Unusual lymphadenopathy diagnosed by endobronchial ultrasound-guided transbronchial needle aspiration

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Abstract

Oxidized cellulose, used as hemostatic in thoracic surgery, may cause in some cases foreign body reactions, and simulate other diseases. We report the case of a 39-year-old man operated on a middle lobe lobectomy for atypical carcinoid. The follow up chest-CT showed enlarged mediastinal lymph nodes, so endobronchial ultrasound-guided transbronchial needle aspiration was performed suspecting recurrence of the tumor. The cytology results showed amorphous fragments such as foreign body reaction secondary to Pahacel®, used as hemostatic during the surgery. A few days later, the patient was re-operated on suspicion of mediastinitis induced by the endoscopic procedure. The aim of this case is to consider the foreign body reaction to Pahacel®, in patients with postoperative thoracic lymphadenopathy. It is also important to remember that in these patients the endoscopic procedures allow the diagnosis but may cause mediastinitis.

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Case Report

A 39-years old man was referred to our Department to perform a bronchoscopy. About six months earlier, the patient underwent a middle lobe lobectomy for an atypical carcinoid that was accompanied by ectopic adrenocorticotropic hormone (ACTH) Cushing's syndrome. After the operation the paraneoplastic endocrinological syndrome resolved and the patient did not suffer any other disorders. The patient, three weeks before coming to our attention, had completed steroid therapy with progressively reduced doses. Six months after the operation, a follow up chest-CT was performed (Figure 1A), which showed a suspect enlargement of subcarinal (18x10 mm) and right paratracheal (19x15 mm) lymph nodes, which appeared to be partly colliquated. The physical examination of the patient was within normal limits. He did not complain of any respiratory symptoms or any other type of disorder. Laboratory investigations revealed normal white blood cells and hemoglobin, electrolytes, kidney and liver function, a mild increase in C-reactive protein (CRP) 0,9 mg/dl. We therefore decided to perform bronchoscopy with enlarged lymph node samples (Figure 2) using endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). During the preparation of the slides for rapid on-site evaluation (ROSE), the material coming out of the needle was gelatinous and very dense with a light pink color. Under the microscope after extemporaneous staining the material showed poor cellularity, acellular material with characteristic elongated and quadrangular fragments (Figure 3). In the meantime, the patient was discharged home, awaiting the results of the bronchoscopy.

The cytological examination showed amorphous fragments of an acellular material, no evidence of malignancy, absence of granulomas and of necrosis was observed. Together with the clinical features of the patient, the diagnosis was suggestive of foreign body lymph node reaction, probably due to surgical material. For this reason, we analyzed the surgical report of our patient and we found out that the material used to control hemostasis was Pahacel®, an oxidized resorbable cellulose (ORC) normally used in thoracic surgery. We concluded that our patient suffered by a foreign body reaction induced by ORC.

After six days from the EBUS, the patient presented to our hospital at Emergency Room with fever, cough, swallowing difficulty and chest pain. A new contrast-enhanced CT was performed (Figure 1B), showing two hypodense formations in the right paratracheal area (48x29 mm) and in the subcarinal area (30x28 mm), which were initially attributable to a colliquated or abscessualised adenopathy.

Therefore, the patient was hospitalized with the suspicion of mediastinitis, and treated with antibiotics (piperacillin-tazobactam 4.5 g/three times per day). After three days the patient underwent via right lateral thoracotomy under general anesthesia. Colliquated masses were confirmed in lymph node regions right paratracheal and subcarinal, confirming the diagnosis of mediastinitis. Microbiological examination was negative for bacteria. The patient's clinical course was regular, and he was discharged home few days later.

Discussion

The use of haemostatic substances is a common practice in surgery and the most commonly substance used is ORC.

Pahacel® is an ORC used in surgical procedures to control capillary, venous and small arterial hemorrhage, it provides rapid hemostasis within 2-3 minutes, and it is absorbed in the body within 7-14 days. It exhibits bacteriostatic and bactericidal properties with the effect on growth and multiplication of gram (+) and gram (-) organisms including aerobic, anaerobic bacteria [1].

