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**TRAHEALNA LOKALIZACIJA INFLAMATORNOG MIOFIBROBLASTNOG TUMORA KOD ODRASLIH: PRIKAZ SLUČAJA**

Authors: **Branislav Oluić**, **Radomir Vešović**, **Zlatibor Lončar**, **Jelena Stojšić**, **Nataša Mujović**, **Dejan Nikolić**. *Vojnosanitetski pregled* (2017); Online First September, 2017.

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TRACHEAL LOCALIZATION OF INFLAMMATORY MYOFIBROBLASTIC TUMOR IN ADULTS: A CASE REPORT

Trahealna lokalizacija inflamatornog miofibroblastnog tumora kod odraslih: prikaz slučaja

Branislav Oluić*, Radomir Vešović†, Zlatibor Lončar¶, Jelena Stojšić‡, Nataša Mujovićǁ, Dejan Nikolić§

*Emergency Center - Clinical Center of Serbia, Belgrade, Serbia.
†Clinic for Thoracic Surgery - Clinical Centre of Serbia, Belgrade, Serbia.
‡Service of Histopathology - Clinical Centre of Serbia, Belgrade, Serbia.
¶Clinic for Physical Medicine and Rehabilitation - Clinical Centre of Serbia, Belgrade, Serbia.
ǁFaculty of Medicine, University of Belgrade, Belgrade, Serbia.
§Physical Medicine and Rehabilitation Department, University Children’s Hospital, Belgrade, Serbia.

Corresponding author:
Radomir Vešović, MD, MSc.
Clinic for Thoracic Surgery - Clinical Centre of Serbia, Koste Todorovića 26, 11000 Belgrade, Serbia.
email: rvesovic@gmail.com
Sažetak

Uvod: Inflamatori miofibroblastni tumor (IMT) je retka neoplazma. Bolest je nepredvidivog toka i nejasne etiologije za čiju definitivnu dijagnozu je potrebna detaljna patohistološka analiza uz primenu imunohistohemije. Mikroskopski ga čine miofibroblastne vretenaste i inflamatorne ćelije u različitom odnosu. Redo se vida kod starijih osoba i nespecifične je simptomatologije. Opisano je prisustvo IMTa na svim anatomskim lokalizacijama, a trahealna lokalizacija je posebno veoma retka.

Prikaz Slučaja: Bolesnica stara 41. godinu javila se u našu ustanovu zbog progresije simptoma sličnih astmi u vidu otežanog disanja, kašlja i brzog zamaranja. Ranije je lečena bronhodilatatornom terapijom bez uspeha. Na kontrolnim ambulantnim pregledima radiografijom grudnog koša uočena je suspektna promena u distalnom delu traheje. Nakon prijema u našu ustanovu učinjene su dijagnostičke metode spirometrija, kompjuterizovana tomografiJA (CT) grudnog koša, nuklearna magnetna rezonanca (NMR) grudnog koša i bronhoskopija. Navedene dijagnostičke pretrage su potvrdile postojanje promene u distalnoj trećini traheje. Učinjena je desna torakotomija sa mobilizacijom pluća i resekcijom traheje i termino-terminalnom (T-T) anastomozom. Histopatološkom analizom operativnog materijala uz primenu imunohistohemije postavljena je dijagnoza IMTa. Bolesnica je četiri godine nakon operacije bez recidiva bolesti.

Zaključak: Za postavljanje dijagnoze IMTa su potrebne detaljne dijagnostičke pretrage, posebno adekvatna histopatološka analiza sa imunohistohemijom. Metod izbora u lečenju IMTa je kompletna hirurška resekcija. Dalje kontrole su neophodne u cilju detekcije mogućih recidiva.

Ključne reči: Inflamatori miofibroblastni tumor, neoplazma, trahea, odrasli, hirurška resekcija.
Abstract

Introduction: Inflammatory myofibroblastic tumor (IMT) is a rare neoplasm. This disease, of unknown etiology, runs an unpredictable course. Its definitive diagnosis calls for detailed histopathological analysis including immunohistochemistry. Microscopically, IMT is composed of myofibroblastic spindle and inflammatory cells in different proportions. It presents infrequently in adults with nonspecific symptomatology. The presence of IMT is described in every anatomical region but the tracheal one is especially uncommon.

Case report: A 41-year-old female patient checked into our institution due to exacerbation of asthma-like symptoms such as shortness of breath, cough and exertion intolerance. She was originally treated as asthmatic patient with bronchodilator therapy with no success. Chest x-ray done during one of outpatient follow-up appointments pointed to a suspected change in the tracheal distal part. After her admission to our institution, the following diagnostic procedures were performed, spirometry, chest computerized tomography (CT) scan, chest magnetic resonance imaging (MRI) and bronchoscopy and the change in tracheal distal third was confirmed. Right sided thoracotomy with mobilization of lung, tracheal resection and termino-terminal (T-T) anastomosis was undertaken. Subsequent histopathological analysis of surgically removed afflicted tracheal part including immunohistochemistry enabled us to definitively diagnose IMT. Four years after surgical resection, patient shows no recidivism of illness.

