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ORIGINAL STUDY

Nasal cavity extramedullary plasmacytoma: literature review and clinical experience

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ABSTRACT

BACKGROUND. Extramedullary plasmacytoma is an extremely rare solitary plasma cell neoplasm that occurs in locations other than bone, without involving the bone marrow. It is commonly located in the upper aerodigestive tract. In the head and neck region, the most frequent location is the sinonasal region.

MATERIAL AND METHODS. A systemic review in accordance with the PRISMA guidelines was done with research works in PubMed, Elsevier database, Cochrane library, Web of Science, Scopus, Crossref and Google Scholar. The search was carried out using the keywords "plasmacytoma and nose", "extramedullary plasmacytoma", "extramedullary plasmacytoma of nose", "plasmacytoma and nasal cavity", and "extramedullary plasmacytoma of nasal cavity".

RESULTS. We analysed 27 research works with a total number of 32 cases. The most common presenting symptoms were nasal cavity bleeding. The disease showed a male preponderance (78.1%). Bone erosion was seen in 7 cases. The histopathological examination showed plasma cells arranged predominantly as a uniform population or sheet-like appearance. A common immunohistochemical marker was CD138 (11 cases). Treatment was primarily radiotherapy (43.7%). We are also reporting a case of a 53-year-old male with plasmacytoma of the middle turbinate managed by wide resection and postoperative radiotherapy.

CONCLUSION. Though a less common condition, in a case of polypoidal-like lesion with bleeding tendency, the clinician should keep in mind the possibility of extramedullary plasmacytoma. The diagnosis is made with histopathological examination and immunohistochemistry of the tissue involved. Treatment can be radiotherapy, surgery, or a combination of modalities.

KEYWORDS: extramedullary plasmacytoma, nasal cavity, plasma cells, immunohistochemistry.

INTRODUCTION

Extramedullary plasmacytomas (EMP) are a group of localized clonal plasma cell neoplasms which are extraosseous in location and without clinico-radiological evidence of another plasma cell neoplasm of bone marrow origin. These are more common in the head and neck region and account for 1% of head and neck malignancies and 2-4% of non-epithelial neoplasms of the sinonasal tract[1]. They are three times more common in males than females and occur usually in the fifth to seventh decade of life[1]. The common sites of occurrence in the head and neck region are mostly extra nodal and include the nasal cavity, sinuses, oropharynx, salivary gland, and the larynx. These can be locally aggressive, causing skull infiltration. Patients usually present with symptoms of nasal obstruction or, less commonly, epistaxis, rhinorrhoea, anosmia, or facial pain. Very rarely, EMP can present as expansive lesions of the sinuses, causing pressure symptoms such as visual blurring[2,3].

The plasmacytoma of the nasal cavity shows a variety of clinical appearances. It can present as a polypoidal lesion, a sessile lesion, a submucosal lesion, or

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an ulcerated lesion. One important differential diagnosis is inverted papilloma, which can be differentiated from the EMPs, with the endoscopic picture. EMPs have a greyish red to grey colour, whereas inverted papilloma has a bright fleshy mass appearance[1,4]. Both these lesions tend to bleed on touch. Another close differential diagnosis is squamous cell carcinoma. All these tumours have an expansile growth and can cause bone erosions or pressure effects. A tissue biopsy with presence of plasma cells is sufficient to rule out inverted papilloma and squamous cell carcinoma.

Diagnosing EMP involves imaging studies, histopathological examination, immunohistochemistry. Commonly used immunohistochemical markers for the diagnosis of EMP include CD138, CD38, CD56, and MUM-1 (Multiple Myeloma Oncogene 1). CD138, also known as syndecan-1, is a glycoprotein expressed on plasma cells. Its presence is a key indicator of a plasma cell origin, helping to distinguish these cells from other cellular components in the tumour[5]. CD56, also called neural cell adhesion molecule (NCAM), is another marker frequently utilized in EMP immunohistochemistry. This marker helps in confirming the plasma cell lineage and can be very helpful in differentiating EMP from other types of tumours[6]. MUM-1 (Multiple Myeloma Oncogene 1), also known as IRF4 (Interferon Regulatory Factor 4), is a transcription factor expressed in plasma cells. Its positive staining indicates the presence of mature plasma cells. Another marker CD79a is found to be positive in 50 % of EMP cases. CD79a is a transmembrane protein seen in B cell neoplasms. As a plasma cell is a matured B cell, few of the plasma cells retains CD79a positivity. Though considered as a less sensitive marker for EMP, CD79a positivity is helpful in the diagnosis of EMP at unusual sites, such as lung and breast. These markers, along with others such as kappa and lambda light chains, help to characterize the immunophenotype of the tumour cells and differentiate EMP from other neoplasms. Additionally, bone marrow biopsy is performed to rule out concurrent multiple myeloma[7].

Surgical excision is considered as a primary modality of treatment in the sinonasal type, especially when the tumour is amenable to complete removal. Treatment approaches also include addition of adjuvant radiation therapy to achieve locoregional control. The prognosis varies, and EMP can either remain localized or progress to multiple myeloma. Regular monitoring and follow-up are crucial to detect any recurrence or progression, emphasizing the importance of a multidisciplinary approach involving haematologists, oncologists, and radiation therapists in managing this uncommon plasma cell disorder. The rate of progression to plasma cell myeloma is about 15%[8,9].