Pierce *et al.* demonstrated that the absorption of ORC occurs because of its dissociation into polyuronic acid and fibrous residue. Polyuronic acid is readily soluble, and its concentration declines within the first 18 h [2]. The fibrous residue is degraded by macrophages commencing within 48 h of implantation. Ultrastructural examination of these macrophages indicated that they do not process fibrous residue, which may explain the resistance of material at sites of implantation for long periods of time, although generally complete reabsorption is achieved within 4±8 weeks [3].

Complicated degradation reactions due to tissue damage in some cases can occur such as provisional matrix formation, acute or chronic inflammation, inducing a granulomatous reaction. This can lead to the creation of foreign body reactions and to the formation of a fibrous capsule, resulting in a pseudotumoral lesion that mimics tumor recurrence [4]. It is estimated that these reactions occur in about 3% of cases [5].

The radiological findings can show an imaging appearance that mimics serious post-operative complications or potentially mimicking disease recurrence in later stages. Differentiating between ORC reaction and post-operative complications or disease progression can be challenging and most encountered on CT mimicking postoperative hematoma, abscess or inadvertently retained surgical foreign body. These other post-operative conditions are often suggested as potential differential diagnostic possibilities in routine clinical prac-

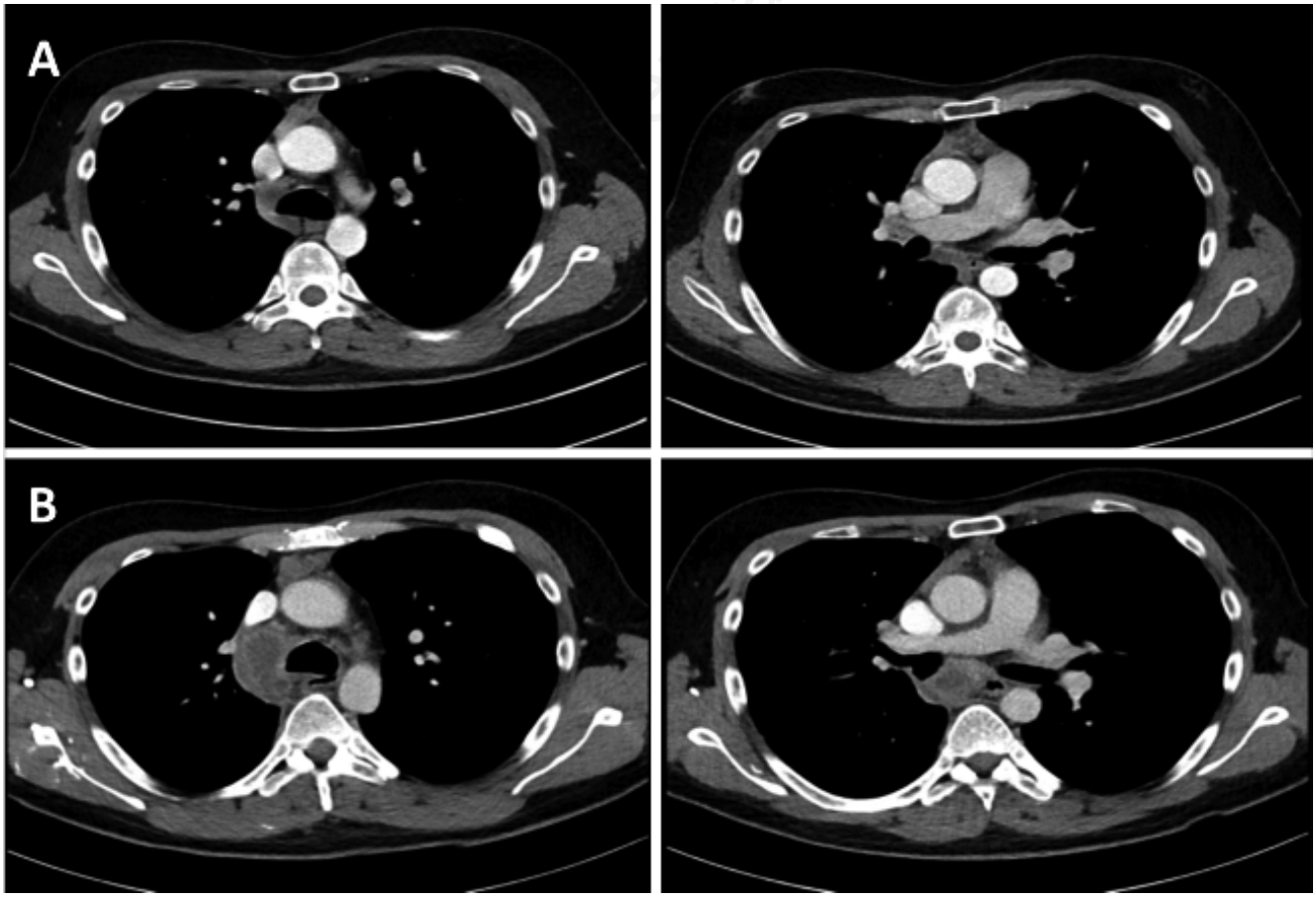

Figure 1. A) Enlarged and partly colliquated lymph nodes before EBUS-TBNA. B) Hypodense formations after EBUS-TBNA.

tice by radiologists not aware of the use of ORC during the surgical procedure or not familiar with appearance of ORC on CT [6]. Frati *et al*. demonstrated that in the post-operative setting, the ability to differentiate ORC reaction from a collection or an abscess on CT, while withholding clinical history about the use of ORC, resulted in correct interpretation in only 11% of the cases [7].

