Extra-skeletal plasmablastic myeloma presenting as palatal growth – An unusual entity

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A B S T R A C T
INTRODUCTION: Multiple myeloma (MM) is characterized by malignant proliferation of plasma cells, monoclonal bone marrow plasmacytosis, the presence of M-protein in serum and/or in urine and osteolytic bone lesions.
PRESENTATION OF CASE: We report a case of a 28-years old female, who was diagnosed to have relapsing extra-skeletal and extra-nodal plasmablastic myeloma, an atypical variant of MM with a poor prognosis. In addition to bone marrow plasmacytosis and the presence of M protein in the serum, the patient had an extramedullary lesion affecting the hard palate.
DISCUSSION: There is a strong correlation with age. The peak incidence is seen in 6th-7th decade. The clinical course in adolescents and young individuals is generally indolent and the survival is longer. Extramedullary myelomas are rare tumors accounting for 0.4% of all head and neck malignancies. CONCLUSION: A case of extraskeletal plasmablastic myeloma presenting as a hard palate growth and that too in young female patient is an extremely rare and requires a multidisciplinary approach for management.

1. Introduction
Multiple myeloma (MM) is a monoclonal plasma cell proliferative disorder accounting for 1% of all malignancies and 10% of malignant haematological neoplasms [1]. It is the second most common haematological neoplasm. The incidence increases with age and the median age at diagnosis is 68. Males are affected more frequently than females. It is extremely rare in young adults below 30 years of age [2,3].

The uncontrolled proliferation of myeloma cells is accompanied by an increase in M-protein. The criteria for the diagnosis of myeloma includes: evidence of M-protein in the serum or urine (usually > 30 g/l); at least 10% plasma cells on a myelogram; demonstration of monoclonal plasma cells on bone marrow biopsy and organ damage [4].

The extramedullary plasmacytomas (EMP) are rare tumors accounting for 0.4% of all head and neck malignancies [5]. They are extremely rare in oral cavity and that too at the time of diagnosis [6]. They indicate extensive disease with poor prognosis.

The prevalence of plasmablastic morphology in newly diagnosed myeloma cases is approximately 10%. Eastern cooperative oncology group has recently confirmed that plasmablastic morphology is a powerful independent adverse prognostic factor for survival [7,8], We, hereby, report a case of a 28-years-old female patient who was diagnosed to have plasmablastic myeloma, considered to be an atypical variant of MM with poor prognosis, presenting as hard palate growth.

2. Case report
A 28 years old female presented to ENT outdoor with complaint of growth over hard palate and pain in the lesion for 2 months. Patient had episodes of bleeding from the growth off and on. The growth was polypoidal, exophytic, firm and bled on touch. The general physical examination did not reveal any abnormality. However, she also had pain in left lower limb and was lathargic most of the times.

Her laboratory reports revealed the following: Hb- 9.6 gm/dl, TLC- 13000/cmm, DLC- P78 L18 M2 E2, platelets were normal. ESR 110 mm/hr, blood urea 35 mg%, S. Creatinine-0.7 mg%, fungal stains and Xpert TB were negative.

Computed tomography (CT Scan) showed an evidence of heterogeneously enhancing nodular oral cavity mass lesion causing destruction of hard palate and alveolar process of maxilla and it was bulging into the nasal cavity (Fig. 1). Further, CT head showed multiple lytic lesions in calvaria (Fig. 2). Positron Emission Tomography (PET) revealed hypermetabolic lytic lesions involving axial and appendicular skeleton. Keeping in view her symptoms, Magnetic Resonance Imaging (MRI) of left knee was also

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performed which revealed diffuse marrow infiltrative disorder possibly leukemia or lymphoma. Biopsy from hard palate growth was done. It showed a diffuse infiltration by medium sized tumor cells, of plasmablastic morphology with fine reticular nuclear chromatin, large nucleus, with very little perinuclear hof (Fig. 3). Immunohistochemistry (IHC) panel applied revealed strong positivity of tumor cells for kappa light chains, while these cells were lambda chains negative. CD38 and CD138 were also positive. CD20, CD5, CD10, CD3, BCL6 and Cyclin D1 were negative. Ki67 index was high (60%). EBER (ebstein barr virus encoded RNA) was also negative, ruling out the differential of plasmablastic lymphoma (Fig. 4). So, a final diagnosis of plasmablastic myeloma was made.

Serum protein electrophoresis yielded hypoalbuminemia and M spike in gamma region (2.4 g/dl), further corroborating the diag-
nosis of plasma cell disorder. Thus, the diagnosis of plasmablastic myeloma was confirmed. The case was discussed in multidisciplinary tumor board. She was taken up for surgery followed by chemo-radiation. But unfortunately, she did not respond well to treatment and finally succumbed to her illness after 6 months.

