Castleman's disease presenting in the lungs: A report of two cases

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Abstract. Castleman's disease (CD) is a rare disease that most commonly occurs in the mediastinum. The lung is a rare site in which CD may occur. The current study reported 2 cases of CD localized in the lungs. Computed tomography imaging identified a high-density mass in the lungs of the two patients. Biopsy and pathological examinations indicated that one case presented features of two CD types (hyaline-vascular and plasma cell types), while the other case suffered from multicentric CD. The present study highlighted the typical clinical features of CD in the lungs. In addition, it is proposed that a diagnosis of CD should be considered for certain patients with masses in the lungs, and a biopsy should be performed to facilitate diagnosis and treatment.

Introduction

Castleman's disease (CD) is an uncommon lymphoproliferative disorder that was initially described by Dr Castleman in 1954 (1). An important pathological feature of CD is hyperplasia of lymphoid follicles, blood vessels and plasma cells (PCs). In addition, CD is one of the common causes of non-neoplastic lymphadenopathy (2,3). The majority (70%) of CD cases have been described in the chest; however, a number of cases have also been described in the abdomen, pelvis, skeletal muscle, head and neck (3,4). Extra-lymphatic sites of involvement may include the lungs, pancreas and parotid gland (3), although the lungs are a rare site in which CD may occur. The present study described two unusual cases presenting CD of the lungs and evaluated the imaging features, highlighting the clinical features of CD in the lungs. Thus, the current study may facilitate the diagnosis, differential diagnosis and treatment of patients with CD.

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Case report

Case 1. The study was approved by the Ethics Committee of Tongji University (Shanghai, China). Written informed consent was obtained from the patient. A 39-year-old female presented to Shanghai Pulmonary Hospital (Shanghai, China) in May 2013, with a mass in the lower lobes of the right lung that had been identified 2 months before. Computed tomography (CT) imaging clarified the presence of a high-density mass in the right lower lung. Compressed bronchiostenosis was identified in the outer and posterior basal segments during bronchoscopy and a lung biopsy revealed lymphocytes in the tissues. Therefore, the patient received anti-inflammatory treatment (cefuroxime, 0.75 g, 3 times/day) for 2 months; however, no evident change was observed in the lesion.

Physical examination identified no enlargement in superficial lymph nodes. Breath sounds were moderately rough and no dry or wet rales were noted. Results of routine laboratory tests and biochemical analysis of blood samples were within the normal ranges. Furthermore, rheumatoid, allergy, lung function and sputum examinations were normal. However, a conventional chest CT scan revealed a homogenous soft-tissue mass in the lower lobes of the right lung, multiple nodules in the two lungs and enlarged lymph nodes in the hilum and mediastinum (Fig. 1). No cysts or necrosis were identified, and latex agglutination and galactomannan tests were negative.

Open lung biopsy was performed and a 3.5x3.0x4.5-cm^3 mass was identified in the lower lobes of the right lung. In addition, numerous 0.3-cm nodes were distributed in the upper and lower lobes of both lungs. Histopathological examination identified lymphoid hyperplasia with numerous PCs and few blood vessels were present in the interfollicular areas of the lymph nodes (Fig. 3A). Subsequent histopathological examinations were used to determine that the patient had features of hyaline-vascular (HV)- and PC-type CD. The mass was excised. No evidence of recurrence was observed during the 6-months follow-up in November 2013.

Case 2. A 40-year-old male presented to the Shanghai Pulmonary Hospital on 2 February 2013, with the symptoms of coughing and shortness of breath. A physical examination revealed numerous hard, mobile lymph nodes in the neck and supraclavicular fossa. Breath sounds were moderately rough and no dry or wet rales were noted. Biochemical analysis of blood samples identified a globulin concentration of 85 g/l (normal range, 20-40 g/l). An abdominal ultrasound identified

