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CASE IMAGE

Crystal-storing histiocytosis and associated marginal zone lymphoma with extensive plasmacytic differentiation

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Key Clinical Message

Crystal-storing histiocytosis (CSH) is a non-neoplastic histiocytic proliferation that results from the intra-lysosomal accumulation of immunoglobulins as crystals. CSH is frequently associated with various B-cell lymphomas or plasma cell neoplasms. CSH can potentially obscure underlying lymphoproliferative neoplasms. This association should always be considered and the tissue should be carefully evaluated.

KEYWORDS

crystal-storing, histiocytosis, immunoglobulin, lymphoma

A 77-year-old man with a history of hypertension and dyslipidemia presented with left lateral cervical pain and swelling. He had no known drug allergies. There was no relevant family history. He had no risk factors for HIV, hepatitis B or C. Review of systems was otherwise unremarkable. He was not an active smoker and had occasional alcoholic drinks. In physical examination, he had an enlarged left tonsil highly suspicious of malignancy. A small left posterior cervical lymph node measuring approximately 1–2 cm was also palpable. No other cervical, axillary, or inguinal adenopathy was noted. There was no hepatosplenomegaly. A cervical and chest computed tomography (CT) scan revealed a 2.2 cm lobulated mass in the left lingular tonsil as well as multiple enlarged left cervical lymphadenopathy. Multiple lung nodules were also identified with an impression of metastatic disease. The biopsy from the tonsillar mass showed unremarkable surface squamous epithelium with submucosal replacement by sheets of crystal-laden histiocytes. There were extensive associated mature-appearing plasma cells, plasmacytoid lymphocytes and aggregates of small lymphocytes (Figure 1). In immunohistochemical analysis, atypical lymphocytes were positive for CD19, CD20, and BCL2 and negative for CD3, CD5, CD10, CD21, CD23,

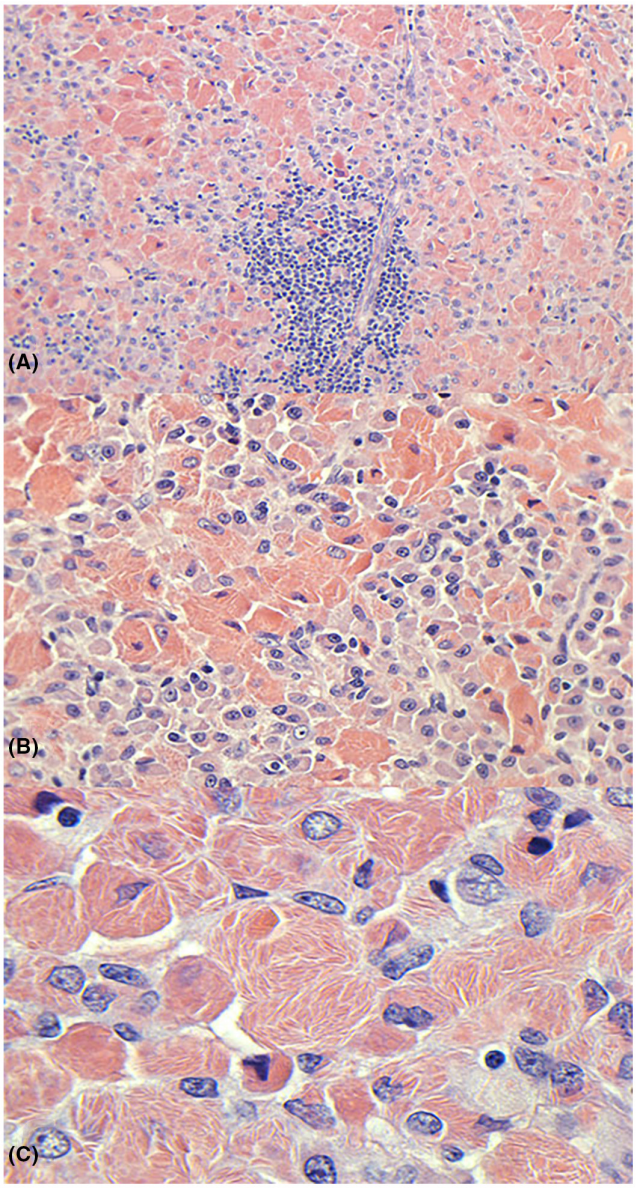

FIGURE 1 Hematoxylin and eosin staining shows sheets of pink staining histiocytes admixed with abundant mature appearing plasma cells and small lymphocytes including lymphoid aggregates (A, 20x; B, 40x; C, 100x).

BCL6, cyclin D1, and MUM-1. Plasma cells were positive for CD19, CD138, MUM-1, IgM, and IgK and negative for CD56, CD117, cyclin D1, IgA, IgG, and IgL (Figure 2). Plasmacytoid lymphocytes showed dual expression of CD20 and CD138 (dim). Histiocytes were positive for CD68 and CD163 and negative for CD1a and S100. Dim expression of Kappa immunoglobulin was noted in histiocytes. Desmin, factor XIIIa, Myf-4, and cytokeratin AE1/AE3 were negative. The proliferation rate evaluated by Ki-67 expression was approximately 1%–2%. In situ hybridization for EBV-encoded small RNA (EBER) was negative.

