# SOLITARY EXTRAMEDULLARY PLASMACYTOMA OF TONSIL - A RARE LOCATION

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**ABSTRACT :** *Extramedullary plasmacytoma is a rare form of plasma cell dyscrasia, in which plasmacell tumours arise outside the bone marrow. The tumor may arise in any part of the body but the vast majority occur in head and neck, primary in the nasal cavity, paranasal sinuses or upper airway. We present here a rare case of extramedullary plasmacytoma arising from the tonsil. The clinical, histolopathology, immunohistochemical findings are reviewed and the management discussed.*

***Key Words : Extramedullary Plasmacytoma (EMP), Tonsil.***

## INTRODUCTION

Extramedullary plasmacytomas (EMP) are rare soft tissue malignant neoplasms composed of plasma cells. They may be primary without evidence of disease in the other foci, or part of systemic involvement during the course of multiple myeloma. Any extramedullary organ or tissues may be involved. The head and neck area, especially the upper respiratory tract with its abundant lymphatic tissue is by far the most common site(90%; Batsakis et al 1964). The vast majority (80%) arise in nasal cavity, paranasal sinuses and posterior wall of the nasopharynx (Webb et al, 1962). Cases of primary growth of EMP in the salivary glands, the orbit, the lacrimal glands, the trachea, the thyroid gland and the larynx have been described (Segas et al, 1993).

Various classifications have been evolved in the past with Willis R A (1960) presenting the following workable pathologic and clinical classification for plasmacytoma.

Group - 1
Plasma cell myelomatosis(Multiple Myeloma, MM)-the generalised bone disease with characteristic roentgenogram, bone marrow findings and frequently abnormal proteins and Bence Jones protein urea. Some of these patients may develop extrameduallary lesion.

Group - 2
Solitary plasmacytoma of the bone -this is a solitary lesion occurring in bone. At the time of diagnosis there is no evidence of generalised disease.

Group - 3
Primary plasmacytoma of soft tissue - these may be single or multiple and occur in submucous tissue of the upper respiratory tract and oral cavity. This is the most common site in this group.

Final classification of individual cases should therfore be tempered by time, as it is possible for an apparent solitary EMP to be the first presenting sign of a generalised disease. The treatment and prognosis of primary EMP are different from that of extra skeletal spread in MM. It is therefore important to look for systemic skeletal involvement in all patients with EMP prior to the institution of therapy (Dolin & Dewar, 1956).

The diagnosis of EMP can be made only on morphologic examination of the tumour. In some circumstances it may be difficult to determine whether the plasma cell proliferation is reactive or neoplastic. EMP shoud be distinguished from non neoplastic conditions such as reactive plasmacytic hyperplasia,plasma cell granuloma (PCG) and pseudolymphoma (PL) (Bahadori & Liebow,1973). Malignancies that can be mistaken for EMP include other haematopoietic neoplasms, malignant melanoma, olfactory neuroblastoma, anaplstic carcinoma and metastases (Kapadia et al, 1981). In addition other small round cell lesions have to be excluded depending on the anatomic site. Apart from conventional haematoxylin and eosin

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stains(H & E), histochemistry, immunohistochemistry and electromicroscopy may be of diagnostic help.

The true nature of primary EMP and its relationship to MM is controversial. Some authors state that primary EMP is a separate entity (Wiltshaw, E. 1976), while others suggest that both EMP and MM are variants of the same disease process (Batsakis et al, 1964). The immunoperoxidase procedures are helpful in demonstrating monoclonal cytoplasmic Ig distribution and morphology of plasma cells in tissue section of bone marrow from myeloma patients(Taylor et al, 1978). The monoclonal Ig pattern is believed to be presumptive evidence of a neoplastic plasma cell proliferation. Long-term follow up and immunoperoxidase study of EMP in relation to Ig content of plasma cells and the presence of any M component in serum or urine may help determine the nature of this process and its relationship to MM.

