Case Report

Nodular pulmonary amyloidosis and obvious ossification due to primary pulmonary MALT lymphoma with extensive plasmacytic differentiation: Report of a rare case and review of the literature

Hua Xiang¹, Zuqun Wu², Zhaoming Wang¹, Hongtian Yao¹

¹Department of Pathology, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, Zhejiang Province, China; ²Department of Respiratory Medicine, The Second Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310009, Zhejiang Province, China

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Abstract: Localized (primary) pulmonary amyloidosis associated with pulmonary low-grade B cell lymphoma is rarely occurred. Here we report an unusual case of nodular pulmonary amyloidosis and obvious ossification due to primary pulmonary mucosa-associated lymphoid tissue (MALT) lymphoma with extensive plasmacytic differentiation in a 59-year-old man; moreover, two bronchial lymph nodes were involved histologically. The patient underwent a left lower lobectomy along with mediastinal lymphadenectomy. He received no adjuvant therapy and the postoperative course was uneventful within the 14 months follow-up period after his initial diagnosis.

Keywords: Nodular pulmonary amyloidosis, MALT lymphoma, ossification

Introduction

Most primary pulmonary lymphomas derive from the bronchus-associated lymphoid tissue and have a B-cell phenotype [1, 2]. These lymphomas may contain amyloid deposits, but this finding is rare, occurring in less than 1% of cases [3].

Herein, we report an extremely rare case of nodular pulmonary amyloidosis and obvious ossification due to primary pulmonary MALT lymphoma with extensive plasmacytic differentiation; moreover, two bronchial lymph nodes were involved histologically. The patient had no obvious symptoms at the time of diagnosis.

Clinical history

A 59-year-old man was informed of the presence of abnormal pulmonary shadow during a physical examination in 2011. Since he was asymptomatic, he was told to follow up chest radiography and computerized tomography (CT) twice a year. In 2013, the abnormal shadow in the left lower lung became larger, so he was referred to the First Affiliated Hospital, College of Medicine, Zhejiang University for examination and treatment. Chest computed tomography scan revealed an irregular shape and well-defined solid mass measuring 9.5 × 6.6 cm at the left lower lobe of lung, with hilar and mediastinal lymph nodes swelling (Figure 1). The diagnosis upon admission was pulmonary soft tissue tumor; the most likely was primary pulmonary chondroma.

No abnormal clinical manifestations were present during the course of disease. All of his laboratory data were within the normal ranges. Bronchoscopic brushing cytology and bronchoalveolar lavage fluid thinprep cytologic test (TCT) were performed, and no tumor cell was found. He had no history of tumor, chronic inflammatory diseases, autoimmune disease or immunodeficiency. The patient underwent a left lower lobectomy along with mediastinal lymphadenectomy. He refused postoperative adjuvant chemotherapy, and there was no recurrence or metastasis been found within the 14 months follow-up period after his initial diagnosis.
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Methods

The resection specimen was fixed in 10% buffered formalin and routinely processed to paraffin wax. Serial sections were stained with hematoxylin and eosin. Immunohistochemistry was performed on 3 μm sections cut from paraffin blocks using avidin-biotin-complex immunoperoxidase technique and the following antibodies: CD20, CD79a, bcl-2, CD138, CD43, CD3, CD5, CD23, CD10, CD21, cyclinD1, bcl-6, kappa and lambda light chain. The diagnosis of amyloid deposition was made based on positive Congo red staining of tissue section.

Pathologic findings

Grossly, the radical lobectomy specimen contained a solid and firm, gray and grayish green mass, measuring 9.5 × 9 × 6.5 cm, and the tumor was confined within the left lower lung (Figure 2A). Hilar and mediastinal lymph nodes were enlarged, and the cut surface of two of which was gray in color (Figure 2B).