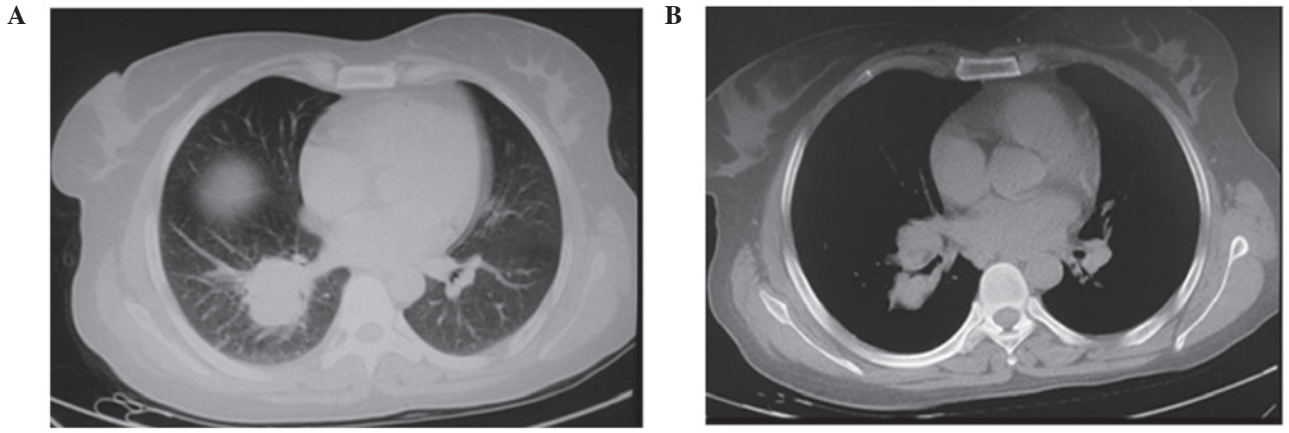

Figure 1. Conventional computed tomography scan of case 1, revealing a well-defined, homogenous mass at the lower lobes of right lungs, as well as enlarged nodes in the hilum and mediastinum. (A) Lung and (B) mediastinal window.

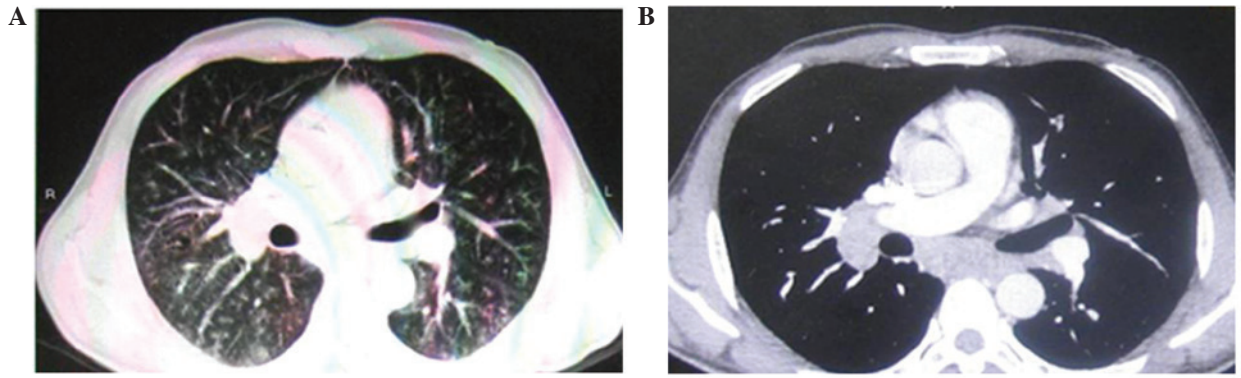

Figure 2. Contrast-enhanced computed tomography scan of case 2, revealing multiple nodules in both lungs, as well as the hilum and mediastinum. (A) Lung and (B) mediastinal window.

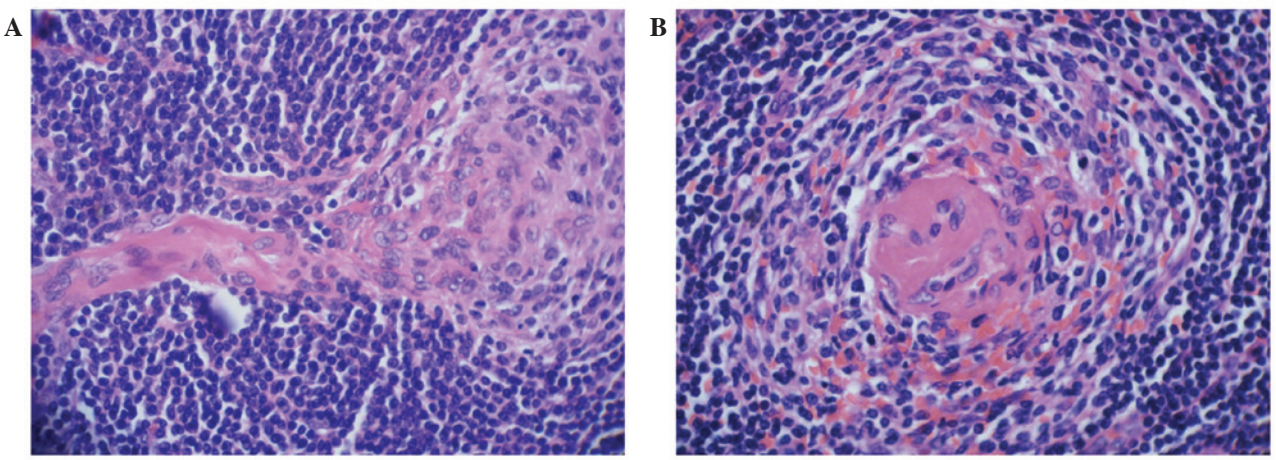

Figure 3. Typical histological features of Castleman's disease, demonstrating (A) numerous plasma cells and few blood vessels in the interfollicular areas in a 39-year-old female; and (B) numerous plasma cells in the interfollicular areas in a 40-year-old male (hematoxylin and eosin staining; magnification, x100).