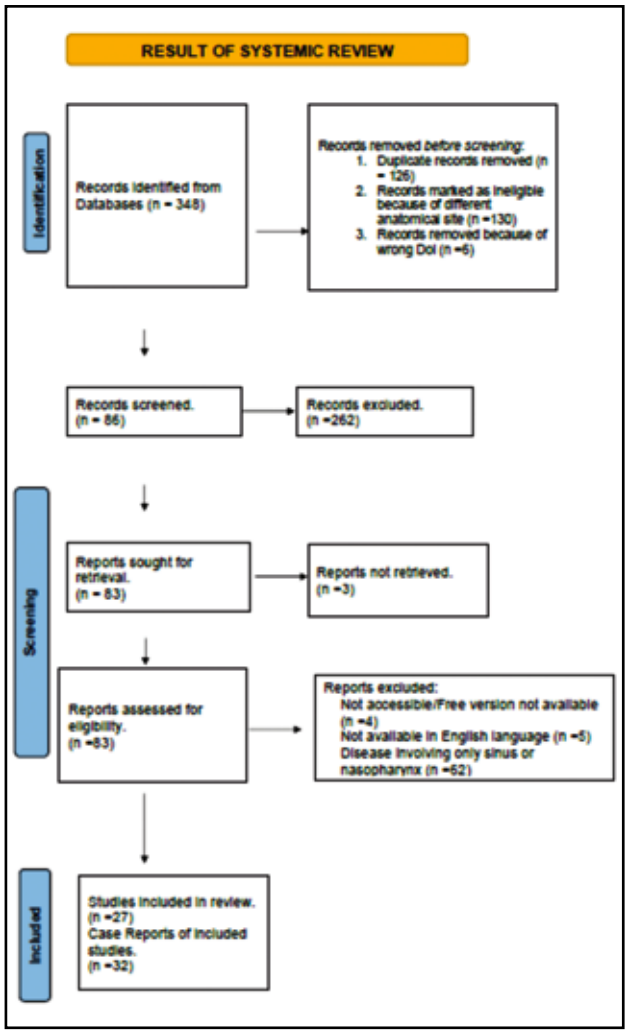


Figure 1. PRISMA flowchart showing selection of articles for review.

MATERIAL AND METHODS

A systematic review of the literature was done in accordance with the PRISMA guidelines[10]. The review was conducted by both authors independently and the data was later compiled in a common Microsoft Excel work sheet. The search was done in PubMed, Cochrane library, Elsevier database, Web of Science, Scopus, Crossref and Google Scholar. The search words included "plasmacytoma and nose", "extramedullary plasmacytoma", "extramedullary plasmacytoma of nose", "plasmacytoma and nasal cavity", and "extramedullary plasmacytoma of nasal cavity". Maximum results were obtained when the Boolean operator "AND" was used with "extramedullary plasmacytoma" and "nasal cavity". Reference sections of the selected articles were also looked into in order not to miss any relevant articles.

The inclusion criteria comprised articles with cases of EMP in any of the nasal cavity sites such as

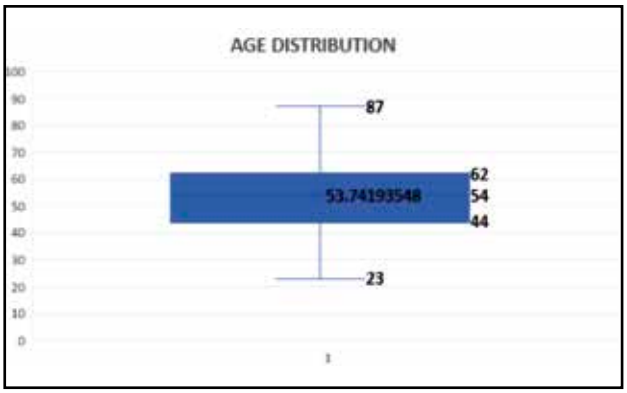


Figure 2. Box and Whisker plot showing age distribution of cases.

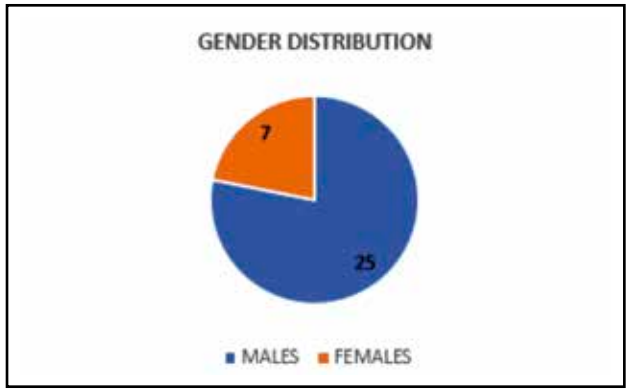


Figure 3. Chart showing gender distribution.

nasal septum, turbinates and/or nasal cavity proper. Literature works where the bulk of the lesion was located in the nasal cavity were also included in the systematic review. Only articles published after 2002 in the English language were considered for the study. Articles with an available English translation were also included in the analysis. Case reports, case series, review articles, and short communications were included.

Articles addressing the disease primarily or isolated lesions of the paranasal sinuses or nasopharynx were not considered for analysis. Literature works which were accessible only through subscriptions and those with incomplete data were also excluded.