Cytological findings are characteristic enough to permit a specific recognition and diagnosis. Our findings showed amorphous fragments of an acellular material, no evidence of malignancy, absence of granulomas and necrosis. This is already described in other studies, in patients with postoperative pseudotumoral lesions induced by oxidized cellulose haemostatic agents. In all cases, oxidized cellulose was seen as acellular, slightly laminated inorganic elongated fragments, fibrillar fragments and a gel-like material resembling colloid and, in various proportions, granulomatous reaction with associated multinucleated giant cells [8,9].

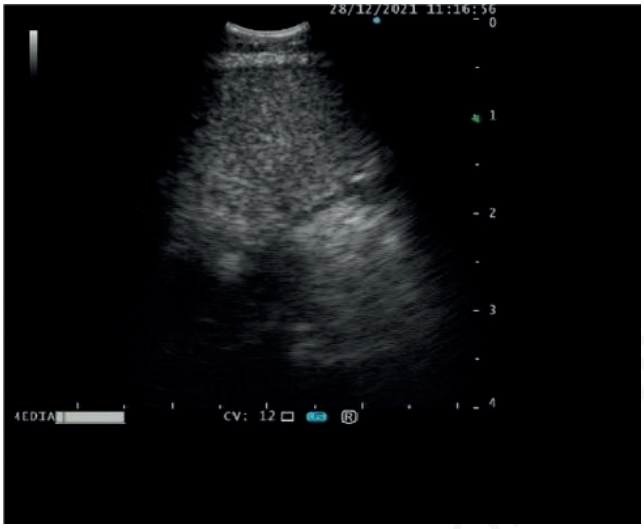

Figure 2. Right paratracheal lymph node.

EBUS-TBNA is a minimally invasive diagnostic technique for peritracheal and peribronchial lymph nodes or masses, and it identifies the puncture site through real-time ultrasound guidance to make accurate sampling from lesions and cytological and histological diagnosis. The sensitivity of EBUS-TBNA is 88-93% and the specificity is 100% in lymph node staging of lung cancer [10]; although several large-scale studies have found no complications associated with EBUS-TBNA [11], infectious complications have emerged as a problem with the increasing use of this procedure. In a Japanese survey, the frequency of infectious complications was reported to be 0.19%. In particular, mediastinitis after EBUS-TBNA was 0.10% of cases [12].

Mediastinitis is an infectious complication due to extension of adjacent disease, hematogenous spread, or direct contamination within the mediastinal space. Criteria for the diagnosis include a positive tissue culture, central chest pain, fever, sternal instability, purulent discharge, or positive blood cultures. The infection could be due to contamination of the bronchoscope's working channel during passage through the oropharynx, which is known to be rich in bacteria, and subsequent passage of the EBUS-TBNA needle through the working channel itself. These theories are supported by the isolation of organisms commonly found in the oropharynx [13,14]. The most common organisms associated with mediastinitis are methicillin-susceptible *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus*, gram-negative bacilli, coagulase-negative staphylococci, *Streptococci viridians* [15].

