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Extramedullary plasmacytoma of the submandibular gland

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Abstract
Extramedullary plasmacytoma in the submandibular region is rare and on initial evaluation must be distinguished from multiple myeloma. The diagnostic evaluation includes appropriate radiological and pathological studies including immunohistochemistry. We report a case of extramedullary plasmacytoma in the submandibular gland. A review of the literature suggests that it has a good prognosis, if multiple myeloma is excluded. This patient was treated by surgical excision followed by radiotherapy.

Key words: Plasmacytoma; Submandibular Gland; Multiple Myeloma

Introduction

Primary extramedullary plasmacytoma is a tumour of atypical neoplastic cells that arises outside the bone marrow in patients without clinical evidence of existing multiple myeloma. Plasmacytomas are characterized by monoclonal expansion of plasma cells that elaborate a single, homogenous immunoglobulin molecule or fragment. The clinical manifestations of plasma cell disorders are directly related to the expansion of these neoplastic cells, the secretion of immunoglobulin molecules and the host's response. Extramedullary progenitor cells differentiate into submucosal plasma cells, which are the origin of extramedullary plasmacytoma. They may remain localized or become disseminated.[1] Patients with plasmacytoma require long-term follow-up to detect possible conversion to multiple myeloma.[2]

Case report

A 32-year-old female presented with a progressively enlarging swelling in her left submandibular region of eight weeks duration. On examination she had a firm, non-tender, mobile swelling which was bimanually palpable. Fine needle aspiration cytology (FNAC) showed atypical plasma cells with mild to moderate nuclear pleomorphism. The patient underwent left submandibular gland excision. Post-operatively the patient made an uneventful recovery. Histological examination revealed a well-circumscribed mass of 2.5 cm $\times$ 1 cm in size composed of a uniform population of immature plasma cells and the surrounding submandibular gland tissue was normal.

Immunohistochemistry demonstrated that tumour cells were positive for lambda light chains and negative for kappa light chains. This indicated a clonal population leading to the diagnosis of a plasma cell neoplasm. The following examinations were undertaken to rule out multiple myeloma: full blood count, urea and electrolytes, creatinine, liver function tests, serum calcium, quantitative immunoglobulins, immunoelectrophoresis, Bence-Jones proteins in urine, bone marrow biopsy and magnetic resonance imaging (MRI) of the skull base to iliac crest were carried out. All investigations were normal. Thus, multiple myeloma was excluded and a diagnosis of primary extramedullary plasmacytoma was made. At three years follow-up, there is no evidence of recurrence.

Discussion

Dalrymple and Henry Bence-Jones first described the neoplastic proliferation of plasma cells characterized by marked proteinuria and bone pain in 1846. In 1873, Rustizky in Kiev coined the term multiple myeloma.[3] Schridde in 1905 was the first person to describe an extramedullary plasmacytoma.

The solitary plasmacytoma of bone is an early manifestation of multiple myeloma and will eventually become disseminated multiple myeloma. Extramedullary progenitor cells differentiate into submucosal plasma cells, that are the origin of extramedullary plasmacytoma. Extramedullary plasmacytoma may remain localized or become disseminated and is a distinct disorder from multiple myeloma since it has a different dissemination pattern and a better prognosis.[4]

Extramedullary plasmacytomas represent less than one per cent of all head and neck tumours.[5] Extramedullary plasmacytoma affects men three to four times more than women and typically occurs in the sixth to seventh decade. Nearly 80 per cent of extramedullary plasmacytomas occur in the submucosal tissues of the upper airway,[6] representing up to four per cent of non-epithelial lesions of the upper respiratory tract.[7] These lesions are important for otolaryngologists to recognise since 80 per cent of extramedullary plasmacytoma occur in the head and neck and 10–20 per cent of cases may present with multiple lesions.[8]

The most common locations for extramedullary plasmacytoma are the nasopharynx and paranasal sinuses, representing approximately four per cent of all non-epithelial tumours of the nasal cavity, nasopharynx, and paranasal sinuses.[5] Other sites include the oropharynx, larynx, tongue, minor salivary glands, thyroid, parotid, orbit, and temporal bone.[7] Outside the head and neck,

