Crystal storing histiocytosis of the tongue as the initial presentation of multiple myeloma

Syed Ali Khurram, PhD,a Allan McPhaden, FRCPath,b W. Stewart Hislop, FRCS,c and Keith D. Hunter, FRCPath,a Sheffield, Glasgow, and Kilmarnock, United Kingdom
UNIVERSITY OF SHEFFIELD, GLASGOW ROYAL INFIRMIARY, AND CROSSHOUSE HOSPITAL

Crystal-storing histiocytosis (CSH) is a rare consequence of abnormal accumulation of immunoglobulins which may arise in a number of different clinical scenarios. In this report, we describe the case of a male patient who presented with an apparently innocuous lesion on the dorsum of tongue which showed the typical features of CSH. Subsequent investigations revealed an associated plasmacytoma, and the patient developed further systemic lesions. The rarity of such lesions presents diagnostic difficulties, yet accurate diagnosis underpins the timely implementation of appropriate therapy. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:494-496)

A 67-year-old male patient presented to his local Oral and Maxillofacial Surgery Department regarding a lump on the posterior dorsum of the tongue. The asymptomatic lesion had been present for ~4 months with no alteration in size or appearance. Otherwise he was medically fit and well. Examination revealed a smooth, circular, and uniformly colored lump of ~8 mm in diameter involving the midline of the dorsum of the tongue. Excisional biopsy of the lesion was carried out under local anesthesia, with the clinical diagnosis of fibroepithelial hyperplasia.

MICROSCOPY
Histologic examination showed mildly hyperplastic and prominently keratinized stratified squamous epithelium overlying connective tissue containing a number of eosinophilic masses with a vague crystalline structure (Fig. 1, A). Most of these appeared to be present within cells, some of which were multinucleated. A mixed population of inflammatory cells, including plasma cells and small lymphoid cells (some of which had crenulated nuclei) were seen scattered between the globules. Histochemical analysis showed that the globules did not stain with either Sirius red or periodic acid–Schiff.

SPECIAL INVESTIGATIONS
Immunohistochemistry demonstrated strong cytoplasmic CD68 expression in most of the cells in the lesion, indicative of their histiocytic lineage (Fig. 1, B). This also demonstrated that most, if not all, of the crystalline globules within the lesion were within the cytoplasm of CD68-positive cells. Immunohistochemistry was negative for cytokeratins, TTF1 (thyroid transcription factor 1), thyroglobulin, desmin, myoglobin, and S100. CD138 and EMA (epithelial membrane antigen) positivity was seen in the plasma cell population, and hematolymphoid markers showed a scattered population with focal accumulations of CD3-positive T cells. The MIB1 proliferation fraction was <5%.

Electron microscopy of the tissue confirmed the intracellular location of the globules. The globules possessed a crystalline structure, but smaller discrete rhomboid-shaped crystals were also seen within the cytoplasm of cells devoid of the large globules (Fig. 1, C). The nature of the material was not evident on electron microscopy, but resembled that presented in previously published cases of crystal-storing histiocytosis (CSH).

Further immunohistochemistry conducted at this point showed extensive expression of IgG by the plasma cell population as well as in some of the large histiocytes, largely as a thin rim adjacent to the crystals. In situ hybridization for kappa and lambda immunoglobulin light chains showed that the plasma cells expressed only kappa light chain, indicating a monoclonal population (Fig. 1, D and E). At this point, the provisional diagnosis of a solitary plasmacytoma of the tongue was made, pending further investigations.

CLINICAL FOLLOW-UP
The patient initially experienced neither postoperative complications nor signs of recurrence, and the biopsy site...
healed satisfactorily. Further investigations, including blood and urine tests, were carried out to investigate the possibility of multiple myeloma which showed a slightly raised mean cell volume (MCV) and a raised erythrocyte sedimentation rate (ESR). Urine analysis did not demonstrate any Bence-Jones protein. Protein electrophoresis revealed no evidence of paraprotein band, although IgG levels were elevated (21 g/L). A bone marrow trephine showed only normal hemopoietic marrow with plasma cell numbers accounting for <5%. No abnormalities were seen on the computerized tomographic (CT) and magnetic resonance imaging scans in the head and neck region, although 2 tiny nodules measuring 3 mm were identified in the chest, the nature of which was uncertain. No evidence of abnormalities was detected on the skeletal survey.

