

Case Report

Pulmonary crystal-storing histiocytosis: a case report and literature review

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Received May 26, 2020; Accepted June 29, 2020; Epub August 1, 2020; Published August 15, 2020

Abstract: Crystal-storing histiocytosis is a rare non-neoplastic histiocytic proliferation disorder which can occur in many anatomic sites. Fewer than 20 cases of pulmonary crystal-storing histiocytosis have been reported, most of which were associated with clonal lymphoproliferative disorder. Herein we report the first case of pulmonary crystal-storing histiocytosis with underlying Sjögren syndrome.

Keywords: Crystal-storing histiocytosis, Sjögren syndrome, lymphoproliferative disorder

Introduction

Crystal-storing histiocytosis (CSH) is an uncommon form of non-neoplastic histiocytic proliferation disorder which can occur in many anatomic sites, but most often occurs in the head and neck [1]. Pulmonary crystal-storing histiocytosis is very rare, and fewer than 20 cases have been reported in the English-language medical literature to date [2]. CSH is frequently associated with underlying lymphoproliferative or plasma cell disorders, but the pathogenesis of this disease is still unclear. Herein we present a 60-year-old woman with pulmonary CSH without underlying lymphoid proliferative disorder but associated with the autoimmune disease Sjögren syndrome.

Case report

A 60-year-old woman with a decades-long history of Sjögren syndrome presented with persistent night cough and sputum for months. A chest computed tomography (CT) exam revealed a 1.5 × 1.1 cm soft tissue nodule with an irregular margin in the lower lobe of her left lung (**Figure 1**, arrow). The radiologic impression could not rule out the possibility of malignancy. The patient underwent a video-assisted thoracoscopic wedge resection of the lower lobe of the left lung.

The pathological examinations of the pulmonary nodule revealed aggregates and sheets of

epithelioid macrophages with small, round to ovoid, bland-looking but often eccentrically placed nuclei and inconspicuous nucleoli (**Figure 2**). The cytoplasm of the macrophages contained abundant plump, brightly eosinophilic crystal materials. The crystal morphology varied from fine needle-like striations to chunky, polygonally-shaped ones. Immunohistochemically, the crystal-storing macrophages expressed the macrophage markers CD68, CD163 (**Figure 3A, 3B**), but they were negative for the S-100 protein and for CD1a (not shown). The crystals were Congo red negative and did not display a green birefringency with polarized light (not shown). The immunohistochemical staining for immunoglobulin light chains revealed a clonal restriction of the κ -light chain and was almost absent of the λ -light chain (**Figure 3C, 3D**). An interstitial infiltration of the mature lymphocytes and some plasma cells was also noted. No cells indicating a diagnosis of malignancy were present in the nodule. The final diagnosis was pulmonary crystal-storing histiocytosis. The patient recovered well and showed no evidence of recurrence after a regular follow-up for three years to date.

Discussion

Crystal-storing histiocytosis (CSH) is a rare condition in which crystalline material accumulates in the cytoplasm of histiocytes. CSH can be classified as localized CSH, defined as affect-

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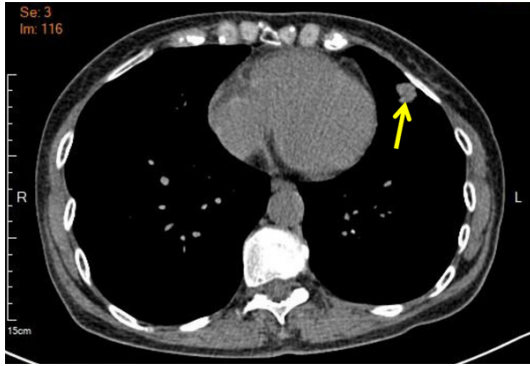


Figure 1. The CT image revealed a 1.5 cm soft tissue nodule with an irregular margin in the lower lobe of the left lung (yellow arrow).

