Int J Clin Exp Pathol 2015;8(6):7482-7487
www.ijcep.com /ISSN:1936-2625/IJCEP0008998

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 Xiang[1], Zuqun Wu[2], Zhaoming Wang[1], Hongtian Yao[1]

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

Received April 11, 2015; Accepted May 27, 2015; Epub June 1, 2015; Published June 15, 2015

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.

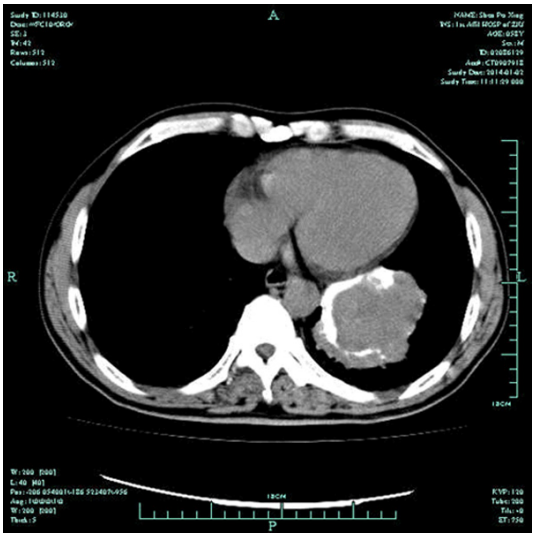

Figure 1. Chest computed tomography scan revealed an irregular solid mass with different density and marginal ossification at the left lower lobe of lung.

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, bcl-6, CyclinD1, Ki-67, 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 sold 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 preexisting 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]".

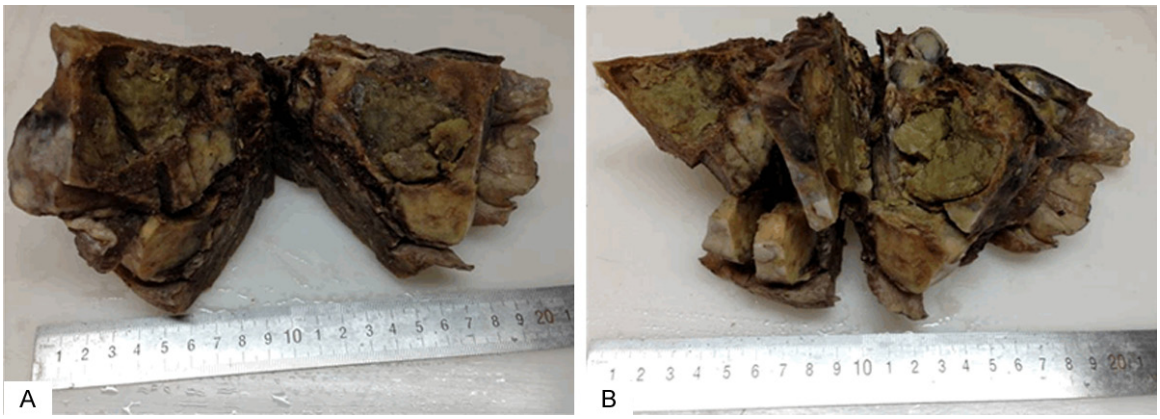

Figure 2. A. The tumor was solid and firm, confined within the left lower lung, the colour of cut surface was gray and grayish green. B. The cut surface of two bronchial lymph nodes was gray in color.