A review of the literature shows location of the tumour in the tonsil to be rare. Appearance of EMP in the region of entire Waldeyer's ring have been reported in 44 cases only (Segàs et al, 1993) with less than half of them arising in the palatine tonsillar region. In the present study we report a rare case of EMP arising from the superior pole of the tonsil which was treated by radiotherapy. The various modalities of treatment, course of the disease, survival and prognostic factors are also discussed.

## CASE REPORT

A 51 year old, otherwise healthy golf course keeper who was a chronic smoker presented to the ENT clinic with complaints of right-sided sore throat for three months. He also experienced odynophagia. There was no history of dysphagia, oral bleeding, dypnoea, dysphonia, earache or loss of weight. Clinical examination revealed a 2 x 1 cm. irregular but firm mass arising from the superior pole of the right tonsil with no involvement of either of tonsillar pillars. The remainder of the ENT examination was unremarkable with absence of any neck nodes. His chest X-ray, full blood count, liver function tests, urea and electrolytes were within normal limits. An incisional biopsy of the mass was taken. Microscopic examination revealed a strip of stratified squamous epithelium with underlying tissue composed of sheets of monomorphic cells with amphophilic cytoplasm and eccentric nuclei(Fig. I). The cells stained positive with methyl green pyronin for plasma cells. The immunoperoxidase stain on formalin fixed paraffin embedded tissue section revealed cytoplasmic monoclonal immunoglobulin(IgG kappa; see Fig. II). The overall appearance was suggestive of a case of extramedullary plasmacytoma. Urinalysis did not show any Bence Jones proteins. Plasma electrophoresis was carried out which revealed a normal pattern with no paraprotein band. Bone marrow biopsy showed normocellular marrow with no evidence of infiltration. CT scan of head and neck revealed small soft tissue mass in the right tonsillar region. No other definite abnormality was seen (see fig. III). A whole body skeletal survey revealed no secondary bony involvement.

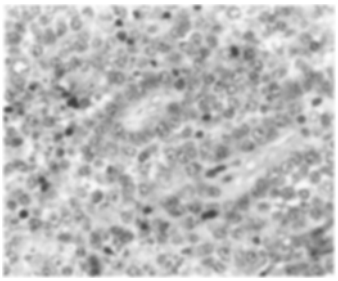

Fig. -I : Microscopic picture of closely packed monomorphic cells with amphophilic cytoplasm with eccentric nuclei (H & E. x 400).

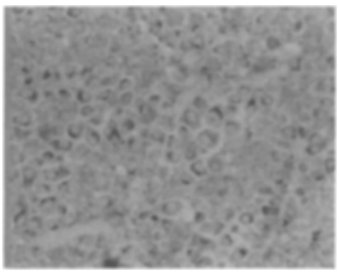

Fig. II : The immunoperoxidase stain revealing cytoplasmic monoclonal immunoglobulin (IgG kappa,. x 400).

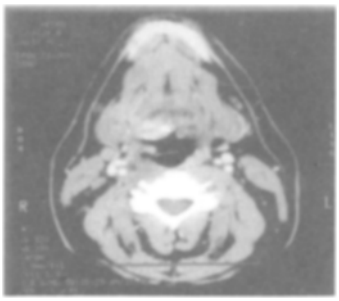

Fig.- III : CT scan (axial view, post contrast) showing soft tissue mass in right tonsil with no nodal involvement.

The patient was treated as a case of solitary EMP with radiotherapy alone (4500 cGY in 20 fractions). Five months following completion of treatment he clinically remains disease-free though he experiences dryness of oropharynx.

## DISCUSSION

Neoplasms of the plasma cell region have been classified as solitary plasmacytomas, multiple or diffused myeloma and plasma luekemia. Solitary plasmacytomas are further characterised as intramedullary and extramedullary (Galton DAG, 1989). The extramedullay plasmacytoma is a malignant plasma cell dysrasia which arises from soft tissue. This is a rare tumour which can be seen in any organ. 90% of these neoplasms occur in the head and neck area with a strong propensity to involve the upper respiratory tract, the nasal cavity and the paranasal sinuses (Webb et al, 1962). Among the malignancies of the above anatomic region, the plasmacytoma constitutes less than 1% (Medini et al, 1980). Outside the head and neck area the EMP is very uncommon but primary tumours in the lung, pleura, stomach, small bowel, colon, ovary, uterus, testes, kidneys, skin and breast has been reported (Segas et al, 1993).