The presumed mechanism underlying the infectious complications is the introduction of oropharyngeal bacteria into deep mediastinal tissues during the transbronchial or transtracheal passage of the needle [16]. Alternative mechanisms for mediastinal infection that complicates EBUS-TBNA include inappropriate instrument sterilization, and contamination through contact with non-sterile surfaces such as slides during sample acquisition and processing between needle passes.

Treatment of EBUS-TBNA-associated mediastinitis commonly involves systemic antibiotic therapy alone; however, several reported cases required thoracotomy with thorax tube drainage supplemented by intravenous antibiotics [17,18].

The biopsy of necrotic structures has been suspected as a potential risk factor for post-procedural infection [19]. Necrosis is

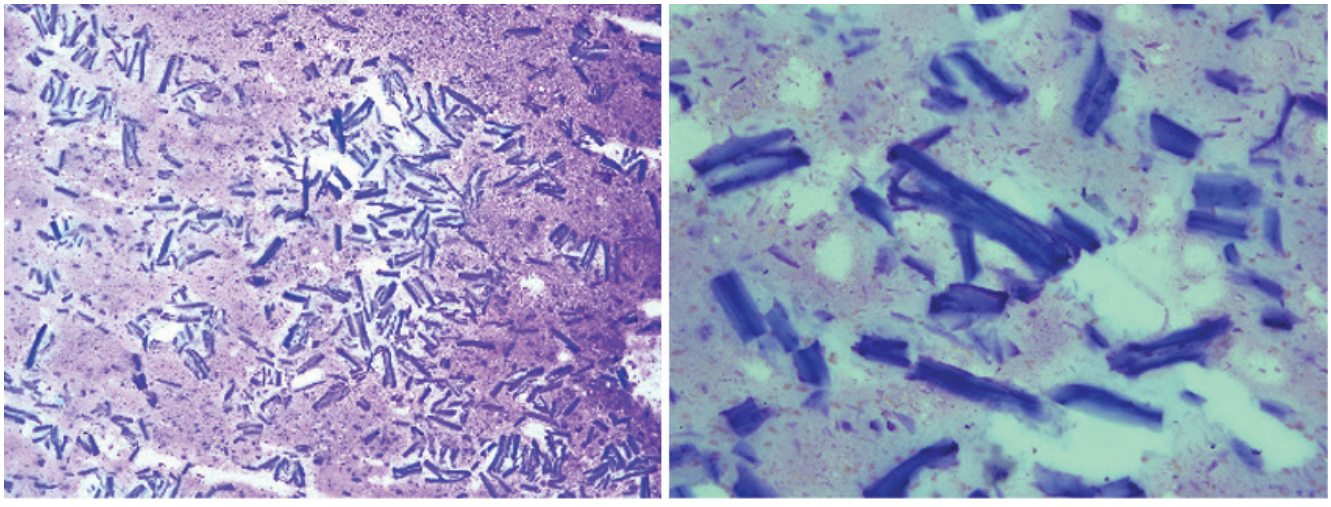

Figure 3. Slides of ROSE showing amorphous acellular material with quadrangular fragments.

related to the avascularity of the lesion, which provides an environment of decreased bacterial clearance and that is relatively shielded from the immune system. It is important to thoroughly examine the chest CT scans before performing the procedure in order, when possible, to avoid biopsy of necrotic lesions [14].

Since mediastinitis after EBUS-TBNA is rare, the diagnosis is sometimes difficult. However, mediastinitis should be considered in the differential diagnosis because of its potentially fatal course. Mild mediastinitis is treatable with antibiotics alone, whereas surgical intervention should be considered without delay in more serious cases [20].

Conclusions

In conclusion, ORC is commonly used in the surgical setting and is sometimes intentionally left *in situ* to promote hemostasis in the post-operative setting. Due to similarities in imaging features of post-operative complications, ORC can be mistaken for potentially serious entities including post-surgical infection and local recurrence of malignancy. Correlation with surgical operative notes, clinical data, and knowledge of the expected imaging appearance of this material, and those of the entities with which it can be confused, can potentially prevent unnecessary intervention. Surgery is the treatment of choice for drug intractable mediastinitis, such as the case reported here.

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