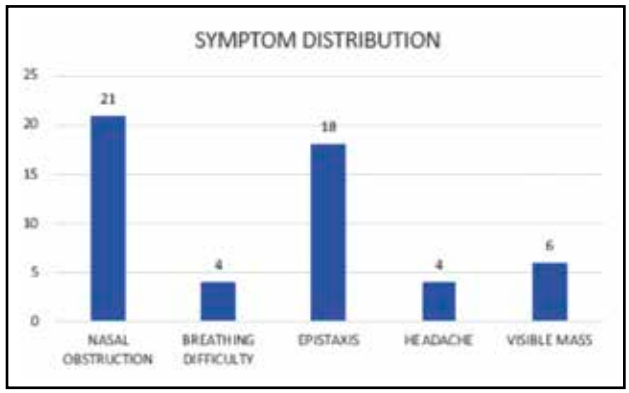


Figure 4. Chart showing the frequency of common presenting symptoms among patients.

RESULTS

A total of 374 articles were found in the database search with the keywords mentioned in the method section. After excluding duplications and articles not available in the English language, a total of 86 articles were screened for data. The inclusion criteria were applied and a total of 27 articles detailing 32 cases were included in our study[3,9,11-35] (Table 1). The selection process of articles is shown in the flowchart (Figure 1).

In the last two decades, the authors were able to find a total of 41 cases of EMP involving the nasal cavity. 4 articles were not accessible because of their payment policy and 5 articles were not in the English language. The lack of data of 9 cases is a limitation for our review.

Among the 32 cases, none of the patient were below the age group of 18. The age group range was 20 to 87 years, with the maximum number of patients in the age group of 44 to 62 years (Figure 2). Out of 32, EMP of the nasal cavity was seen in 25 males and 7 females (Figure 3).

The most common presenting symptom was epistaxis, followed by nasal obstruction. Patients also reported some non-specific symptoms such as dizziness (1 patient), cough (1 patient), neck pain and paroxysms of sneezing (1 patient). 4 patients presented with a history of a visible mass inside the nasal cavity (Figure 4). Diagnostic endoscopic examination was of limited use because of the presence of blood clots, blood-tinged crusts, or tendency for bleeding. CT was the most preferred radiological investigation of choice. Only CT scans with or without contrast were performed on 22 patients. Both CT and MRI were done in 5 cases, while in 4 cases only MRI was performed.

Isolated nasal cavity involvement was seen in only 14 cases, while the majority of cases were involved with one or more sinuses, with/without involvement of the nasopharynx. Two cases had extensive sites involvement, one with spine and the other one with discrete laryngeal involvement.

Bony destruction was seen in 7 cases and all those cases had extensive involvement of the nasal and paranasal sinus region (Table 2, Figure 5). The authors noted that there is no uniformity in selecting the IHC panel and in certain cases with the microscopic ap-

Table 1. Recent reported cases of extramedullary plasmacytoma of sinonasal origin.

Author/ Publishing year	Patient details Age/Gender	Presenting symptoms	Nasal endoscopy	Radiologic investigation	Radiological scan findings	Microscopic findings	IHC	Treatment
Ashraf et al.[3] 2013	20y/M	Paroxysms of sneezing Expectoration of a brown coloured mass	Not available	CT	Soft tissue mass in the left nasal cavity without bony destruction and septal deviation to the right side	Pure population of plasma cells with small, round, eccentric nucleus with perinuclear halo and abundant basophilic cytoplasm	Not available	Endoscopic excision
	48y/M	Epistaxis	Soft friable polypoidal mass occupying the left nasal cavity	CT	Mass involving the left medial canthus and base of the nasal pyramid	Sheet of discohesive neoplastic plasma cells with eccentric hyperchromatic nuclei with irregular chromatin distribution	CD38 positivity	Endoscopic excision followed by RT – 4400 cGy over 1 month
	60y/M	Epistaxis	Friable bloody tumour mass at the right middle meatus	Not available	Not available	Sheets of plasma cells	CD38, EMA positivity	Tissue biopsy followed by RT (Complete details not available)
Hazarika et al.[9] 2011	31y/M	Swelling in the right maxillary region involving the upper alveolus Right-sided nasal obstruction Right nasal discharge	Highly vascular mass in the region of the right upper alveolus and hard palate extending to the right nasal cavity	CECT	Moderately enhancing lesion in the right maxillary antrum with bony erosions extending to the right ethmoid sinus, sphenoid sinus, nasal cavity, and nasopharynx	Respiratory epithelium overlying an encapsulated tumour composed of sheets of plasma cells	Not available	Default treatment
	60y/M	Right-sided nasal obstruction Epistaxis	Highly vascular mass arising from the posterior end of the right inferior turbinate, filling the right choana	CT	Moderately enhancing soft tissue lesion arising from the right posterior end of the septum going to the nasopharynx, without bony erosion	Ulcerated hyperplastic respiratory epithelium overlying dense infiltrate of mature plasma cells, plasmacytoid cells with vesicular predominant nucleoli, Russel bodies and neutrophils. Stroma showed abundant eosinophilic material resembling amyloid	Not available	RT 30 Gy in 10 fractions followed by endoscopic laser excision of the residual lesion
Corvo et al.[11] 2013	51/F	Nasal obstruction (right > left) Epistaxis	Pale reddish broad tumour occupying 96% of the right nasal cavity and adhered to the lateral wall, intraorally a rough-surfaced tumour in the right gingivobuccal sulcus from the right incisor to the right first molar. Septal deviation to the left noted	CT	Expansive tumour lesion occupying both nasal fossae (right > left), with bone erosion at the level of the inferior and medial wall of the right maxillary sinus and the hard palate	Neoplastic growth in the chorion consisting of a mantle of plasma cells in a monotonous arrangement	Kappa chain donality with plasmacytoma features	RT 4870 cGy in 27 sessions followed by surgical excision after 12 months from diagnosis with degloving and transantral access
Hu et al.[12] 2020	64y/M	Nasal congestion Epistaxis Headache Decreased sense of smell Nasal odour	Red purulent outflow in the right nasal cavity, new biological stuffing with an unknown source and bleeds on touch	CT	Heterogenous right maxillary sinus and nasal cavity lesion; bone resorption in the medial wall of the right maxillary sinus	Ciliated columnar epithelium with diffusely arranged plasmacytoid tumour cells in the stroma	LPositive for CD79a, CD138, CD56, 30% Ki-67, vimentin	Removal of the polypoidal mass from the nasal cavity, uncinectomy and removal of the polypoidal mass from the right maxillary sinus
Rawat et al.[13] 2010	85y/M	Right nasal visible mass Epistaxis	Reddish pink mass completely occluding the right nasal cavity with the septum pushed to the right side	CT	Right nasal cavity mass	Undifferentiated large round cell tumour	Positive for CD79a, CD138, CD 56 with kappa light Chain restriction	Endoscopic excision of the mass followed by RT, 40 Gy in 20 sessions