The appearance of EMP in the region of Waldeyer's ring is very uncommon (Segas et al, 1993). The majority of the tumours occur in men about three times as often as in women and are generally seen in the 50-80 age group (Gorenstein et al, 1977). The predominant symptom in patients with EMP of the orpharynx is upper airway obstruction and bleeding from tumour. The upper airway obstruction varies according to the size and location of the mass. Patients complain of difficulty in swallowing solid food or dysphagia or a sensation of a foreign body. Bleeding from the surface of the tumour occurs frequently and is related to the growth of the tumour as well to trauma due to lesion caused by hard food (Wollersheim et al, 1984). In our case the patient complained of soreness in the throat and pain on swallowing with no history of any bleeding. On physical examination a pharyngeal mass is detected which can originate from any site of the Waldeyer's ring. Ulceration of the mass can occasionally be seen Although not often clinically ulcerated, the submucoal EMP tend to be vascular and bleeds easily, with microscopic foci of surface necrosis and acute inflammation seen in some cases on histologic examination. 10-25% of the plasmacytomas may develop metastases to submandibular or cervical lymphnodes (Moss, W. T., 1987). No cervical lymphnode involvement was found in our patient.

The diagnosis of EMP can be made only morphologically because of the non-specific clinical presentation and radiologic appearance. Most primary EMP of the head and neck arise in the submucosa of the upper air and food passages although in occasional cases with local bone destruction, the possibility of an osseous origin is difficult to exclude with absolute certiainty. On histologic examination, closely packed masses of immature or atypical plasma cells of varying differentiation and a scant stroma are seen with replacement of normal tissue. The cytoplasm of plasma cells is strongly pyroninophilic. A characteristic concentrically arranged lamellar rough endoplasmic reticulum and prominent Golgi apparatus are seen on electromicrocroscopy. Identification of a single type of Ig using the immunoperoxidase method is considered evidence of the neoplastic nature of the plasma cell proliferation (Taylor et al, 1978).

The radiographic manifestations of EMP depend upon the size, location and extent of tumour. When confined to submucosa mucosa it is visible as a soft tissue mass which may block sinus orifices(Gromer & Duvall, 1973). Multiple sites of simultaneous tumour development may be apparent (Batsakis et al, 1964). Bony invasion occurs in approximately one-third of patients and can be suspected if pain in a major clinical symptom (Gromer & Duvall, 1973). It may be visible on plain film but tomography is usually necessary to define the degree of destruction. Not infrequently, a small tumour is visible clinically and large bulky tumour masses within the nasal cavity and sinuses are demonstrated radiographically, often with marked bony destruction. Calcification within primary tumours has not been observed and metastatic deposits outside the liver, spleen and lymphnodes have not been reported.

Diagnostic difficulties may arise in differentiating EMP from benign reactive plasmacytosis as well as other malignant disorders(Kapadia et al, 1982). Careful attention should be given to proper fixation and processing of tissue. It is better to adequately excise rather than biopsy a polypoid mass or enlarge lymphnode or tonsil in order to avoid crush artefacts. Reactive plasma cell proliferation, as seen in PCG and in some cases PL, may mimic well differentiated EMP and be impossible to distinguish on histologic grounds alone. Reactive plasma cells may have atypical features such as binucleation and the presence of nucleoli. In PCG there is a supporting stroma of granulation tissue or hyalinized tissue and other reactive cells such as lymphocytes and lipid laden macrophages are intermixed with the plasma cells (Bahadori & Liebow, 1973). In PL the polymorphic inflammatory infiltrate is composed predominantly of mature lymphocytes, plasma cells and reactive histiocytes. Germinal centres may be readily found and varying degrees of fibrosis are present(Kelly et al,

1977). The demonstration of intracellular polyclonal Ig using the immunoperoxidase stain on the tissue sections permits the differentiation of reactive plasma cell lesions from EMP.