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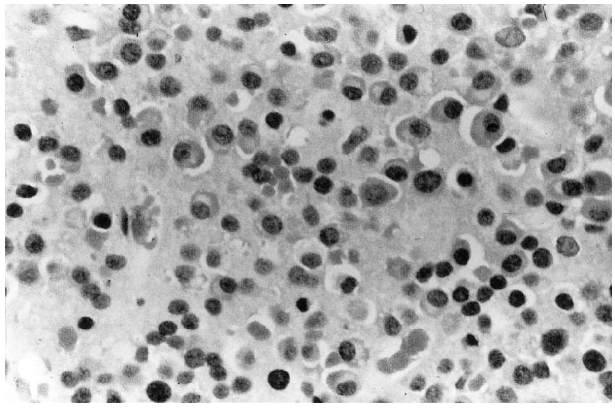

FIG. 1

Well-circumscribed tumour composed of uniform immature plasma cells together with few lymphocytes (H & E; ×200).

extramedullary plasmacytoma has been reported in the pleura, mediastinum, spermatic cord, ovary, intestines, kidney, pancreas, breast, and skin.

Extramedullary plasmacytoma of the submandibular gland is extremely rare. Most of the symptoms related to extramedullary plasmacytoma can be related to their specific location in the head and neck.

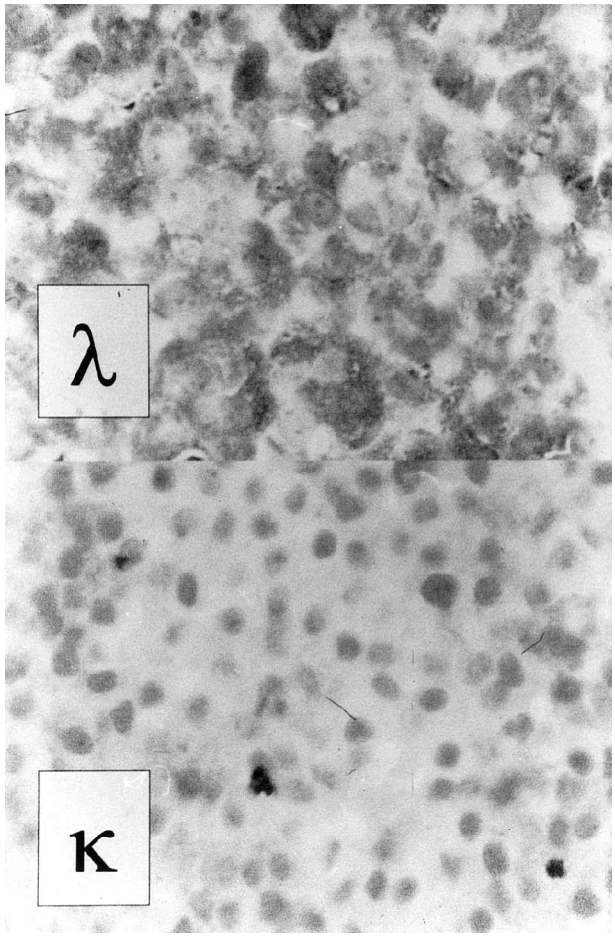

FIG. 2

Immunohistochemical labelling for immunoglobulin shows Immature plasma cells with granular cytoplasmic positive for lambda light chains (cytoplasm dark due to immuno-peroxidase reaction product). Tumour negative for kappa light chains; (cytoplasm unstained; immunoperoxidase with H & E counterstain; ×200).

In a series of 20 patients of extramedullary plasmacytoma of the head and neck 80 per cent of patients presented with the complaint of a mass or swelling, 35 per cent with airway obstruction, 35 per cent with epistaxis, 20 per cent with localised pain, 15 per cent with proptosis, 10 per cent with nasal discharge, 10 per cent with regional lymphadenopathy, and five per cent with a VIth nerve palsy.[9] Other presentations reported include the Collet-Sicard variant of the jugular foramen syndrome, bilateral maxillary sinus involvement, and a midline forehead swelling, reminiscent of a Pott's puffy tumour, from a frontal sinus lesion. Cervical lymph node metastasis occurs in 12–26 per cent of cases at initial presentation.[10]

FNA is not diagnostic but the presence of abnormal plasma cells should raise the suspicion of a plasma cell neoplasm. FNA does not usually yield sufficient material for detailed immunohistochemistry, making diagnosis difficult. FNA can be used to differentiate from squamous cell carcinoma. Biopsy of the lesion is the first step in confirming the diagnosis. Deep biopsies must be taken since the tumour is submucosal and the mucosa may be thickened from an inflammatory reaction.