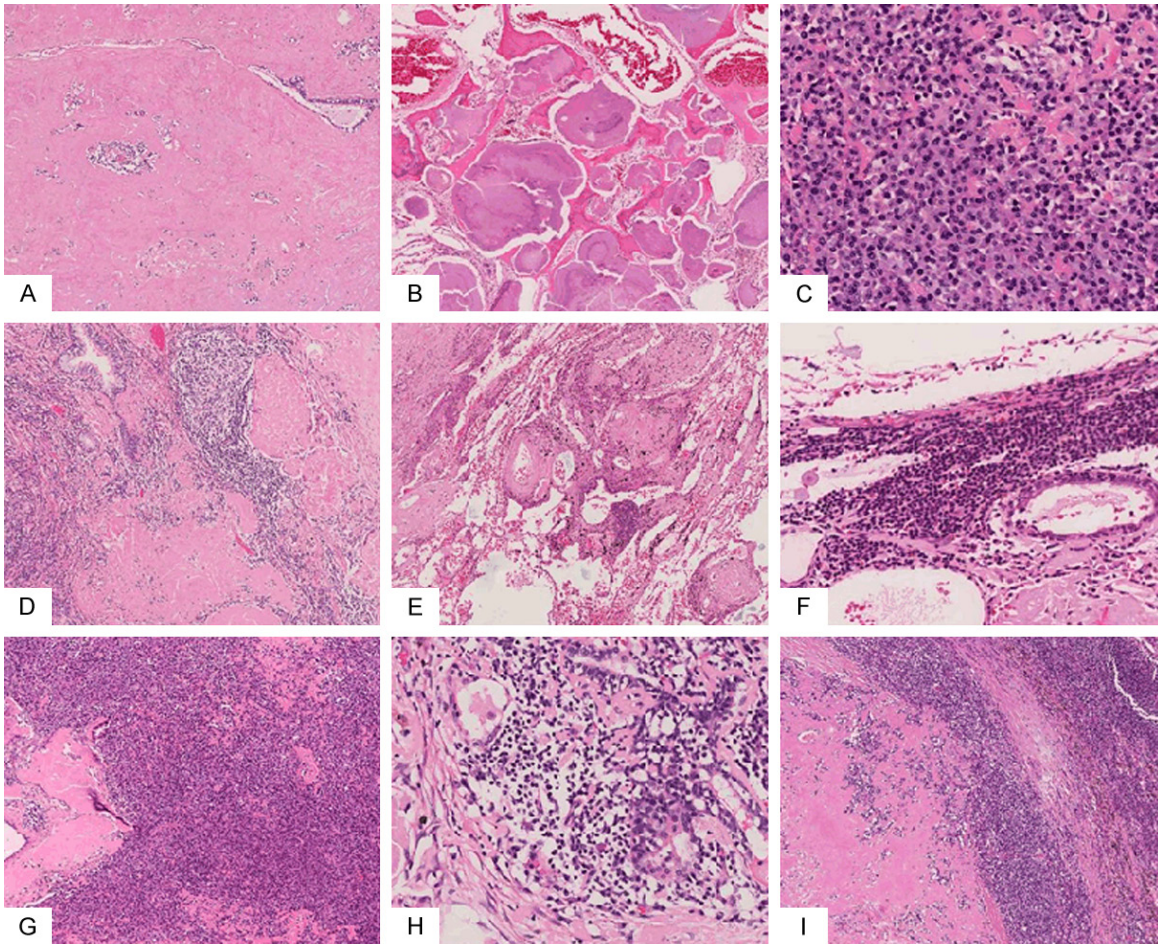

Figure 3. Histologic findings. A. Extensive eosinophilic amorphous material deposition. B. Obvious metaplastic ossification accompanied by a granulomatous reaction. C. Focal aggregates of lymphocytes with extensive plasmacytic differentiation. D. Reactive lymphoid follicles with germinal centers. E. 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).