Microscopically, extensive eosinophilic amorphous material deposition and metaplastic ossification dominated the lesion (Figure 3A, 3B), accompanied by a granulomatous reaction. Focal aggregates of lymphocytes with extensive plasmacytic differentiation presented within and at the periphery of the nodule, and reactive lymphoid follicles with germinal centers were formed (Figure 3C, 3D). At low magnification, the nodule was well circumscribed; however, pleural infiltration and lymphatic tracking with the mononuclear infiltrate cuffing pulmonary veins and lymphatics were observed (Figure 3E, 3F). The lymphoplasmacytic infiltration was intense and lacked a gradient from the center of the nodular lesion to its periphery (Figure 3G). In some areas, these cells infiltrated the pulmonary bronchiolar epithelium and formed lymphoepithelial complexes (Figure 3H). Amyloid deposits were seen within the walls of blood vessels. Moreover, extensive amyloid deposition, with neoplastic lymphoplasmacytic aggregated at the periphery, was also observed in two bronchial lymph nodes (Figure 3I).

In immunohistochemical studies, these cells were positive for CD20, CD79a, bcl-2, CD138, lambda light chain, and focally positive for CD43, but negative for CD3, CD5, CD23, CD10, CD21, cyclinD1, bcl-6 and kappa light chain (Figure 4A-H). Aberrant antigen expression of CD20/CD43 (coexpression of CD20 and CD43 by lymphocytes) was observed. In addition, the diagnosis of extensive amyloid protein deposition was made based on positive Congo red staining (Figure 4I).

Discussion

Mucosa-associated lymphoid-tissue lymphoma (MALT), also known as marginal-zone lymphoma, is the most frequent form of primary pulmonary lymphoma [4]. MALT lymphoma is rare, composing less than 1% of all primary lung malignancies [5]. The average age of onset is 50-60 years (range 12-79 y). Most patients are asymptomatic at the time lymphoma been diagnosed, although cough, dyspnea, hemoptysis, and chest pain may occur. Majority of patients are identified by incidental findings on radiography. Although MALT lymphomas are often described in association with autoimmune disorders, most commonly Sjögren’s syndrome, they may also develop in a patient with no pre-existing condition [6-9]. The present case met criteria for primary pulmonary lymphoma defined by Stalzstein as a tumor that “originally involved only the lung, or the lung and its regional lymph nodes, and in which there is no evidence of dissemination of the tumor for at least 3 months after the diagnosis is established [10]."
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Figure 2. A. The tumor was solid and firm, confined within the left lower lung, the colour of cut surface was gray and grayish green. B. The cut surface of two bronchial lymph nodes was gray in color.

Figure 3. Histologic findings. A. Extensive eosinophilic amorphous material deposition. B. Obvious metaplastic ossification accompanied by a granulomatous reaction. C. Focal aggregates of lymphocytes with extensive plasmacytic differentiation. D. Reactive lymphoid follicles with germinal centers. E. Lymphatic tracking. F. Pleural infiltration by neoplastic lymphocytes. G. The lymphoid infiltrate was intense and lacked a gradient from the center of the nodular lesion to its periphery. H. Lymphoepithelial lesion was found in a part of the bronchiolar epithelium. I. Extensive amyloid deposition, with neoplastic lymphoplasmacytic aggregated at the periphery was observed in bronchial lymph nodes. (A, B, D, E, G and I: × 100; C, F and H: × 400).
Amyloidosis involving the lung shows three main histologic presentations that are described as nodular pulmonary amyloidosis (NPA), tracheobronchial amyloidosis and diffuse alveolar septal amyloidosis [11, 12]. In some instances, such nodules may also relate to preexisting chronic inflammatory conditions or may be associated with autoimmune conditions such as Sjögren's syndrome. The majority of NPA relate to an underlying lymphoplasmacytic neoplasm in the spectrum of MALT lymphoma has been verified in a few reported cases [8, 13-18]. In our patient, there was no evidence of extrapulmonary organ involvement with amyloidosis. Moreover, findings on blood and urine chemical analyses, including serum immunoelectrophoresis for light chains, were negative, consistent with the diagnosis of primary (localized) pulmonary amyloidosis.