Microscopically, an extramedullary plasmacytoma appears as a monocellular proliferation of plasma cells set in a sparse matrix. Nuclear and cellular atypia may be minimal or prominent. The plasma cells have round eccentric nuclei with dense nuclear chromatin clumps arranged along the nuclear membrane in a cartwheel fashion. The cytoplasm is abundant, slightly basophilic, and a perinuclear halo typically appears and corresponds to the Golgi apparatus. Plasmacytic, plasmablastic and anaplastic subtypes have been described, but histological appearance is not a reliable indicator of biological activity.[1] Local amyloid deposits have been found in 11–38 per cent of cases but systemic amyloidosis is very rare.

Using immunohistochemical techniques, a monoclonal staining pattern can be seen demonstrating either one heavy chain class, one light chain type, or both, as found in multiple myeloma and other B-cell neoplasms. Histopathological examination cannot distinguish multiple myeloma from an extramedullary plasmacytoma, further evaluation is necessary to exclude the presence of systemic disease and confirm the diagnosis of extramedullary plasmacytoma.

Investigations to be done are full blood count, bone marrow biopsy, serum biochemistry including calcium, blood urea nitrogen, creatinine, uric acid, serum protein, serum and urine electrophoresis, and a skeletal survey to rule out multiple myeloma. Further investigations such as immunoglobulin assay, Cal25, Epstein-Barr (EB) virus, and MRI of the skull base to iliac crest are also recommended.[11]

Normal bone marrow examination, absence of lytic bone lesions on skeletal series, and low paraprotein levels are necessary to establish the diagnosis of extramedullary plasmacytoma. High levels of paraprotein in the serum or urine should raise the clinician's suspicion of a disseminated process, since paraprotein levels correlate directly with tumour burden.[12]

After a diagnosis is confirmed, extramedullary plasmacytoma can be staged as follows: Stage I is localized and a controllable disease, Stage II is local extension or involvement of the lymph nodes, and stage III is disseminated disease.[13] Forty per cent of extramedullary plasmacytomas spread beyond the site of presentation and its draining lymph nodes. Of these, 62 per cent have soft tissue and visceral deposits, including skin, liver and subcutaneous tissues and 81 per cent developed lesions in bone.[8]

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The treatment of extramedullary plasmacytoma is surgery or radiotherapy or both. Extramedullary plasmacytomas are radiosensitive and radiotherapy is the treatment of choice.[2] However, surgery is recommended in cases that are localized and can be removed with minimal morbidity.[7] Surgery or radiation can then be used for salvage in the cases of local recurrence. Abemayor, *et al.* in 1988,[11] recommended radiation therapy, with surgery only for diagnostic purposes or to remove residual disease. Chemotherapy is used for disseminated disease.[14]

Long-term follow-up has shown the local recurrence rate to be 21 per cent for radiotherapy alone and 20 per cent for surgery alone. The recurrence rate was 46 per cent for patients treated with combined therapy, which probably reflects the fact that more extensive disease was being treated, and 35 per cent of patients developed disseminated disease regardless of initial treatment. Patients who developed local recurrences were more likely to develop disseminated disease.[15] Factors associated with poor prognosis include the presence of bone destruction, large primary tumour, recurrence, and tumours located in the sphenoid, maxillary sinus, orbit, or larynx. Histological appearance and lymph node involvement are not reported to be of any prognostic significance. Seventeen to 31 per cent of patients diagnosed with extramedullary plasmacytoma will develop multiple myeloma.[9] Cases of recurrence have been reported 28 and 36 years after initial treatment, in the literature; hence long-term follow-up is mandatory. The prognosis is good provided that multiple myeloma has been excluded.[16] Kaplan Meirs survival estimates for plasmacytoma of the head and neck region are 95 per cent survival at one year, 82 per cent survival at five years and 72 per cent survival at 10 years.[2]

Conclusion

Extramedullary plasmacytoma of the submandibular region is rare and on initial evaluation must be distinguished from multiple myeloma. FNA is not diagnostic but the presence of abnormal plasma cells should raise a clinical suspicion of plasmacytoma. The diagnosis evaluation includes appropriate radiological and pathological studies including immunohistochemistry. It is important to recognize the clinical manifestations of plasma cell neoplasms of the head and neck, and perform a full evaluation to rule out systemic disease. All patients require regular long-term follow-up to monitor for disease progression, dissemination or recurrence.

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