Diagnosis of extra-nodal marginal zone lymphoma (EN-MZL) with associated crystal-storing histiocytosis (CSH) was made.

CSH is a rare non-neoplastic histiocytic proliferation that results from the intra-lysosomal accumulation of immunoglobulins as crystals. There are localized and generalized forms of CSH, the former being more frequent. The main sites of disease are the head and neck, lung, kidney, bone marrow, and lymph nodes, although nearly any site can be involved. CSH has been reported to show a prominent association with lymphoproliferative or plasma cell disorder including lymphoplasmacytic lymphoma, marginal zone lymphoma, monoclonal gammopathy of undetermined significance, or multiple myeloma.[1] CSH is usually associated with immunoglobulin kappa light chain restriction without any association with a specific type of Ig heavy chain. Extensive involvement by CSH can potentially obscure the underlying neoplasm making the recognition of the neoplasm challenging.[2,3] While the prognosis of generalized forms of CSH is usually poor, in localized forms, the prognosis is variable depending upon the extent of tissue involved and the underlying condition of the patient. In general, the prognosis and overall survival in patients with localized CSH associated with marginal zone lymphoma are comparable to age and sex-matched patients with MZL without CSH.

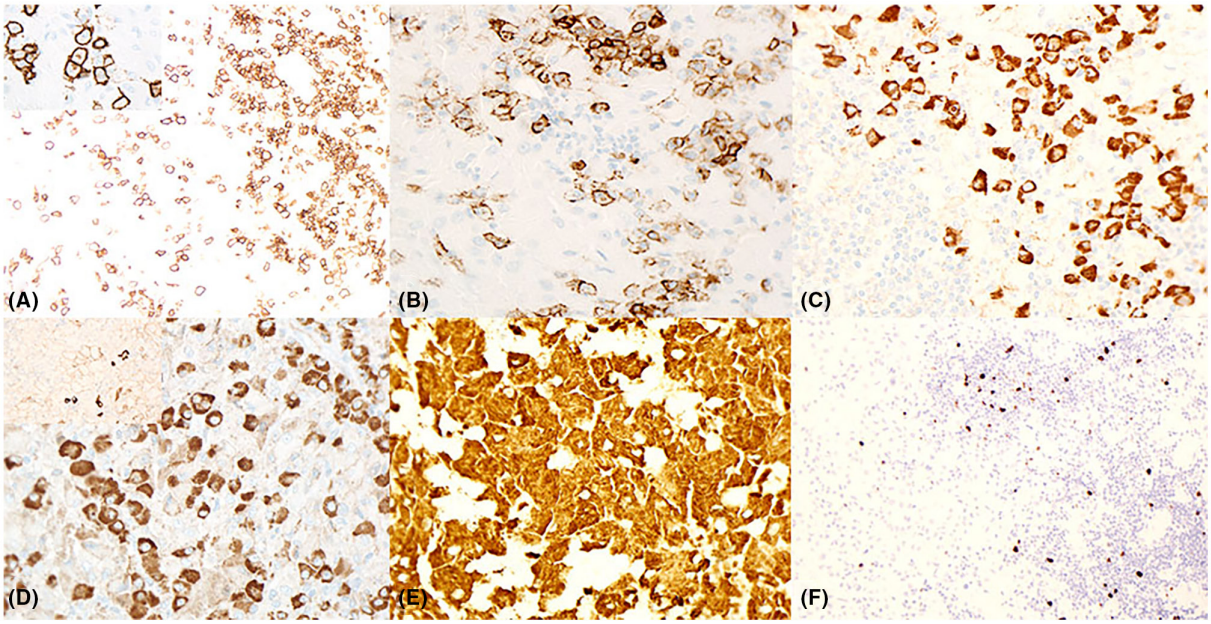

FIGURE 2 Immunohistochemical staining shows infiltrating B cells (A, CD20, 20x) including larger immunoblasts/plasmablasts (A inset, CD20, 100x) admixed with aggregates of plasma cells (B, CD138, 40x). Plasma cells are positive for IgM (C, 40x) and IgK (D, 40x) but not for IgL (D, inset, 40x). Histiocytes show strong positivity for CD68 (E, 40x) but not for CD1a or S-100 (not shown). The proliferation rate determined by Ki-67 was low (F, 20x).

AUTHOR CONTRIBUTIONS

Ayah Al-Qaderi: Conceptualization; data curation; formal analysis; writing – original draft; writing – review and editing. **Ali Sakhdari:** Conceptualization; data curation; formal analysis; investigation; supervision; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declared no conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The University Health Network guidelines for IRB (REB) mentioned that case studies that involve three or fewer patients do not require UHN REB review.

CONSENT

Based on the principles of publication of medical research involving human subjects, this manuscript does not provide any of the subject's identifying information. Therefore no written informed consent was obtained from the patient or the patient's parent/guardian.

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