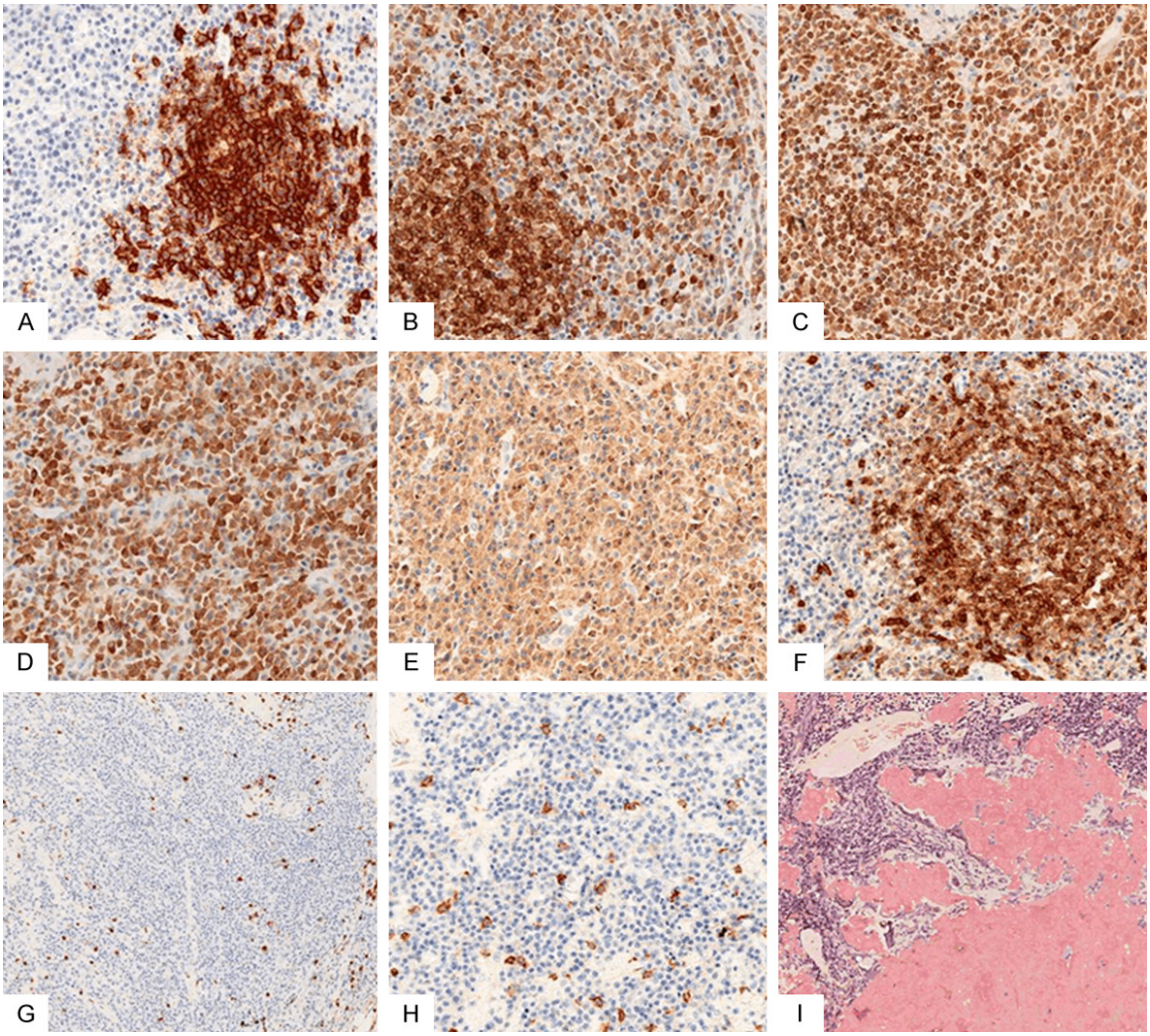

Figure 4. Histochemical and immunohistochemical findings. The Lymphoma cells were positive for CD20 (A), CD79a (B), bcl-2 (C), CD138 (D), lambda light chain (E), CD43 (F), and negative for CD3 (G) and kappa light chain (H); Extensive amyloid protein deposition was confirmed by Congo red staining (I). (A-F, H: × 400; G and I: × 200).

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

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 histologically. 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. Mlika 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.

Acknowledgements

This study was supported by the grants from Natural Science Foundation of Zhejiang Province, China (No. Y2110146).

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

References

[1] Li G, Hansmann ML, Zwingers T, Lennert K. Primary lymphomas of the lung: morphological, immunohistochemical and clinical features. Histopathology 1990; 16: 519-531.

[2] Herbert A, Wright DH, Isaacson PG, Smith JL. Primary malignant lymphoma of the lung: histopathologic and immunologic evaluation of nine cases. Hum Pathol 1984; 15: 415-522.

[3] Dacic S, Colby TV, Yousem SA. Nodular amyloidoma and primary pulmonary lymphoma with amyloid production: a differential diagnostic problem. Mod Pathol 2000; 13: 934-940.

