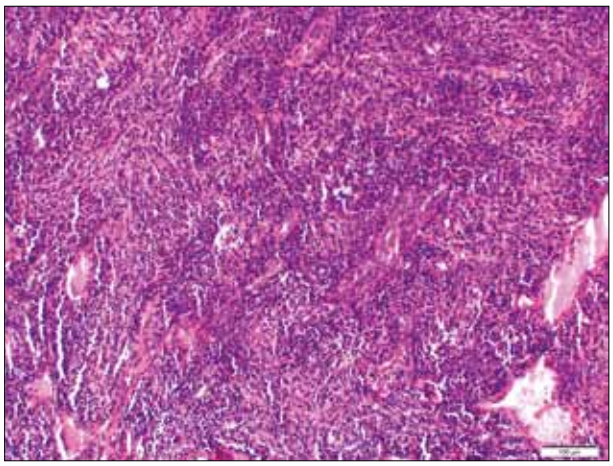

Figure 3. The tumor was composed of bundles of uniform spindled cells and inflammatory cells – lymphocytes, plasma cells and histiocytes (H&E; ×200)

Case no. 2

A 42-year-old man, former smoker, reported to a doctor because of irritating cough and blood-stained sputum. The symptoms had lasted for three months. CT of the thorax and bronchoscopy had been performed at another hospital. The tumor was noticed in the lumen of the right main and intermediate bronchus, arising suspicion of a carcinoid, but a malignant tumor of low malignant potential of mesenchymal origin was diagnosed via immunohistochemical analysis of bioptic samples.

The patient was admitted to our hospital two months later in order to perform an endoscopic resection of the entire tumor. The CT of the thorax showed infiltration of 40×30×30 mm in size, localized in medial basal segment of the right lung. A lobular, bleeding tumor emerging from the distal portion of the right main bronchus was registered on repeated bronchoscopy (Figure 4).

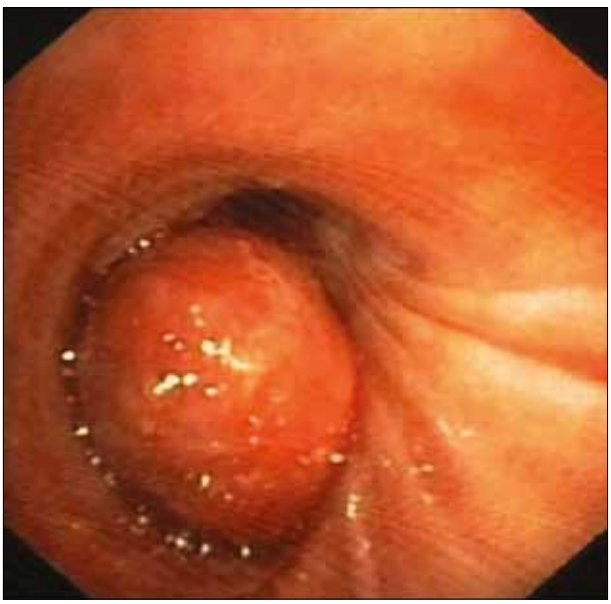

Figure 4. A rigid bronchoscopy shows the tumor inside the distal part of the right main bronchus before resection

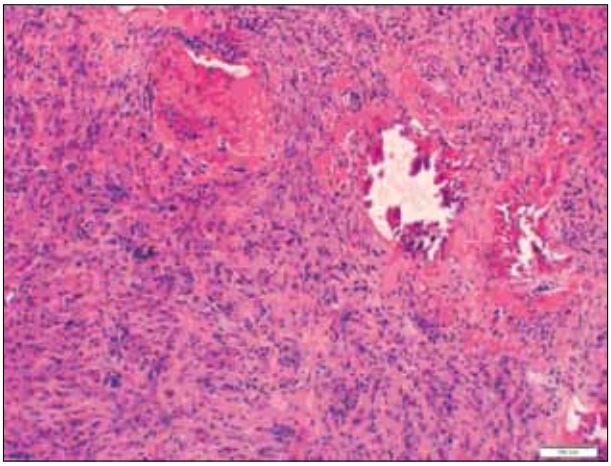

Figure 5. The bronchoscopy sample consisted of connective tissue with keloid-type hyalinization, lymphoplasmacytic infiltration of the lesion, presence of peripheral calcifications (H&E; ×100)