Kadian et al.[14] 2021	54y/F	Nasal obstruction Breathing difficulty	Large polyp growing from the left inferior turbinate, causing 100% obstruction	CT	Left inferior turbinate lesion	Plasmacytoma	Not available	Left inferior turbinectomy with postoperative RT 45Gy in 25 fractions
Ishtiaq et al.[15] 2018	59y/M	Recurrent right epistaxis Right-sided facial pressure Occasional breathing difficulty through the right nasal cavity	Firm haemorrhagic mass in the right-side nasal cavity extending from the floor to almost two-thirds of the distance towards the posterior aspect of the nasal cavity	CT	Polypoidal mass in the right supero-medial nasal cavity at the middle meatus occluding the right superior nasal cavity	Plasma cell myeloma	Lambda chain clonality	RT 5040 cGy to the nose and 4000 cGy to neck nodes followed by endoscopic removal of the residual lesion
	61y/M	Right side maxillary sinus pain Ipsilateral epistaxis Rhinorrhoea	Bloody tumour mass occupying the right nasal cavity	CT MRI with contrast	CT – Heterogenous lesion involving the right maxillary sinus and nasal cavity with bone erosion (alveolar superior bone) MRI – hyperintense in T1, fluid attenuated, inversion recovery in FLAIR sequences and hypointense in T2 in the right maxillary sinus	EMP	CD138+ with kappa light chain restriction	RT 60 Gy, with history of recurrence 5 years later, treated with bortezomib/ dexamethasone and autologous bone marrow transplantation
Cantone et al.[16] 2017	60y/M	Right nasal obstruction Ipsilateral epistaxis Rhinorrhoea	Bloody tumour mass occupying the right nasal cavity	CT MRI with contrast	Soft tissue lesion involving the right nasal cavity and ethmoid sinus; no bone erosion. MRI – hyperintense signal in T1 and FLAIR sequence with hypointense in the T2 sequence in the right nasal fossa	EMP	Diffuse positivity for CD138	RT 60 Gy with history of three episodes of recurrence
	37y/F	Left nasal cavity obstruction	Bloody tumour mass occupying the left nasal cavity	CT and MRI	Left maxillary sinus and nasal cavity tumour lesion	EMP	CD 138+ with kappa light chain restriction	RT 40 Gy with two cycles of VAD and autologous BMT
Palacios et al.[17] 2002	62y/M	Small palpable mass in the left nostril	Darkish red submucosal mass in the left pyriform aperture area	CT	Soft tissue mass in the left anterior nasal cavity with periosteal reaction	Plasmacytoma	Not available	RT followed by surgical excision
Ando et al.[18] 2018	51y/M	Nasal bleeding Nasal obstruction	Not available	CT	Polypoidal lesion in the left nasal cavity	Large diffuse proliferation of plasmablastic tumours with centrally or peripherally located large round nuclei with prominent nucleoli. Abundant eosinophilic cytoplasm with perinuclear halo	CD3, CD56, EBER 1, CD138 positivity	CHOP regimen followed by 30 Gy / 10 fraction RT
Pantazidou et al.[19] 2021	51y/M	Nasal obstruction Dizziness Photophobia and diplopia of the left eye Cervical stiffness and pain Headache	Not performed due to cervical instability	CECT	Heterogenous soft tissue mass filling the left nasal cavity, with signs of mass effect of the left medial wall of the maxillary sinus, with no signs of erosion. Extensive osteolytic damage to the left lateral mass of the atlas, with disruption of the anterior arch and erosion of the transverse ligament	Plasmacytoma	CD138, CD56, CD79a, 30% ki-67, vimentin positivity	Not available