Conclusion: Definitive IMT diagnosis requires detailed diagnostic tests, most importantly, an adequate histopathological analysis including immunohistochemistry. Complete surgical resection is the treatment of choice in case of IMT. Further monitoring of patients is necessary due to risk of recurrence.

Keywords: Inflammatory myofibroblastic tumor, neoplasms, trachea, adult, surgical resection.

Introduction

Inflammatory myofibroblastic tumor (IMT) is an infrequent mesenchymal tumor of unclear etiology and more frequent occurrence among children and young adults in the first two decades of life (1, 2). The most common incidence is in the lungs as peripheral nodes
while its manifestation in the trachea is extremely rare. According to the World Health Organization (WHO), IMT is a lesion composed of myofibroblastic spindle cell population accompanied by an inflammatory infiltrate of plasma cells, lymphocytes, and eosinophils (2) and its diagnosis depends upon relevant histopathological analysis. Before its definitive diagnosis, detailed histopathological analysis is necessary that includes an immunohistochemistry (3, 4). Even though it is previously being considered a benign ailment, latest research indicates its recurrence potential or malignant nature, depending upon proliferative index (Ki-67) (5). Surgical resection is the method of choice in its treatment with the excellent chance of patient survival (1). We report a 41-year-old female patient with IMT of the trachea.

Case report

A 41-year-old female patient was admitted to our institution due to the exacerbation of asthma-like symptoms. In the months prior to admission, she experienced difficulties breathing, cough without sputum and exertion intolerance. The worsening of those symptoms over time and their appearance even at rest were noted. She was originally treated with bronchodilator therapy with no effects. During one of outpatient follow up visits, chest x-ray showed a change in the distal left wall of the trachea (Fig. 1) and she was referred to our hospital.

Upon admission, pulmonary function test parameters informed of the severe obstructive ventilatory defect of upper respiratory tract FEV1% - 32%, FVC% - 84%, Tiff 29%.

Laboratory analysis values fell within their respective reference intervals. CT of the thorax exposed semicircular thickening of the size 32x15 mm at the level of the distal third of trachea, above bifurcation, that significantly reduced tracheal lumen (Fig. 2).

Subsequently, chest MRI revealed that on a distance of approximately 16mm from tracheal carina, laid a tumor that filled the lumen almost in its entirety (free lumen is of magnitude of 8x4mm approximately) and its dimensions were 11x19x33mm (Fig.3).

Repeated bronchoscopy disclosed the tumorous lesion on the XIII tracheal ring that blocked two thirds of tracheal lumen (Fig.4). Histopathological findings revealed chronic inflammation and squamous metaplasia of respiratory epithelia of trachea only.
After completed preoperative procedure, right sided thoracotomy was performed with mobilization of lung and resection of trachea in the length of approximately 3cm and termino-terminal (T-T) anastomosis.

Microscopically, unencapsulated inflammatory myofibroblastic tumor contained a mixture of spindle cells arrayed in fascicles or arranged in storiform pattern. These cells with oval nuclei and inconspicuous nucleoli had abundant lightly eosinophilic cytoplasm. Mitoses and cytologic atypia were not found. Admixed with the spindle proliferation, is an inflammatory infiltrate containing a numerous lymphocytes, and a prominent number of plasma cells associated with lymphoid follicles. Histiocytes were also obtained including some Touton type giant cells (Fig.5a and Fig.5b). Immunohistochemically, all of tumor cells expressed vimentin (Fig.5c) and some of them smooth-muscle-actin (SMA) (Fig.5d). Anaplastic lymphoma kinase (ALK) expression was detected in some of tumor cells (Fig.5e). Cytokeratin-AE1/AE3 was not expressed, excluding spindle cell type of lung carcinoma and in like manner S-100 protein, excluding neuroectodermal tumor. Ki67 was not found in any of examined tumor cells.

Postoperative course proceeded with no complications. Patient was released from the hospital on the tenth postoperative day. From there on, she has been undergoing regular follow-up visits and four years after the procedure, the patient shows no recidivism of the illness.

**Discussion**

IMT is a rare mesenchymal tumor most commonly located in the lungs making only 0.04% of all lung tumors (1), while its presence in the trachea is exceptionally uncommon (6, 7). Etiology of this tumor is uncertain. Explanations provided for IMT development are the following: an inflammatory reaction as a result of a trauma, an autoimmune reaction or an infection. However, in the majority of reported IMT cases, no trauma or infection was detected prior to the diagnosis (8, 9). As of late, IMT is widely recognized as a mesenchymal tumor with low malignant potential in view of its observed characteristics: local recidivism and invasion, metastasis, malignant transformation and certain genetic transformation such as chromosome translocation ALK genes in reported cases (5, 10).