Several types of poorly differentiated neoplasms may be mistakenly diagnosed as EMP including undifferentiated or metastatic carcinomas, olfactory neuroblastoma, Walsenstroms macroglobulinemia and granulocytic sarcoma(Bahadori & Liebow, 1973). The non-lymphoid malignancies which are negative for intracytoplasmic IgM are distinguished by their characteristic histochemical electromicroscopic features. However, in some poorly differentiated round cell malignancies the correct diagnosis can be established only after the combined use of morphology, histochemistry, immunohistochemistry, or electromicroscopy.

Evaluation of the extent of disease is essential for proper management of this patient. The treatment and prognosis defers according to whether the EMP is primary or secondary. The majority of patients with primary EMP do not have a demonstrable monoclonal component in serum or urine probably because of low tumour cell mass at onset. The detection of monoclonal protein in serum or urine does not preclude the diagnosis of primary EMP, although large amount of Ig should suggest a higher tumour cell mass usually seen with disseminated disease(Woodruff et al, 1979). Monoclonal Ig is found in 97% of patients with MM when immunoelectrophoresis is performed on serum and urine and an abnormal skeletal survey in 75% (Kapadia, S. 1980). Thus a bone marrow aspirate or biopsy, serum and urine electrophoresis and skeletal survey should be performed at diagnosis in each case of EMP to search for evidence of MM.

EMP are high radiosensitive. They often respond to a dose of radiation of 2000-3000 rads with complete clearance. The majority of mucosal and small EMP can be controlled by 3000 and 4000 rads. If there is no dissemination, these patients are usually cured of their disease. For the large EMP, one should attempt to irradicate the local tumour, the final radiation dose should be determined by the size of the tumour, the extension to involved bone, muscle and other deep structures and the completeness of the regression following a certain dose of radiation. Others have recommended a uniform dose of up to 5000-6000 rads in the treatment of these tumours (Mill & Griffith 1980). Radical surgery is not usually indicated. Treatment with chemotherapy and steroids is indicated in patients with secondary EMP and when dissemination occurs in the course of primary EMP.

The prognosis is more favourable in patients with primary EMP not associated with MM. Although a small proportion of these patients have a rapidly progressive course with dessemination and death in a few months about 33-75% survive five years (Wiltshaw, E. 1976). Dissemination eventually occurs in 35-50% of patients with primary EMP months to years later, at times as late as several decades after diagnosis (Batsakis et al, 1964). Bone pain anaemia, renal impairment, bronchopneumonia and other infections may herald the onset or complicate the course of MM. Once MM occurs infection and renal failure are the commonest causes of death(Kapadia S., 1980)

Woodruff et al, have suggested that the good prognosis of head and neck EMP is probably related to the fact that they are localised at onset and that very large tumours are uncommon. Patients with large EMP should be considered for post-radiation chemotherapy. Regional lymphnode involvement, local bone destruction and persistence of primary tumour after radiation are not necessarily poor prognostic indicators. dissemination is an ominous sign and the most common causse of death.

The differences in the clinical course of primary EMP and MM and a more favourable prognosis for the former, would seem to lend weight to the argument that they are separate entities(Wiltshawm, E. 1976). However, there appears to be more compelling consideration that favour a unified concept which incorporates primary EMP and MM into a continum or spectrum of monoclonal plasma cell neoplasms (Batsakis et al, 1964). These include morphological similarities, the evolution of EMP to MM and finally the demonstration of cytoplasmic monoclonal immunoglobin in primary EMP which is identical to that found in bone marrow and serum or urine at the time of dissemination. The patients with primary EMP disease which does not evolve to multiple myeloma may reflect a difference in rate of tumour growth or cure after local radiation therapy.

## CONCLUSION

Multiple myeloma or generalised myeloma is a disease of unknown aetiology. This disease almost always commences in the bone marrow, has an insidious onset and is

always diagnosed at an advanced stage. Tumours containing plasma cells indistinguishable from those cells occuring in MM may arise in upper airway passages, oral cavity and other extramedullary areas. These are known as EMPs. A certain number of patients will ultimately develop generalised disease. Others die from local invasion and the remainder show no further evidence of tumour either locally or at a distant site following treatment. The extent of primary tumour at onset and development of dissemination after local control with radiation therapy are factors that affect survival the most. The importance of a detailed work up in each case to establish the presence or absence of dissemination cannot be overemphasised.