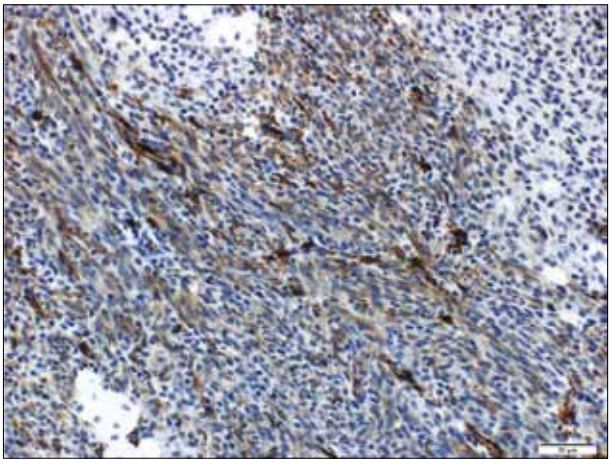

Figure 6. Strong SMA positivity was seen in spindle cells (×200)

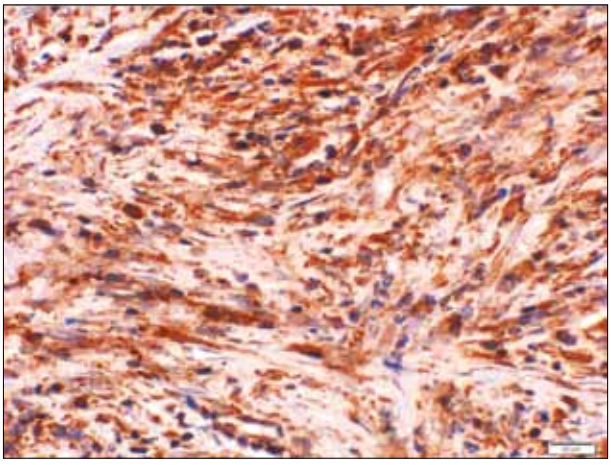

Figure 7. Strong CD117 positivity was seen in spindle cells (×400)

The extracted bronchoscopy sample consisted of connective tissue with keloid-type hyalinization, slight lymphoplasmacytic infiltration of the lesion and presence of peripheral calcification. The sample was diagnosed with IMT (Figure 5). Due to profuse hemorrhage from the mouth, an emergency surgery was performed six days after the bronchoscopy. A sleeve resection of the right intermediate bronchus was performed, with a length of 12 mm starting from the origin of the bronchus to the upper lobe. A prior location of the tumor stem which was bleeding actively was also found. The detached tumor was located in the right main bronchus. Pathohistologically observed, spindled cells were SMA (Figure 6), desmin, vimentin and CD117 positive (Figure 7), and ALK, CD34 and panCK negative, which confirmed the IMT diagnosis. The patient has been feeling well and has had no recurrence for 21 months after the surgical treatment.

Case no. 3

A 32-year-old man, non-smoker, reported to a doctor because of intermittent pain on the left side of his thorax that had lasted for six months. The radiograph of the thorax, left basally, showed a round shadow and the patient had been sent to our hospital.

The CT of the thorax showed a round nodule with a diameter of 15 mm, left basally, in the ninth segment. Left anterolateral minithoracotomy and atypical resection of the left lower lobe were also performed. A marginal extract of the lung was submitted for ex tempore analysis. A soft, yellowish nodule with a diameter of 15 mm was located at the intersection. The pathologist declared that this is a benign process, primarily an IMT. At the permanent paraffin sections, spindle cells arranged in storiform configuration were mixed with lymphocytes, plasma cells and histiocytes. Vascular and bronchioloalveolar elements were present inside the tumoral mass (Figure 8). An immunohistochemical analysis was applied, and the final IMT diagnosis was as follows: spindled cells – panCK, ALK, desmin and CD34-negative (Figure 9) and CD117, SMA and vimentin – positive (Figure 10). Ten months after the surgery there has been no recurrence of the disease.

DISCUSSION

IMT in the lung was first described in 1939, and in the trachea in 1978 [1, 13]. Hartmann and Shochat [14] diagnosed IMT in 56% of patients, out of 78 benign lung tumors. Unlike Cerfolio et al. [4] (0.04%), Golbert and Pletven [15] had a significantly higher incidence (0.7%), which is most likely a consequence of a pediatric population included in the study. One hundred and eighteen patients with benign lung tumor were operably taken care of at the Institute for Pulmonary Diseases of Vojvodina (2009–2013), of which two (1.7%) had IMT in the lung and one patient was with localization in the trachea. We have thereby confirmed the view that this is a rare tumor.