IMT of respiratory organs is most frequently related to ambiguous symptomatology involving difficulties breathing, cough and fatigue (11). Dyspnea as the most common tracheal IMT clinical symptom is manifested early in the course of illness because of tracheal obstruction (10).
However, forming the correct diagnosis is usually delayed when symptoms are as vague and common and having in mind the low illness incidence (3).

IMT of trachea is generally located in the distal third of trachea (12).

Identifying an IMT preoperatively is hindered because of its cellular pleomorphism feature even after an adequate bronchoscopy (11,13). Its diagnosis is ordinarily being confirmed after surgical resection (13). The above argument also demand immunohistochemistry analysis (3,4).

Upon morphological pattern and immunohistochemistry results we diagnosed IMT. Until the 2004 WHO lung tumor classification, inflammatory myofibroblastic tumor of the lung was categorized as “inflammatory pseudo tumor” (14). Characteristic morphology of unencapsulated tumor is a mixture of spindle cells in fascicular and storiform pattern and collagen, accompanied with lymphocytes, plasma cells and histiocytes. Using vimentin expression, we confirmed mesenchimal proliferation and using focal SMA expression myofibroblastic origin of tumor was confirmed. Absence of S-100 proliferation excluded neuroectodermal origin of tumor and absence of Cytokeratin-AE1/AE3 expression allowed exclusion of spindle cell carcinoma, although according to the literature their presence could be observed in some IMTs. Its focal reactivity is potentially explained by alveolar entrapment. We did not find Ki67 expression and that could be a good prognostic sign that we don't expect local tumor recurrence after the tumor was removed completely. We were guided by IMT diagnosis recommendation of both the 2004 and the more recent 2015 WHO classification of lung tumors (14, 15). In described tumor ALK was expressed in some cells. Cessna et al. in 2002 found that 40% of IMTs expressed ALK in some of tumor cells (16).

Since IMT could imitate other lesions such as lymphoproliferative diseases, certain expert opinions call for histopathological confirmation before the surgical resection that could shed light on whether less invasive procedure like the endoscopic removal can be implemented. Nonetheless, it is widely accepted that in the case of tracheal IMT with transmural propagation or recidivism, the complete surgical resection of the afflicted part of the trachea is recommended (3,4,7,11,12).

Due to the small number of reported cases of tracheal IMT, till 2013, there were only 11 recorded cases of tracheal IMT in adults, we can't say anything definitive about its recidivism rate (8). This is the first reported case of tracheal IMT in adults for our hospital.
Radiotherapy is being used in patients when surgery is not applicable or they are inoperable with limited results (3,4,12).

In the course of IMT treatment, beside surgical resection as the method of choice, corticosteroids are being prescribed as well. Results of their use are varied, from ineffective to complete illness remission (2,17,18). The adoption of chemotherapy in IMT treatment did not produce satisfactory results (19).

After complete IMT removal, the prognosis is usually excellent, and with several recidivism cases being reported, subsequent regular follow-ups of patients are recommended (7,12).

**Conclusion**

Inflammatory myofibroblastic tumor is rarely thought of considering its vague clinical course and nonspecific radiographic findings. It can not be ignored especially in the pediatric population. Surgical resection is the method of choice in treatment of inflammatory myofibroblastic tumor. When tumor is resected in its entirety, this method yields an excellent rate of patient survival. Histopathological examination and diagnosis supported by immunohistochemistry are necessary to determine the histological type of tumor and its biological behavior. Other treatment techniques (chemotherapy, radiotherapy, corticosteroids) are being used less frequently and with lower success rates. Further monitoring of patients is necessary in order for recidivism to be detected.
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FIGURES:

Figure 1.

Figure 2.
Figure 5.

FIGURE LEGENDS:

Fig. 1. Chest X-ray (CXR) showing a lesion on the left distal wall of the trachea (arrows).

Fig. 2. Computed Tomography (CT) showing a mass on the left tracheal wall with intraluminal propagation.

Fig. 3. Magnetic resonance imaging (MRI) scan demonstrating a tumor of the left lateral tracheal wall, with lumen reduction.

Fig. 4. Bronchoscopy showing a stenosis of the trachea as a result of a tumor mass at the level of the XIII tracheal ring.

Fig. 5. Figure 5: a) Unencapsulated proliferative cells is present in deeper layers of tracheal wall. Respiratory epithelia is with squamous metaplasia, H&E x10. b) Mixture of small spindle cells with prominent, hyperchromatic nuclei and histiocytes with clear nuclei intermingled with lymphocytes and plasma cells, H&E x20; c) Small spindle cells expressed, Vimentin x40; d) Majority of cells express SM-Actin x40; e) ALK-P expression in some cell is specific for myofibroblastic tumor of the lung, ALK-P x40.