CASE REPORT

Multiple inflammatory nodules: a differential diagnosis of new pulmonary nodules in oncology patients

Atul B. Shinagare\textsuperscript{a,b}, Gina Cunto-Amestyc and Fiona M. Fennessya\textsuperscript{a,b}

\textsuperscript{a}Department of Imaging, Dana-Farber Cancer Institute, 44 Binney Street, Boston, MA 02115, USA; \textsuperscript{b}Department of Radiology, Brigham and Women’s Hospital, 75 Francis Street, Boston, MA 02115, USA; \textsuperscript{c}Department of Pathology, Brigham and Women’s Hospital, 75 Francis Street, Boston, MA 02115, USA

Corresponding address: Atul B. Shinagare, MD, 33 Pond Ave, Apt B 514, Brookline, MA 02445, USA.

Email: ashinagare@partners.org

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Abstract

New pulmonary nodules in an oncology patient are often considered metastatic unless proven otherwise. However, the possibility of an inflammatory cause needs to be considered in this setting. Clinicopathologic correlation is always needed in such cases to establish a diagnosis, especially before initiating a new treatment. The multiplicity of inflammatory nodules in this case, in the form of multiple pulmonary nodules and a spinal soft tissue mass, can be a considerable diagnostic challenge. The potential ramifications of not being familiar with inflammatory pseudotumors and not knowing when to suggest it involve unnecessary and incorrect patient treatment including chemotherapy, and may have medicolegal implications for the radiologist. Therefore all radiologists, especially those involved in oncologic imaging, need to be aware of this entity.

Keywords: Sarcoma; pulmonary nodules; inflammatory nodules.

History

A 70-year-old male shipyard worker with exposure to asbestos and lead, and a childhood history of polio, was being followed up for unclassified dermal sarcoma of upper back, which was resected with negative margins. A baseline staging computed tomography (CT) scan was unremarkable. A routine follow-up CT scan after 6 months showed multiple (approximately 20 in number) new nodules up to 2 cm in size, scattered in both lungs with a lower lobar predominance (Fig. 1). An enhancing soft tissue nodule measuring 2 cm in size was seen at the right T4–5 intervertebral foramen (Fig. 2). There was erosion of the adjacent lamina and pedicle. This nodule was protruding into the spinal canal without any significant mass effect on the spinal cord. There was no associated lymphadenopathy in chest or abdomen. The patient remained asymptomatic during this period, and inflammatory markers such as C-reactive protein were normal.

Because a metastatic process was the primary concern, a thoracoscopic wedge excision of two of the peripheral lung nodules from different lobes was performed. On microscopy, an admixture of lymphocytes, plasma cells and eosinophils were seen in the affected lung tissue. Focal areas of fibrosis were present in areas of inflamed lung (Fig. 3). Gram, fungal and acid fast stains were negative for microorganisms (not shown). The possibility of inflammatory pseudotumor was considered on the initial pathology report, but considering the absence of abundant myofibroblasts, a final pathologic diagnosis of chronic pneumonitis was given. In view of multiple nodules scattered throughout both lungs, and the concomitant presence of a mass at the intervertebral foramen, the final clinical and radiological impression was that of an inflammatory process resembling an inflammatory pseudotumor. No treatment was offered, and follow-up CT performed after 18 months showed resolution of the lung nodules (not shown). The intervertebral foramen lesion had also resolved, leaving behind only the persistent bony defect (Fig. 4).
Discussion

There is a broad differential for this case that needs to be considered. The presence of new pulmonary nodules and a soft tissue mass at the intervertebral foramen causing erosion of the lamina on the follow-up scan of a patient with history of malignancy obviously raises concern for metastatic disease. The differential diagnosis may also include an aggressive lymphoma, which can present with pulmonary nodules and extranodal soft tissue masses, but this type of presentation would be unlikely in the absence of lymphadenopathy. Multiple lung nodules may be seen in association with granulomatous diseases such as sarcoidosis. However, absence of interstitial thickening and hilar lymphadenopathy make sarcoidosis unlikely. As this patient had a long history of asbestos exposure, asbestosis is a possibility. However, asbestosis was excluded because of the absence of pleural plaques and interstitial lung disease. Inflammatory causes such as Wegener granulomatosis or rheumatoid arthritis were considered less likely because the patient was otherwise asymptomatic. Tuberculosis must also be considered, although it is unlikely in view of lack of symptomatology, and lack of associated findings such as mediastinal lymphadenopathy, parenchymal consolidations or cavities, and pleural effusions. In addition, spinal tubercular involvement usually starts in vertebral body, causes destruction of the intervertebral disc and is associated with a pre- or paravertebral soft tissue. A discrete solid nodule at the intervertebral foramen is therefore an unlikely presentation of tuberculosis.