Etiology and pathogenesis of IMT have been the subject of numerous debates and controversial views. Most studies support the notion that this tumor is a consequence of an inflammatory reaction after a trauma, autoimmune reaction or a recurrent infection [16, 17]. Although the tumor grows slowly and locally, it may recur, show local invasion and give rise to distant metastasis. Therefore, according to more recent notions, it is considered

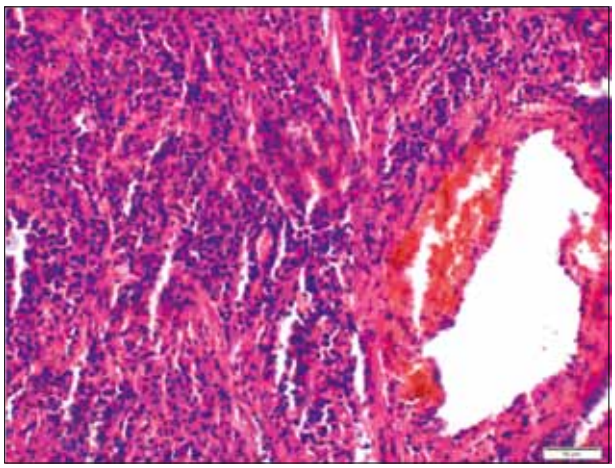

Figure 8. Vascular elements were present inside the tumoral mass (H&E; ×200)

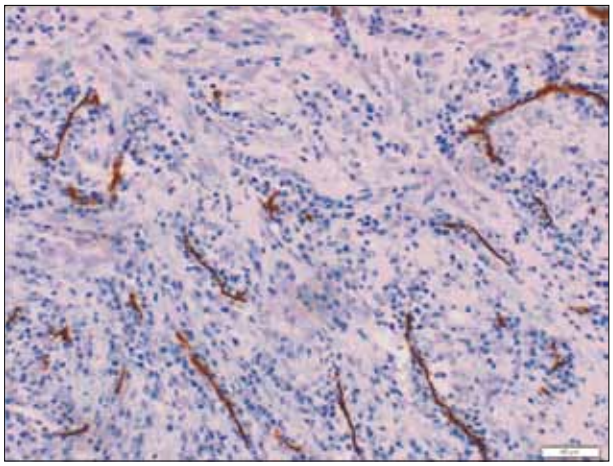

Figure 9. Immunoreactivity of the myofibroblasts for CD34 was not observed (×200)

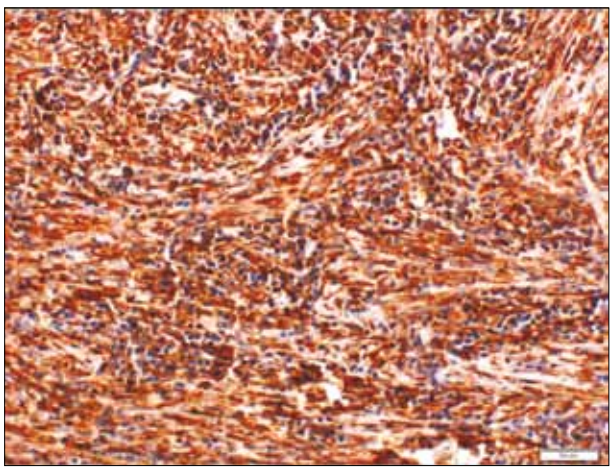

Figure 10. Diffuse strong vimentin positivity was seen in spindle cells (×200)

a malignant soft tissue tumor of low malignant potential, rather than a reactive lesion [18]. According to Cerfolio et al. [4], it is most appropriate to categorize IMT into non-invasive (asymptomatic, small tumors, without invasion of surrounding structures) and invasive (invasion of surrounding structures, nuclear atypia, mitotic activity). The authors recommend performing a wedge resection of non-invasive forms, and lobectomy or pneumonectomy of invasive ones, depending on the localization of the tumor [4]. Regardless of the treatment, long-term monitoring of patients is necessary, since there have been described recurrences even several years after the initial resection [19].