Fig. 1. A, Hematoxylin-eosin–stained section showing eosinophilic globular deposits with a scattered associated infiltrate of immune cells (×40). B, Expression of CD68 demonstrates that the deposits are contained within the cytoplasm of macrophages (×40). C, Electron microscopy demonstrates the crystalline nature of the globular deposits and shows dispersed crystals within the cytoplasm of other cells. D, E, In situ hybridization for (D) kappa light chain and (E) lambda light chain confirms the monoclonal nature of the plasma cell infiltrate (×2).
In light of the investigations, a definitive diagnosis of an isolated plasmacytoma involving the dorsum of the tongue was made and local radiotherapy administered to the primary site in tongue.

However, within a few months of completion of the radiotherapy, the patient reported significant loss of appetite, weight loss, and general malaise with blood investigations showing a significant fall in hemoglobin and a sharp rise in the ESR and serum IgG. A repeat of the investigations showed a small level of paraprotein in peripheral blood and low-level Bence-Jones protein positivity. A CT scan showed a 10 × 2.7 cm paravertebral mass within the thorax, and CT-guided biopsy showed histology consistent with a plasmacytoma. Keeping in mind the aggressive nature of the lesion, the patient was started on bortezomib (Velcade) and dexamethasone, which resulted in a significant clinical improvement within a week.

**DISCUSSION**

Crystal-storing histiocytosis is a rare condition and has been most commonly described in relation to clonal lymphoplasmacytic disorders, such as multiple myeloma and lymphoplasmacytic lymphoma. Intracellular deposition of immunoglobulin crystals has been reported in a wide range of tissues, including lungs, gastrointestinal tract, skin, bone marrow, liver, and cervical lymph nodes, with, in some rare cases, no evidence of a lymphoproliferative disorder. CSH may involve multiple organs simultaneously; however, there are only 3 reports describing CSH in oral tissues, involving the parotid gland, nasopharynx and tongue.

In the present report, we describe the first report of a patient in whom CSH involving the dorsum of the tongue was the presenting lesion of a monoclonal plasma cell disorder. Furthermore, this lymphoplasmacytic neoplasmic disease subsequently progressed to multiple myeloma over a period of 1 year. Solitary plasmacytoma of the base of tongue is well established in the literature, but more commonly presents with a primarily cellular mass or with amyloidosis. The only previously reported case of massive crystal storing histiocytosis in the tongue was secondary to polyclonal hypergammaglobulinemia with no evidence of a lymphoplasmacytic neoplasm.

The histologic features presented difficulties in diagnosis and raised a number of differential diagnoses. The crystalline inclusions in CSH may be deposited in parallel arrays and mimic the histologic features of adult rhabdomyoma. Initial examination of the histologic features in the present case suggested a follicular pattern such as seen in thyroid gland. However, careful examination of the hematoxylin-eosin features reveals the intracellular nature of these inclusions. Nevertheless, it is important to exclude unusual presentations of skeletal muscle or thyroid lesions as part of the diagnostic process. The identification of eosinophilic crystalline inclusions in a diagnostic biopsy can be challenging, because immunohistochemistry can give equivocal and relatively nonspecific results. The use of electron microscopy in the present case provided a fuller description of the crystalline nature of these inclusions and aided in the process of resolving the differential diagnosis.

**REFERENCES**


Reprint requests:
Dr. Keith D. Hunter
Clinical Senior Lecturer in Oral Pathology
Oral and Maxillofacial Pathology
School of Clinical Dentistry
University of Sheffield
Claremont Crescent
Sheffield S10 2TA
United Kingdom
k.hunter@sheffield.ac.uk