Belic et al.[20] 2013	44y/M	Right-sided epistaxis Right nasal obstruction	Dark red soft polypoidal tumour slightly bleeding on touch, in the right nasal cavity, arising from the last third of the septum, extending to the choana, obstructing the nasal cavity	CECT	Heterogenous soft tissue mass in the right nasal cavity, arising from the posterior septum, with mass effect on the medial wall of the right maxillary sinus	Intermediate differentiation extramedullary tumour of plasma cell origin	CD79α, CD138, CD38, MUM-1 and lambda positivity	Endoscopic excision followed by RT 50 Gy in 25 fractions
Ching et al.[21] 2002	63y/M	Right nasal blockage	Not available	CECT	Soft tissue mass filling the entire nasal cavity, with erosion of the nasal septum	Not available	Not available	RT
Lomeo et al.[22] 2007	32y/M	Asymmetrical facial pain Right periorbital swelling Blurred vision Nasal pressure Right nasal congestion with epistaxis	Red polypoidal mass eroding into the right middle turbinate and right osteomeatal complex	CT	Homogenous mass in the right maxillary area with extension to the fronto-ethmoid and periorbita, not involving the ipsilateral globe	EMP	Not available	Image guided endoscopic sinus surgery with post operative RT
Erkal et al[23] 2006	87y/F	Visible left nasal mass with epistaxis and difficulty in breathing	Friable lesion arising from the left maxillary sinus, extending to the nasal cavity and nasopharynx	MRI with contrast	T1 sequences – Soft tissue lesion posterior to the left maxillary sinus, obliterating the left nasal cavity, extending to the left nasopharynx, frontal and sphenoid sinus	Atypical plasma cells, characterized by eccentric nuclei and abundant cytoplasm that invaded the vascularized stroma beneath the stratified columnar epithelium	Kappa light chain positivity	RT 50 Gy in 25 fractions
Nakamura et al.[24] 2016	39y/F	Right nasal obstruction	Not available	MRI	Mass lesion in the right nasal cavity	Proliferation of large atypical plasmacytoid cells with enlarged nuclei and prominent nucleoli	CD138 positivity, kappa light chain restriction	RT 46 Gy in 23 fractions
Shahrizal et al.[25] 2009	54y/M	Epistaxis from right nostril Right-sided nasal blockage Hyposmia	Smooth bulbous mass in the right nasal cavity, attached to the anterior one third of the right middle turbinate with covering mucosa normal and in continuity with that of the turbinate	CT	Smooth spherical lesion arising from the right middle turbinate and obstructing the right osteomeatal complex	Fragmented polypoidal structures made of congested stroma infiltrated with sheets of ovoid neoplastic cells with eccentric hyperchromatic pleomorphic nuclei and occasional prominent nucleoli	Negative for MNF116, L26, CD45RO. Kappa and lambda light chain staining inconclusive	Excision
Meziane et al[26] 2011	42y/M	Headache Right nasal obstruction	Budding tumour of the right nasal cavity	CT	Mass on the right nasal cavity and maxillary sinus	Proliferation of plasma cells	CD 38 positivity, lambda restricted light chain	Spontaneous regression
Micozdadioglu et al.[27] 2009	70y/M	Nasal obstruction	Dark red mass in the right side of the septum, blocking the nasal cavity	CT	Mass located in the anterior part of the right nasal cavity with thinning of the nasal septum, mass not discriminated from the middle and inferior concha	Diffuse atypical plasma cell infiltration with ulcerated surface epithelium destroying the nasopharyngeal glands	CD 38 positivity, and kappa chain positivity with negative for lambda light chain	Trans nasal endoscopic excision

Adoga et al.[28] 2020	28y/F	Recurrent unprovoked left nasal bleeding	Fleshy finger-like mass filling the left nasal cavity extending from the roof, and bleeding easily on contact	CECT	Contrast enhancing isodense mass filling up the left nasal cavity with lateral deviation and erosion of the medial wall of the left maxillary sinus and extension to the left ethmoid sinus	Sheets of plasmacytoid cells, discrete, moderately pleomorphic with eccentric nuclei and prominent nucleoli. Abundant eosinophilic cytoplasm with perinuclear halo, with tumour cells invading the fibro-collagenous stroma	CD 10 and CD 38 positivity	Endoscopic surgical excision
Cheng et al.[29] 2021	23y/M	Progressive nasal congestion and nasal mass	Not available	MRI	Right nasal cavity mass, irregular thickening of the posterior wall of the nasopharynx, left arytenoid mass	Cytoplasmic red stained tumour cells with uniform size and nuclear deviation	Positive for CD79a, CD 99, MUM1, Lambda light chain, CD 38, Ki 67(20%+), EBV-EBER	PAD 3 courses, VRD 2 courses, CHOP 4 courses, decitabine-chidamide 9 courses
Windfuhr[30] 2002	60y/M	Left side palpable mass with slight breathing impairment.	Dark red submucosal mass at the pyriform aperture on the floor of the left nasal cavity	Not available	Not available	Monomorphous population of plasma cells	Monotypic lambda light chains, positive for CD138, Syndecan, and CD3 positivity in intermingled cells	RT 55 Gy in 28 fractions followed by surgical excision under microscopic vision
Baek et al.[31] 2005	65y/F	Left-sided nasal obstruction and blood-tinged crusting	Dark red mass on the left nasal septum	CT	Mass protruding from the mid part of the septum without involving the underlying septal framework	Uniform population of plasma cells	Kappa light chain positivity	Endonasal endoscopic excision
Raghuram et al.[32] 2022	45y/M	Epistaxis	Fragile mass attached to the roof of the left choana	MRI	Polypoidal mass in the left posterior nasal cavity, iso- to hypointense on T2 and T1 images	Sheets of plasmacytoid cells	Positive for CD138, MUM1, Lambda light chain, cyclin D1, Ki 67(60% +)	Endoscopic sinus surgery
Hu et al.[33] 2023	45y/F	Epistaxis Cough Dizziness, headache Nasal congestion Hyposmia	Pink neoplasm in the right nasal cavity with blood crust and pseudo membrane on the surface, enlargement of the maxillary sinus	MRI	Isointense on T1 and hyperintense on T2 images	Round cells, uniform in size, rich cytoplasm, skewed in nucleus.	Positive for CD138, CD 38, MUM 1, CD79a, BCL-2, Kappa light chains	Endoscopic resection followed by 52 Gy RT
Urso et al.[34] 2021	60y/M	Nasal congestion Rhinolalia	Not available	CT	Round lesion with exophytic growth placed in the medium and inferior meatus of the posterior left nasal cavity	EMP	Not available	VMAT 50 Gy in 25 fractions
Padhi et al.[35] 2020	75y/M	Left-sided nasal blockage	Pink polypoidal mass arising from the left nasal orifice	CT	Mass arising from the left nasopharynx with rightward deviation of the nasal septum	Large, atypical cells with variably eccentric nuclei, fairly abundant amphophilic cytoplasm, prominent nucleoli, occasional binucleated forms, a few Dutcher bodies, increased mitosis, and apoptosis	Positive for CD38, CD138, CD79a, MUM1, Kappa, IgA, BCL-2, CD 43, Ki 67-60%	RT 40 Gy