IMT of the respiratory tract is usually diagnosed in men under 40 years of age [20, 21, 22]. Bahadori and Liebow [2] involved in their study one third of patients younger than 20 years, where the youngest one was 13 months old. Our patients were 49, 42 and 39 years old. Two out of three patients that we presented were former smokers, had nonspecific respiratory symptoms of the disease: cough (2/3), difficulty in breathing (1/3), chest pain (1/3), prior pneumonia (1/3), hemoptysis (1/3), hoarseness and stridorous breathing (1/3). Weight loss and poor appetite were noted only in the patient whose tumor was localized in the trachea. These results are in correlation with the results of Cerfolio et al. [4] and Mondelo [23].

Over 80% of IMT cases in the respiratory system are localized at the periphery of the lung parenchyma [24, 25]. We have shown various anatomical localizations of the tumor: peripheral node (case no. 3), endobronchial polyp (case no. 2) and endotracheal polyp (case no. 1). Regardless of the localization, preoperative diagnostics of IMT is insufficient. CT scans of the tumor show a nonspecific shape of a coin, whereas in bronchoscopic samples there are often only inflammatory cells [7, 24]. Therefore, surgery is crucial from the standpoint of diagnostics and treatment, where ex tempore analysis is primarily used to exclude malignancy [26, 27, 28]. In cases no. 1 and 2 we diagnosed IMT based on bronchoscopic samples, while in the third case we intraoperatively excluded malignancy and suspected the existence of IMT, which was confirmed on paraffin sections.

IMT is a 15–40 mm well-circumscribed, non-encapsulated, firm, yellowish-white node [2]. The sizes of tumors in our patients (18, 15 and 25 mm) are in correlation with the published data [26, 29]. Histologically, all three tumors consisted of bundles and vortices of uniform spindled cells and inflammatory cells. Immunohistochemically observed, spindled cells were the following: SMA (2/3), desmin (1/3), CD117 (3/3), vimentin (3/3) positive, and CD34, ALK and panCK negative in all patients. Since IMT is a rare tumor, a small sample which we processed immunohistochemically indicated a myofibroblastic differentiation of spindled cells, which was consistent with the results of a much larger series [29].

As our patients did not have any contraindications for surgical treatment, we opted for complete surgical, i.e. endoscopic resection of the tumors in order to avoid possible recurrences. Data on tumor recurrences are limited due to small number of cases. They have been recorded in 4% of the cases in the respiratory system, whereas they are more frequent in extrapulmonary localization (25%). Most authors believe that recurrence is the consequence of an incomplete initial surgical or endoscopic resection [30]. We have been monitoring our patients clinically, radiologically and bronchoscopically for 26, 21 and 10 months and have not recorded any recurrences.

Bearing in mind that our patients have undergone a complete resection of the tumor, we expect a good prognosis of the disease.

Inflammatory myofibroblastic tumor in the respiratory system is rare. Complete surgical or endoscopic resection should be the choice of treatment. After the complete removal, prognosis is generally excellent and recurrences are rare. Since this tumor has unpredictable biological behavior, long-term monitoring of patients is necessary.

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Инфламаторни миофибробластни тумори дисајног система: приказ три болесника с различитим клиничким презентацијама и лечењем

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КРАТАК САДРЖАЈ

Увод Инфламаторни миофибробластни тумор је ретко и недовољно испитано обољење. Макроскопски је добро ограничен, неинкапсулиран, чврст, обично жуто-бео чвор. Хистолошки је саздан од вретенастих и инфламаторних ћелија: лимфоцита, плазма ћелија и хистиоцита, укључујући Тутонов тип вишеједарних џиновских ћелија.

Приказ болесника Први болесник, мушкарац стар 49 година, жалио се на промуклост и код њега је дијагностикован инфламаторни миофибробластни тумор у трахеји. Други болесник, мушкарац стар 42 године, кашљао је и имао сукрвичав испљувак, а инфламаторни миофибробластни тумор је био у десном главном и интермедијарном бронху. Трећи болесник, мушкарац стар 32 године, жалио се на болове у грудном кошу, а инфламаторни миофибробластни тумор код њега се испољио као солитарни периферни чвор у левом доњем режњу. У свим случајевима тумор је ресециран бронхоскопски и хируршки.

Закључак Инфламаторни миофибробластни тумор у плућима и душнику је редак. Комплетна ресекција, када је могуће, требало би да буде избор лечења. Након потпуног уклањања тумора прогноза је обично изврсна, а рецидиви су ретки.

Кључне речи: инфламаторни миофибробластни тумор; плућа; душник

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