hepatosplenomegaly and enlarged retroperitoneal lymph nodes. In addition, a contrast-enhanced CT scan revealed multiple nodules in the two lungs and enlarged lymph nodes in the hilum and mediastinum (Fig. 2). The mass was markedly and homogeneously enhanced relative to the muscles. No cysts or necrosis were identified. The patient underwent a lymph node biopsy to determine a definitive diagnosis. Pathological examination of the biopsy revealed lymphoid hyperplasia with numerous PCs in the interfollicular areas. Thus, a final histological diagnosis of PC-type multicentric CD was determined (Fig. 3B). Steroids were administered as the initial treatment strategy (prednisone, 40 mg/day). Subsequently, the sizes of

the lymph nodes in the neck, supraclavicular fossa, hilum and mediastinum reduced following 2 weeks of treatment; however, no evident changes were identified in the lung mass. CHOP chemotherapy (cyclophosphamide, hydroxydaunorubicin, Oncovin and prednisone) with Mabthera was proposed as a follow-up treatment in February 2014. However, the patient refused further treatment.

Discussion

CD is a rare disease characterized by hyperplasia of the lymphoid follicles (5). The current study reported 2 cases of CD localized in the lungs. Analysis of the 2 cases indicated that a diagnosis of CD should be considered when a mass is identified in the lungs. The findings of the present study may facilitate the diagnosis, differential diagnosis and treatment of patients with CD.

CD has two clinical subtypes: Multicentric and unicentric (localized) (6). The unicentric variant of CD is the most common type and is localized to a single lymph node chain or area (5). In adults, 90% of localized CD cases are HV-type and predominantly occur in young adults (3). The thorax (mediastinum) is the most common site of localized CD; however, a number of cases have been described in other locations, such as the abdomen and neck (3,4,7,8). The multicentric variants of CD are less common, accounting for only 10-20% of cases and commonly occurring in an older age population (3). Disseminated lymphadenopathies with systemic illness, such as fever, weight loss and abnormal laboratory results, are the common clinical features of multicentric CD. Furthermore, it is associated with POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M protein and skin changes) (3). CD may also be classified into HV-type, PC-type and mixed-type CD, according to its histological features (6). HV-type is characterized by hyperplasia and vascular proliferation in the interfollicular region, while PC-type is characterized by polyclonal PCs within the interfollicular zone (9). In the current study, case 1 suffered from mixed-type CD and case 2 presented PC-type CD. A previous study has demonstrated that the HV type was present in 75-90% of CD cases, the PC type in 10-25% of cases and the mixed type in 1-4% of cases (10). Multicentric CD is predominantly of PC type (2), which is consistent with the histological features of case 2 of the present study.

Radiological examinations, such as CT scans, can provide important information regarding CD tumors, including tumor site, characteristics and association with other tissues (3). The imaging features of CD are associated with its histological type, with previous reports demonstrating that different enhancement patterns of HV- and PC-type CT (4,11). Homogenous high enhancement is typically observed in HV-type CD due to the abundance of blood vessels. By contrast, PC-type CD typically exhibits absent or mild homogenous enhancement. However, a number of previous studies have described increased vascularity of PC-type CD on contrast-enhanced CT images (4,11). In the 2 cases in the present study, suffering from PC-type CD, homogenous enhancement was observed, which is consistent with previous studies (4,11).

The majority of localized CD cases can be cured by resection of the involved lymph nodes (3) and surgery has been proposed as the gold standard for the treatment of unicentric CD (12). For multicentric and aggressive CD, steroid treatment and/or systemic chemotherapy are required (3). However, for multicentric CD, surgical resection is rarely possible due to disseminated lymphadenopathy. Thus, a standard treatment course has yet to be established for patients with multicentric CD. In such cases, systemic therapy with steroids alone or in combination with other agents, including methotrexate or antiproliferative agents, is typically administered. In addition, it has been demonstrated that the prognosis of PC-type CD is worse compared with that of HV-type CD (3). Steroids were used in the present study in case 2, and the size of the lymph nodes were also reduced. However, no obvious changes were observed in the mass in lungs, which indicated that combined therapy with chemotherapy drugs are required.

In conclusion, CD is a rare lesion that is frequently misdiagnosed as lymphoma, thymoma, sarcoidosis or metastatic tumor, since non-specific symptoms or imaging findings are observed. The findings of the current study indicate that a diagnosis of CD should be considered for certain patients with masses in the lungs, particularly when accompanied by enlarged lymph nodes at distinct sites.

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