Abbreviations: BMT – Bo ne Marrow Transplantation, CECT - Contrast Enhanced Computerised Tomography, CHOP - Cyclophosphamide, Hydroxydaunorubicin, Oncovin (Vincristine), Prednisone, CT -Computerized Tomography, MRI - Magnetic Resonance Imaging, PAD – Bortezomib (PS-341), Adriamycin, Dexamethasone, RT - Radiotherapy, VAD - Vincristine, Adriamycin, Dexamethasone, VMAT - Volumetric Modulated Arc Therapy.

Table 2. Details of sites of bone destruction.

Bone destruction site	Frequency
Nasal cavity and sinus	4
Nasal cavity and septum	1
Nasal cavity and nasopharynx	1
Nasal cavity and spine	1

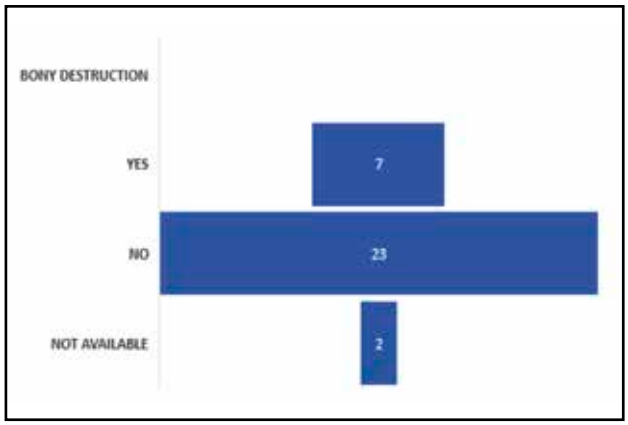


Figure 5. Chart showing frequency of bone erosion among cases.

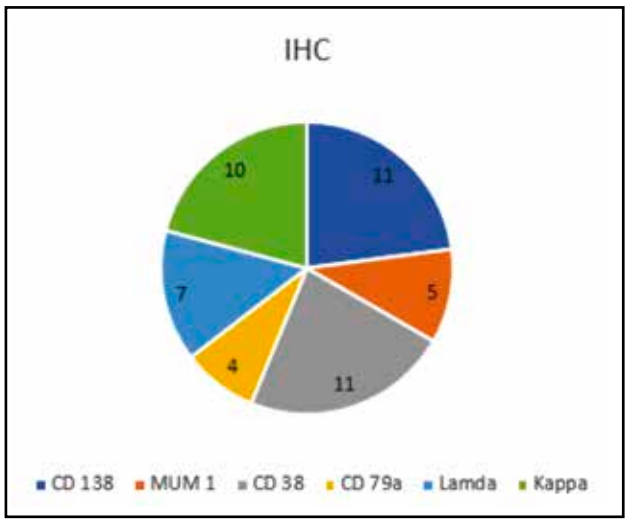


Figure 6. Frequency of positive IHC markers.

pearance of the lesion, the diagnosis of EMP was made. With the data available, 11 cases reported with positivity of CD138 and CD38. The clonality of immunoglobulin is an important factor in determining the neoplastic nature. In our review, only 19 cases were checked for either kappa or lambda chain restriction. The distribution showed 10 cases with kappa chain restriction and 7 cases with lambda chain restriction. Inconclusive results were observed for lambda and kappa chain with one case. The diagnosis was made based only on the H and E staining characteristics of the lesion (Figure 6).

27 cases had typical morphology of plasma cells, 3 cases exhibited plasmacytoid cellular features and one case each presented with plasmablastic and undifferentiated morphology (Table 3). The most commonly observed pattern of arrangement of cells was a sheet-like form (25%) (Table 4).

Surgery was the preferred method of treatment (17 cases). 7 patients underwent only surgical treatment, while in 3 patients, surgery was performed after attempted Radiation therapy. In 7 cases, surgery with postoperative radiotherapy was done. Radiation therapy was the only treatment modality in 10 cases. In 4 cases, various chemotherapeutic regimens were attempted due to the failure of either surgical or radiation therapy or a combination of both. 2 cases underwent bone marrow transplantation because of multiple remissions. Interestingly, one patient had a history of spontaneous regression (Table 5).