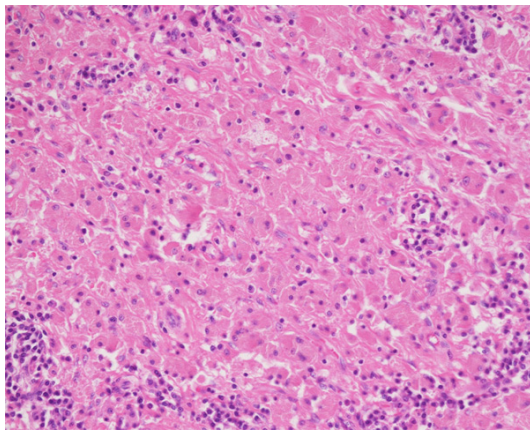


Figure 2. Aggregates and sheets of epithelioid macrophages with small, round to ovoid, bland-looking nuclei. Note the brightly eosinophilic crystal materials in the cytoplasm (H&E stain, 100x).

ing a single body site or organ, or defined as generalized disease with the involvement of two or more sites [1]. The common sites for localized CSH are the lungs, kidneys, bone marrow, orbit, oropharyngeal and sinonasal mucosa. Generalized CSH has been observed in virtually every organ of the body, with the most frequent involvement in the bone marrow, liver, lymph nodes, spleen, kidneys, and the gastrointestinal mucosa [1]. Importantly, nearly all CSH cases (over 90%) are associated with an underlying clonal lymphoproliferative or plasma cell disorder such as multiple myeloma, lymphoplasmacytic lymphoma, monoclonal gammopathy of unknown significance (MGUS) or B-cell lymphoma. In those CSH cases not associated with a clonal disorder, most of the cases are associated with chronic inflammation or autoimmune abnormality conditions such as

rheumatoid arthritis, Crohn's disease, or *Helicobacter pylori* gastritis [2]. In our case, the patient suffered from the autoimmune disease Sjögren syndrome that had not been reported before.

Histopathologically, CSH is characterized by sheets of epithelioid macrophages with bland, round-to-ovoid, often eccentrically located nuclei with small nucleoli. The cytoplasm contains brightly eosinophilic crystals. Immunohistochemically, the crystal-containing macrophages are invariably positive for CD68 but negative for the S100 protein, CD1a, Langerin, and cytokeratin. The crystals' morphology is variable, from fine needle to rhabdoid, chunky forms. In addition, the crystals are Congo red negative and non-birefringent. Interestingly, immunostaining for the immunoglobulin light chain in the crystals shows a clonal restriction with the κ -light chain in virtually all cases. The exact pathogenesis of CSH is not well understood, but the immunoglobulin structure alterations and aberrant folding are possible mechanisms [3, 4].

The differential diagnosis of pulmonary CSH includes a diverse group of histiocytic abnormalities occurring in the lungs [5]. For example, the accumulation of interstitial or alveolar macrophages containing pigment such as carbon pigments, hemosiderin, and silica crystals, may be confused with the crystal-containing macrophages of CSH. However, the lack of any brightly eosinophilic needles or polygonal-shaped crystals may distinguish the different diagnosis. In eosinophilic pneumonia or Churg-Strauss syndrome, there are many macrophages containing Charcot-Leyden crystals which may resemble the crystals in CSH. However, the abundant eosinophils in the background should provide clues to the correct diagnosis. Langerhans cell histiocytosis containing macrophage-like cells with abundant eosinophilic cytoplasm are also in the differential diagnosis. It can be distinguished by the presence of elongated or clefted nuclei and positive immunohistochemical staining for CD1a, S100 protein, and Langerin. Erdheim-Chester disease, a rare histiocytic disorder, is characterized by aggregates of bland-looking macrophages with abundant pale eosinophilic foamy cytoplasm. The cells are CD68 positive, CD1a negative and show variable staining with the S100 protein. Granular cell tumor is a benign neoplasm com-