Various inflammatory processes, including inflammatory pseudotumor as well as inflammatory reactions to infection, trauma or malignancies have overlapping pathogeneses and distinction can only be made with histopathology, at times requiring panels of immunostains.
in difficult cases. As the radiologic features of all these inflammatory entities are identical, in this review we focus on the most commonly known entity, the inflammatory pseudotumor.

Plasma cell granuloma or inflammatory pseudotumor has many synonyms: inflammatory myofibroblastic tumor, inflammatory myofibrohistiocytic proliferation, histiocytoma, xanthoma, fibroxanthoma, xanthogranuloma, fibrous xanthoma, xanthomatous pseudotumor, plasma cell–histiocytoma complex, plasmacytoma, and solitary mast cell granuloma.

Inflammatory pseudotumor can occur at any age, with over half the cases occurring in patients younger than 40 years. They are one of the most common lung tumors in the pediatric population. Inflammatory pseudotumor occurs in both genders and in all ethnic groups. Lung and orbit are the most common sites, although they can occur almost anywhere in the body, such as skull base, thyroid, liver, spine, spleen, lymph nodes and other tissues. The cause of this entity is unknown, and the pathogenesis is unclear. An association with infections such as mycobacteria, actinomycetes, Epstein–Barr virus or nocardia has been suggested; others have proposed an association

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**Figure 2** (a) Coronal reformatted CT image (window level 50, window width 350), showing an enhancing soft tissue mass at the intervertebral foramen (arrow), causing erosion of the adjacent portion of the lamina (curved arrow). (b) Axial CT image, bone window (window level 600, window width 3000), showing the defect caused by the mass at the intervertebral foramen (arrow), causing erosion of the adjacent pedicle and lamina (curved arrows).

**Figure 3** Low power photomicrograph stained with hematoxylin and eosin showing an admixture of lymphocytes, plasma cells and eosinophils in the affected lung tissue with focal areas of fibrosis in the areas of inflammation.

**Figure 4** Axial CT image (window level 50, window width 350) on the follow-up scan, at the same level as Fig. 2b. The previously detected intervertebral foramen mass has completely disappeared with a persistent bony defect (curved arrows).
with trauma or malignancy[7]. Some consider it to be a mesenchymal neoplasm with prominent secondary inflammation, especially in view of the potential for aggressive behavior[4–6]. Histologically, inflammatory pseudotumor consists of a variably dense polymorphic infiltrate of lymphocytes, plasma cells, histiocytes, and occasional eosinophils on a background of spindle cells or myofibroblasts arranged in short fascicles with a whorled architecture. The inflammatory infiltrate may be dense enough to obscure the underlying spindle cells. Three predominant histologic types are known: fibrous histiocytic pattern, which is the most common type and is characterized by spindle-shaped myofibroblasts arranged in whorls; an organizing pneumonia pattern, which is characterized by parenchymal infiltrate of mononuclear cells, histiocytes and fibroblasts and airways filled with histiocytes and fibroblasts; and the least common lymphohistiocytic pattern, which is characterized by lymphocytes and plasma cell infiltration with minimal fibrous connective tissue[4].

Pulmonary manifestations may include cough, dyspnea, chest pain, hemoptysis and some patients may have an increased sedimentation rate, anemia or thrombocytosis. However, most patients are asymptomatic[8]. The imaging appearance of inflammatory pseudotumor is non-specific and reliable differentiation from other causes of pulmonary nodules is not possible based on radiological features. Inflammatory pseudotumor is commonly first detected on a chest radiograph, which usually shows a solitary, well-circumscribed lobulated mass or an ill-defined, consolidative opacity[9]. Multiple nodules may be seen in 5% of cases[9]. There is a predilection for the lower lobes[4]. Most are parenchymal (85%); however endobronchial (10%) and endotracheal (4%) lesions may be seen[3]. The appearance on CT is variable, usually seen as a heterogeneous enhancing mass or multiple lung nodules. Magnetic resonance images usually have a high signal intensity on T1-weighted images[4]. In a report of 28 cases of pulmonary inflammatory pseudotumor, calcification was seen in 18% of cases, and cavitation was present in 11% of cases[3].

The clinical course of the inflammatory pseudotumor is usually benign. Treatment is required only to relieve its local effects. Complete surgical resection with open thoracotomy is usually the preferred treatment, especially with solitary and large tumors. Other treatment options include steroid treatment, rigid bronchoscopic removal or observation[3]. Radiotherapy and chemotherapy have also been tried in some cases[10]. Rare cases show a recurrence or metastases[11]. Occasional cases showing spontaneous regression[12,13] have also been reported.

This case represents a rare, but very important differential that needs to be considered in oncology patients with new pulmonary nodules. The potential ramifications of not being familiar with inflammatory pseudotumors and not knowing when to suggest it are vast, both for the patient and the radiologist. Therefore this disease entity is one that all radiologists interpreting imaging studies on cancer patients need to be aware of.

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