DISCUSSIONS

Plasma cell neoplasms encompass a spectrum of neoplasms characterized by monoclonal proliferation of terminally differentiated B cells – plasma cells. These are a group of diseases which include plasma cell myeloma, plasmacytoma, monoclonal immunoglobulin deposition disease, and plasma cell neoplasm with associated paraneoplastic syndrome[36]. Plasma cell myeloma is a relatively common haematolymphoid neoplasm associated with multifocal proliferation of plasma cell in the bone marrow, whereas plasmacytomas, which are localized proliferations of clonal plasma cells without involvement of the bone marrow, are relatively less common. Plasmacytoma can be osseous, which mainly involves the axial skeleton and bones with active haematopoiesis. Extraosseous plasmacytoma, also called extramedullary plasmacytomas, are even rarer. This was first described by Schridde in the year 1905[9]. The incidence rate of EMP is 0.1 per 100,000 persons. The mucosa of the upper air tract is the most commonly involved. Other involved sites are the gastrointestinal tract, lymph nodes, bladder, thyroid, breast, and CNS. EMP is a diagnosis of exclusion. A thorough clinical and laboratory evaluation, along with bone marrow examination, is necessary to rule out any possibility of

Table 3. Histomorphology of plasma cells and differentiation pattern.

Morphology	Frequency
Plasma cells	27
Plasmacytoid	3
Undifferentiated	1
Plasmablastic	1
Atypical cells	3
Differentiated cells	2
Intermediate differentiation	1

Table 4. Arrangement of plasma cell in tissues.

Arrangement	Frequency
Uniform population	8
Sheets	6
Infiltrative	1

Table 5. Treatment modalities offered.

Treatment	Frequency
Surgery	10
Radiation	14
Surgery with postoperative radiation therapy	7
Chemotherapy	4
Spontaneous regression	1

plasma cell myeloma, as secondary involvement in extramedullary sites is much more common than de novo occurrence.

The diagnosis of EMP is made using the international myeloma working group diagnostic criteria, which include: no M protein in serum and/urine, extramedullary tumour of clonal plasma cells, normal bone marrow, normal skeletal survey and no related organ or tissue impairment[37].

Age

The disease is more commonly observed in elderly males aged above 40 years. In our review, the average age was 52.68 years with a median of 56.51 years. However, the literature showed seven cases of EMP in the age group less than 40 years, out of which one patient was undergoing treatment for human immunodeficiency virus (HIV)-related disease. The simultaneous occurrence of HIV and EMP has not been reported elsewhere; hence, the role of HIV in the pathogenesis of EMP cannot be established. HIV diseases are known to cause lymphomas of the head and neck region. The same mechanisms may lead to the pathogenesis of EMP[9]. This is also supported by a case reported by Nakamura et al.[24], where a case of EMP was seen in a known case of mucosa-associated lymphoid tissue lymphoma (MALToma) following treatment with rituximab. The CD20 inhibitor has also been associated with histological transformation of MALT lymphoma into plasmacytoid changes[24]. Though considered to be a disease of the 5th and 6th decade, two cases have been noted in the age group of more than 80 years[13,23].

Clinical picture

In our systemic review of 32 cases, the lesion showed a right-sided preponderance, with a ratio of 5:4. Clinical features usually depend on the site of the tumour and tumour mass size. Anjos Corvo et al.[11] reported a case of giant sinonasal EMP with expansile features, where the patient presented with a history of nasal obstruction and self-limiting nasal bleed. The majority of the EMPs of the sinonasal region present with nasal obstruction leading to difficult nasal breathing, nasal discharge, not responding to conservative management, or self-limiting spontaneous epistaxis. EMPs can also cause headache, anosmia, or chronic cough[12]. In our review, 4 patients reported complaints of pain in the craniofacial area, such as headache or facial pain, and only one patient exhibited bone destruction in radiological studies. Another rare presentation is the presence of a visible nasal mass in cases of long-standing or neglected EMPs of sinonasal origin[13,17]. The tendency to bleed upon manipulation sometimes prompts the surgeon to perform an office-based nasal endoscopy. In such situations, it might be difficult to clearly delineate the exact characteristics of the lesion. Due to the rarity of the condition, the initial diagnosis in most of the cases was nasal polyp or inverted papilloma with polypoidal changes. The clinical history of epistaxis may lead the clinician towards the diagnosis of malignancy of the nasal cavity.

Radiological evaluation

The choice of radiological investigation is still a topic of debate. Computerized tomography scans are considered as the first line of investigation, either with or without contrast. Plasmacytomas appear as soft tissue lesions with heterogenous intensity on contrast-enhanced CT scans. The tumour may show bony erosions, which can present as sclerotic or lytic lesions. The expansive nature of these lesions can

sometimes lead to pressure necrosis of bony structures. The bone erosion may mimic other malignant lesions of this region, such as squamous cell carcinoma, adenocarcinoma, lymphoma, or distant metastasis from other primary sites. In the present review, 7 cases reported with signs of bone destruction and the CT scan was the radiological investigation in all of these cases. The enhancing property of these lesions is variable. In our analysis, 4 cases were noted to have heterogenous enhancement, and two cases exhibited moderate enhancement.