[4] Cadranel J, Wislez M, Antoine M. Primary pulmonary lymphoma. Eur Respir J 2002; 20: 750-762.
[5] Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. Cancer 1972; 29: 252-260.
[6] Kurtin PJ, Myers JL, Adlakha H, Strickler JG, Lohse C, Pankratz VS, Inwards DJ. Pathologic and clinical features of primary pulmonary extranodal marginal zone B-cell lymphoma of MALT type. Am J Surg Pathol 2001; 25: 997-1008.
[7] Bégueret H, Vergier B, Parrens M, Lehours P, Laurent F, Vernejoux JM, Dubus P, Velly JF, Mégraud F, Taytard A, Merlio JP, de Mascarel A. Primary Lung Small B-Cell Lymphoma versus Lymphoid Hyperplasia: Evaluation of Diagnostic Criteria in 26 Cases. Am J Surg Pathol 2002; 26: 76-81.
[8] Nakamura N, Yamada G, Itoh T, Suzuki A, Morita-Ichimura S, Teramoto S, Shijubo N, Koba H, Satoh M, Abe S. Pulmonary MALT lymphoma with amyloid production in a patient with primary Sjögren's syndrome. Intern Med 2002; 41: 309-311.
[9] Papiris SA, Kalomenidis I, Malagari K, Kapotsis GE, Harhalakis N, Manali ED, Rontogianni D, Roussos C, Moutsopoulos HM. Extranodal marginal zone B-cell lymphoma of the lung in Sjögren's syndrome patients: reappraisal of clinical, radiological, and pathology findings. Respir Med 2007; 101: 84-92.
[10] Saltzstein SL. Pulmonary malignant lymphomas and pseudolymphomas: classification, therapy, and prognosis. Cancer 1963; 16: 928-955.
[11] Utz JP, Swensen SJ, Gertz MA. Pulmonary amyloidosis. The Mayo Clinic experience from 1980 to 1993. Ann Intern Med 1996; 124: 407-413.
[12] Howard ME, Ireton J, Daniels F, Langton D, Manolitsas ND, Fogarty P, McDonald CF. Pulmonary presentations of amyloidosis. Respirology 2001; 6: 61-64.
[13] Lim JK, Lacy MQ, Kurtin PJ, Kyle RA, Gertz MA. Pulmonary marginal zone lymphoma of MALT type as a cause of localised pulmonary amyloidosis. J Clin Pathol 2001; 54: 642-646.
[14] Wieker K, Röcken C, Koenigsmann M, Roessner A, Franke A. Pulmonary low-grade MALT-lymphoma associated with localized pulmonary amyloidosis. A case report. Amyloid 2002; 9: 190-193.
[15] Kawashima T, Nishimura H, Akiyama H, Hirai K, Yamagishi S, Okada D, Kinoshita H, Enomoto Y, Okamoto J, Nakajima Y, Takeuchi S, Iijima Y, Furuhata K, Nakayama K, Izumo T, Koizumi K, Shimizu K. Primary pulmonary mucosa-associated lymphoid tissue lymphoma combined with idiopathic thrombocytopenic purpura and amyloidoma in the lung. J Nippon Med Sch 2005; 72: 370-374.
[16] Georghiou GP, Boikov O, Vidne BA, Saute M. Primary pulmonary amyloidosis due to low-grade B cell lymphoma. Asian Cardiovasc Thorac Ann 2007; 15: 69-71.
[17] Satani T, Yokose T, Kaburagi T, Asato Y, Itabashi M, Amemiya R. Amyloid deposition in primary pulmonary marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue. Pathol Int 2007; 57: 746-750.
[18] Grogg KL, Aubry MC, Vrana JA, Theis JD, Dogan A. Nodular pulmonary amyloidosis is characterized by localized immunoglobulin deposition and is frequently associated with an indolent B-cell lymphoproliferative disorder. Am J Surg Pathol 2013; 37: 406-412.
[19] Cadranel J, Wislez M, Antoine M. Primary pulmonary lymphoma. Eur Respir J 2002; 20: 750-762.
[20] Troch M, Streubel B, Petkov V, Turetschek K, Chott A, Raderer M. Does MALT lymphoma of the lung require immediate treatment? An analysis of 11 untreated cases with long-term follow-up. Anticancer Res 2007; 27: 3633-3637.
[21] Addis BJ, Hyjek E, Isaacson PG. Primary pulmonary lymphoma: a re-appraisal of its histogenesis and its relationship to pseudolymphoma and lymphoid interstitial pneumonia. Histopathology 1988; 13: 1-17.
[22] Cavalli F, Isaacson PG, Gascoyne RD, Zucca E. MALT Lymphomas. Hematology Am Soc Hematol Educ Program 2001; 241-258.
[23] Wang B, Zhang C, Wang B, Zhang L. Comparisons of surgery and/or chemotherapy in the treatment of primary pulmonary mucosa-associated lymphoid tissue lymphoma. Ann Thorac Cardiovasc Surg 2015; 21: 109-113.
[24] Mlika M, Ayadi-Kaddour A, Marghli A, Ridène I, Maalej S, El Mezni F. A rare pulmonary lesion association. Rev Pneumol Clin 2012; 68: 303-306.