Nodular amyloidomas (NA) of the lung are non-neoplastic inflammatory nodules containing eosinophilic amyloid deposits and a reactive lymphoplasmacytic infiltrate. In some instances, the extensive amyloid deposits may obscure an underlying low-grade malignant lymphomas (ML), and it is in this group that morphologic confusion with NA occurs. Studies have found that NA can be separated from ML utilizing both histologic and immunohistochemical features [3]. Key discriminating morphologic features between the two entities included lymphatic tracking of the cellular infiltrate, pleural infiltration, sheet-like masses of plasma cells and

Figure 4. Histochemical and immunohistochemical findings. The Lymphoma cells were positive for CD20 (A), CD79a (B), bcl-2 (C), CD138 (D), lambda light chain (E), CD43 (F), and negative for CD3 (G) and kappa light chain (H); Extensive amyloid protein deposition was confirmed by Congo red staining (I). (A-F, H: × 400; G and I: × 200).
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reactive follicles. Lesional circumscription, vascular and bronchial destruction, lymphoepithelial lesions, and granulomas were not helpful discriminators. At low magnification, all NA demonstrated well circumscribed masses of dense amorphous eosinophilic material with the histochemical and tinctorial properties of amyloid. The central mass of amyloid like material was relatively paucicellular, with a predominant mononuclear infiltrate present at the periphery of the lesion; Plasma cells were present, but a sheet-like distribution of plasma cells (greater than 20 cells in aggregate) was not observed. In addition, no pleural infiltration was observed. While patients with low-grade ML tended to have intense lymphoid infiltrates that did not show a significant intensity gradient from the center of the mass to its periphery, and tended to demonstrate lymphatic tracking at the edge of the amyloid mass, with the mononuclear infiltrate cuffing pulmonary veins and lymphatics; moreover, there was often seen a sheet-like distribution of uniform plasmacytic elements forming broad sheets. Germinal centers were more often associated with ML than with NA. Immunohistochemical features indicating a dominant CD20 (+), CD79a (+) B-cell population, light chain restriction, and aberrant antigen expression of CD20/CD43 (coexpression of CD20 and CD43 by lymphocytes) were helpful discriminators and provided supports for the diagnosis of ML.

Little study on treatment of primary pulmonary MALT lymphoma is available and consensus on its treatment is also absent. Some authors advocate a watch-and-wait policy, given the disease’s indolence [19]. Troch et al. observed 11 patients with pulmonary MALT lymphoma that were not treated immediately and found signs of spontaneous tumor regression in six patients [20]. In general, surgical resection is reserved for localized tumors, and chemotherapy is given for bilateral or diffuse involvement. The prognosis of primary pulmonary MALT lymphoma is generally favorable in most cases, with 5-year survival rate of more than 80% and median survival time of more than 10 years [21]. Some case reports have demonstrated that adjuvant chemotherapy is not related to prognosis in MALT lymphoma [22]. The present case received no adjuvant therapy and the postoperative course was uneventful, though two bronchial lymph nodes were involved histo-

logically. Recently, Wang et al reported that for patients with confined lesions for which conventional biopsy cannot be performed, surgical excision plays an important role in clarifying the diagnosis and obtaining good therapeutic results and a good prognosis [23].

In summary, pulmonary MALT lymphoma may be associated with localized amyloid deposition and should be discriminated from localized pulmonary amyloidosis. The histologic and immunohistochemical features of the current case are in line with those reported in medical literature. Mika et al reported that localized amyloidosis associated with a pulmonary MALT lymphoma seems to have a better prognosis than a disseminated amyloidosis [24]. Because of the rarity of the case reported, the pathogenesis of the association between pulmonary MALT lymphoma and localized amyloidosis remains unknown and the therapeutic method is controversial. The clinical behavior and treatment of this unique malignant neoplasm require further studies on more cases.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Zuqun Wu, Department of Respiratory Medicine, The Second Affiliated Hospital, College of Medicine, Zhejiang University, 88 Jiefang Road, Hangzhou 310009, Zhejiang Province, China. Tel: +86-571-87783552; Fax: +86-571-87783552; E-mail: chzewzq@163.com

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