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## REFERENCES

1. Bahadoria M., and Liebow A. A.,(1973) Plasma cell granuloma of the lung. Cancer, 31 : 191 - 208.
2. Batsakis J. G., Fries G. T., Goldman R. T., Karlsberg R. C.,(1964) Upper respiratory tract plasmacytoma. Arch. Otolarnygol. 79 : 613 - 618.
3. Dolin S., Dewar J. P., (1956) Extramedullary plasmacytoma. Am J. Path 32 : 83 - 103.
4. Galton D. A. G., Myelomatosis in Hoffbrand A. V., Lewis S. M.,(eds) (1989) Postgraduate Haematology. Oxford, Heinemann Professional Publishing, 18 : 474 - 97.
5. Gorenstein A., Neel H. B., Devine K. D. (1977) Solitary extramedullary plasmacytoma of the larynx. Arch Otolaryngol 103 : 159-61.
6. Gromer R. C., Duvall A. J. (1973) Plasmacytoma of the head and neck. Journal of Laryngology & Otology 87 : 864-872.
7. Kapadia S. B., (1980) Multiple myeloma : A clinicopathologic study of 62 consecutively autopsied cases. Medicine, 59 : 380-392.
8. Kapadia S. B., Barnes L., Deutsch M. (1981) Non-Hodgkin's lymphoma of the nose and paranasal sinuses : A study of 17 cases. Head and Neck Surg., 3: 490-499.
9. Kapadia S. B., Desai U., Cheng V. S., (1982) Extramedullary Plasmacytoma of the head and neck. A clinicopathologic study of 20 cases. Medicine 6 : 317-329.
10. Kelly A. G., Rosas- Uribe A., Kraus S. T., (1977) Orbital lymphoma and pseudolymphomas. A clinicopatholic study of eleven cases. Am. J. Clin. Pathol., 68 : 377-386.
11. Medini E., Rao Y., Levitt S. H.(1980) Solitary extramedullary plasmacytoma of the upper respiratory and digestive tracts. Cancer 45 : 2893-6.
12 Mill W. B., Griffith R.(1980) The role of radiation therapy in the management of plasma cell tumor. Cancer, 45 : 647-652.
13. Moss W. T.(1987) Radiation therapy of tumors of the nasal cavity and paranasal sinus, in Thawley S. E., Panje W. R. (eds) Comprehensive Management of Head and Neck Tumors. Philadelphia, Saunders, 18 : 344-52.
14. Taylor C. R., Russell R., Chandor S., (1978) An immunohistologic study of multiple myeloma and related conditions, using an immunoperoxidase method. Am. J. Clin Pathol., 70 : 612-622.
15. Webb H. E., Harrison E. G., Masson J. K., Solitary extramedullary myeloma (plasmacytoma) of the upper part of the respiratory tract and orpharynx. Cancer 15 : 1142-55.
16. Willis R. A.(1960) Pathology of Tumors, 3rd ed. London Butterworth : P 791.
17. Willshaw E. (1976) The natural history of extramedullary plasmacytoma and its relation to solitary myeloma of bone and myelomatosis. Medicine, 55 : 217-238.
18. Woodruff R. K., Whittle J. M., Malpas J. S.(1979) Solitary plasmacytoma I : Extramedullary soft tissue plasmacytoma. Cancer 43 : 2340-2343.
19. Wollersheim H. C. H., Holdrinet R. S. G., Haanen F.(1984) Clinical course and survival in 16 patients with localized plasmacytoma. Scand J Haemotol 32 : 423-428.
20. Segas J., Skoulakis H., Katrinakis G., Tzardis M.(1993) Solitary Extramedullary Plasmacytoma of the oropharynx : A rare location. ENT Journal. Vol 72, No. 11, 743 -745.