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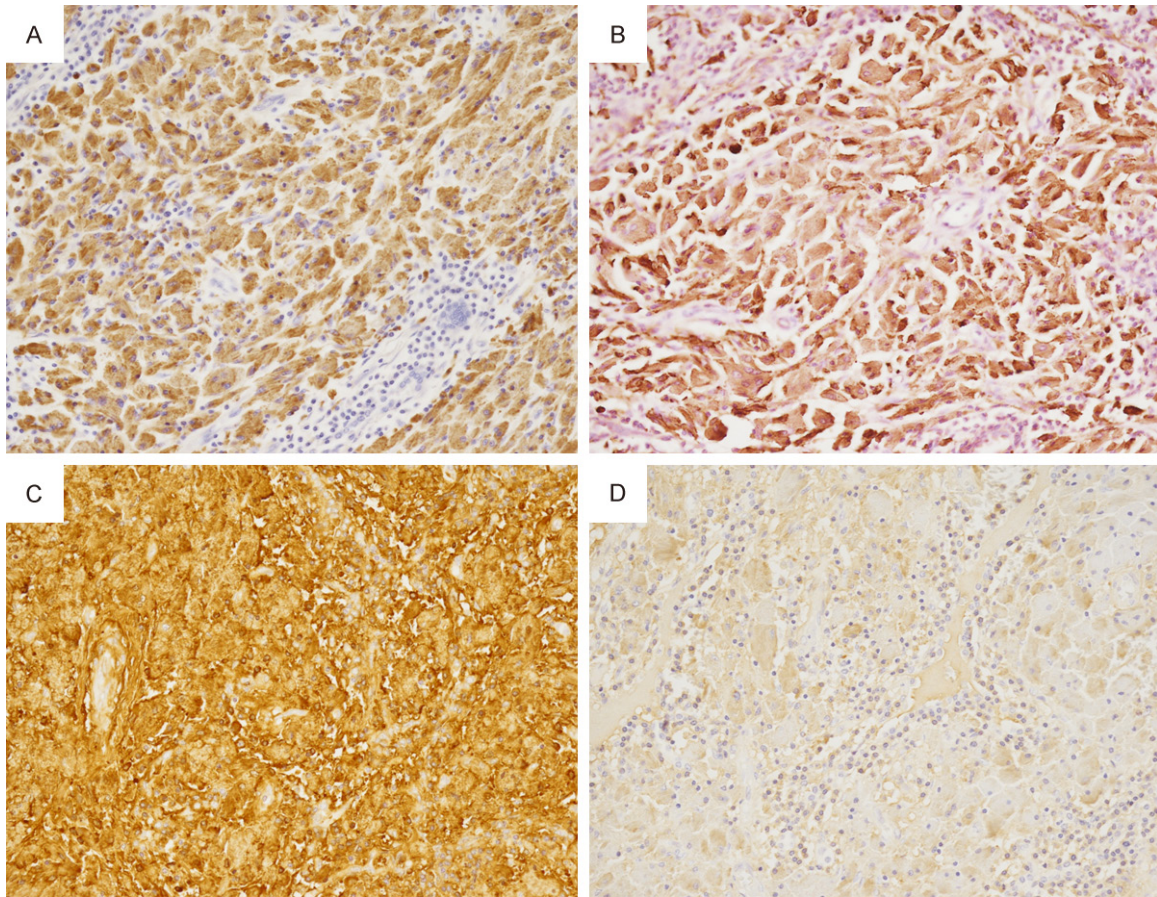


Figure 3. Immunohistochemical studies: (A) the crystal-storing macrophages express CD68 and (B) CD163. Staining for the immunoglobulin light chains revealed a clonal restriction of the κ -light chain (C), and was almost absent of the λ -light chain (D) (200x).

posed of cells with granular eosinophilic cytoplasm [6]. The tumor cells are usually S100 protein, CD68, neuron specific enolase, and CD56 positive but negative for GFAP, HMB-45, and CD1a. Pulmonary clear cell sugar tumor is another rare benign neoplasm which is composed of round to polygonal epithelioid cells with abundant clear to eosinophilic cytoplasm. The pulmonary clear cell sugar tumor belongs to the PEComa family, and these tumor cells are positive for HMB-45 and Melan-A but negative for CD68 [7]. Although most of the CSH patients have clonal lymphoproliferative disorders, a few patients suffer from autoimmune diseases such as rheumatoid arthritis and Crohn's disease. To our knowledge, this CSH patient who also had Sjögren syndrome was the first such case reported.

Albeit rare, pulmonary CSH should be considered in a differential diagnosis involving a prolif-

eration of macrophages with abundant eosinophilic cytoplasm. The presence of intracytoplasmic clonal immunoglobulin crystals along with the positive CD68 staining of the macrophage-lineage are key to the diagnosis. In addition, because generalized CSH is always accompanied by clonal lymphoproliferative disorders such as multiple myeloma or other autoimmune diseases, the need for a systemic evaluation should be stressed to rule out the possible generalized disease.

Disclosure of conflict of interest

None.

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