3. Discussion

Plasma cell dyscrasias are a group of disorders characterized by monoclonal plasma cell expansion. Predominately a disease of the elderly, the peak incidence is between 60 and 70 years [2,3]. Five patients with Multiple Myeloma (MM) of less than 30 years of age have been reported from India, during the last 10 years, which constituted only 3.3% of all MM cases [9]. The diagnosis of MM requires 10% or more clonal plasma cells in the bone marrow or the presence of a biopsy proven plasmacytoma, along with evidence of end-organ damage i.e. anaemia, hypercalcemia, lytic bone lesions, or renal failure [4].

Depending on their site of development and clinical features, plasma cell neoplasms have been divided into: a) Solitary extramedullary plasmacytoma (b) Solitary bone plasmacytoma (c) Multiple myeloma (d) Multifocal form of multiple myeloma (e) Plasmablastic sarcoma [10]. Extramedullary plasmacytoma (EMP) is a localized collection of monoclonal plasma cells, arising within soft tissues in an extraskelatal site. They can either be — Primary (true) plasmacytoma (without evidence of systemic disease) or extramedullary manifestation during the course of multiple myeloma. Schridde reported the first case of EMP in 1905 [11]. The most commonly affected site is the nasal cavity/paranasal sinuses (43.8%) followed by nasopharynx (18.3%), the oropharynx (17.8%) and larynx (11.1%). EMP affects males 3–4 times more than females with a median age of 55 years [12]. The etiology of EMP is still unknown. Because of its presentation in the mucosa of the upper aero-digestive tract (78%), chronic stimulation by inhaled irritants or viral infection has been implicated as causative factor [13]. The clinical presentation varies according to the site of involvement.

Extramedullary involvement of multiple myeloma is uncommon at diagnosis and is caused by haematogenous spread. Plasmablastic myeloma represents a small morphological subtype of multiple myeloma and is associated with a poor prognosis. Extramedullary dissemination of myeloma usually occurs several years after the initial diagnosis of myeloma, but sometimes the extramedullary myeloma can present at the time of diagnosis [14]. In the present case, it could not be determined whether the extramedullary mass developed concurrently with the myeloma, subsequently to the primary myeloma or whether this was a primary extramedullary plasmacytoma that then progressed to a frank myeloma.

Histopathologically, the tumor is characterized by a dense homogenous infiltrate of plasma cells. The plasma cells have round eccentric nuclei with dense chromatin clumps arranged along the nuclear membrane in a cartwheel fashion. Plasmacytic, plasmablastic and anaplastic cell types have been described.

The treatment of extramedullary plasmacytoma is still controversial. Some advocate radiotherapy while others prefer surgical excision. Most clinicians recommend a combined approach (surgery and radiotherapy) for the management [14]. High-dose melphalan followed by autologous stem cell transplantation (SCT) remains the first-line therapy for young high-risk multiple myeloma patients who are responsive to conventional induction chemotherapy (vincristine or thalidomide, doxorubicin and dexamethasone). The patient in our case was managed surgically and subsequently subjected to radiotherapy. She was also offered stem cell transplantation. Because of the tendency of EMP to progress into disseminated multiple myeloma, a life-long follow-up of these patients is recommended. Compared to other subtypes, plasmablastic morphology has poor prognosis with high risk of complications, relapse or refractory disease, despite these aggressive treatment approaches [15].

Myeloma needs to be differentiated from other monoclonal gammopathies and plasmablastic lymphoma. Morphological features can be used to distinguish plasmablastic lymphoma from well-differentiated plasma cell neoplasms. However, highly aggressive plasma cell myeloma may contain a predominance of plasmablasts, which can closely resemble the malignant cells of plasmablastic lymphoma [16]. However, the distinction depends on clinical features. In addition, the presence of Epstein–Barr virus (EBV) infection is much more strongly associated with plasmablastic lymphoma than with plasma cell neoplasms [17]. In practice, it is very difficult to distinguish these by using morphologic criteria only. Thus, in this study we used clinical, radiological and laboratory data as well as pathological findings to identify plasma cell myeloma, and then performed a comprehensive panel of lymphoid and plasma cell-related markers, to compare plasmablastic lymphoma and plasmablastic plasma cell myeloma.

4. Conclusion

A case of extraskeletal plasmablastic myeloma presenting as a growth of hard palate and that too in young female patient is an extreme rarity and to the best of our knowledge, has never been reported in literature. A multidisciplinary approach is required for the optimal diagnosis and management of extramedullary plasmacytoma.

Conflicts of interest

There is no conflict of interest amongst the authors.

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Ethical approval

As it is a case report, ethical approval has been exempted by our institution.

Consent

Written informed consent was obtained from the patient’s guardian for publication of this case report and any accompanying images.

We state that the work has been reported in line with the SCARE criteria [18].

We also declare that there are no conflicts of interest amongst the authors.

Author contribution

Sanjay Kumar – Supervised the article and did the final editing
Namita Bhutani – Reviewed the literature and wrote the article
Sant P Kataria – Gave important inputs regarding the management of the case
Rajeev Sen – Managed the investigative work-up of the patient.

Guarantor

Pradeep Kajal.
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