Another radiological imaging modality is the magnetic resonance imaging, which is more useful in cases of extension into the orbit or doubtful cases of intracranial extension. The use of MRI offers the added advantage of radiation-free environment.

A whole-body PET-CT is useful in cases of multiple site involvement.

CT and MRI imaging complement each other and should be the investigations of choice. It is important to note that radiological imaging alone is not conclusive for the diagnosis. These investigations help the clinician in planning the treatment modality and approach[21,38].

Histopathology and immunohistochemistry

Histopathological examination, along with other ancillary techniques, helps establish the diagnosis. IHC aids in determining the plasma cell origin and clonality. Histological examination reveals diffuse sheets of plasma cells and also help rule out other lymphomas with plasmacytic differentiation. One out of 32 patients in our review exhibited plasmablastic cells and one had an undifferentiated cellular architecture. Interestingly, both of these cases were found to have limited disease. Marginal zone lymphoma and lymphoplasmacytic lymphomas are the two mature B cell neoplasms that can show extensive plasmacytoid features. However, extensive sampling of the tissue may reveal areas with a B-cell component. IHC shows CD138, CD38, and MUM-1 positivity. There is reduced weak expression of CD56 and cyclinD1 compared to plasma cell myeloma. The CD20 expression in the neoplastic cells should raise the possibility of lymphomas over plasmacytoma[2,3,5].

Though rare, these tumours can progress to multiple myeloma; however, the rate of progression is much lower with EMP as compared to solitary bone plasmacytoma. In our review, none of the patients reported progression of the disease, although a few cases reported relapse at the local site.

The Wiltshaw et al. classification[39] is the most accepted clinical staging system for soft tissue plasmacytomas. In this classification, stage 1 denotes limited extramedullary site involvement, stage 2 indicates involvement of regional lymph nodes and stage 3 is characterized by the presence of distant metastasis. It is of utmost importance to rule out other benign and malignant neoplasms in cases of stage 2 and 3 soft tissue plasmacytomas. Benign neoplasms mimicking EMPs may include lesions with the presence of plasma cells seen in chronic granulomatous conditions such as rhinoscleroma and plasma cell granulomas. To differentiate from other pathologies, one important factor to note is clonality. Monoclonal origin points towards EMPs whereas multiclonal origin is suggestive of an inflammatory pathology in most cases. The use of IHC is helpful in reaching the correct diagnosis in such confusing scenarios[1,2].

The diagnosis of EMP is incomplete without a bone marrow examination. It is imperative to rule out any involvement of the bone marrow as extramedullary involvement can also be seen in cases of the aggressive form of primary marrow disease, such as multiple myeloma. One simple screening tool to rule out myeloma is examining for the presence of Bence Jones protein (BJP) in the urine, which is a homogenous immunoglobulin light chain. The absence of BJP in urine favours the diagnosis of EMP. The excess of BJP points towards increased production of either light chain kappa or lambda, which further warrants serum electrophoresis. To summarize, EMP is a diagnosis of exclusion[1-4,40,41].

Treatment

The treatment protocol includes various modalities like radiation therapy, chemotherapy, surgery, a combination of different modalities and, finally, bone marrow transplantation. The cornerstone of management strategies is to achieve a good locoregional and distant site disease-free interval. There is no consensus on the choice of primary treatment. The role of surgery as a single modality treatment is controversial, as incomplete excision may necessitate adjuvant therapies. However, in cases where patients are not motivated for frequent follow-up visits and investigations, this approach can be considered. The quality of life following different treatment methods has to be evaluated in detail to reach a consensus on treatment strategies.

The management mainly involves surgery, where complete removal of the mass should be ensured, followed by radiotherapy. The surgical approach is usually endoscopic transnasal, but, in extensive and expansive lesions, lateral rhinotomy may be necessary. As the tumour is highly radiosensitive, local radiation therapy has shown equal results to surgery in terms of locoregional control. The choice of treatment should be based on the extent of the lesion, as very large lesions causing complete nasal obstruction may not benefit symptomatically from radiation therapy. The side effects of radiation can further cause morbidity to the patient[42]. Neoadju-

vant radiotherapy followed by surgery is also a treatment protocol which was carried out in 5 of the cases. Postoperative radiotherapy may help to achieve a better locoregional control.

Chemotherapy is indicated only in relapse and refractory cases or cases where the surgery is not possible. Jacevičiūtė et al.[43] suggested the administration of chemotherapeutic agents in the anaplastic variant of EMPs. The widely used chemotherapeutic drugs include cyclophosphamide, melphalan, lenalidomide, bortezomib, cisplatin, doxorubicin and bendamustine. Newer immunological agents included in the chemotherapy regimens are daratumumab (anti CD38) and elotuzumab (SLAMF7 antibody of IgG1 type). Daratumumab is used in combination therapy, whereas elotuzumab can be an effective monotherapeutic agent. In a recalcitrant case reported by Cheng et al.[29], various chemotherapeutic regimens were administered in an attempt to achieve remission of the disease. The treatment included 3 cycles of PAD (Bortezomib, Doxorubicin, Dexamethasone), followed by two cycles of VRD (Daratumumab plus Bortezomib, Lenalidomide, Dexamethasone) and 4 cycles of CHOP (Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone). The disease control was achieved with 9 cycles of decitabine and chidamide. In a 51-year-old case reported by Ando et al.[18], the lesion was managed with CHOP regimen followed by radiotherapy. In a case reported by Cantone et al.[16], bortezomib was administrated for the recurrence of the lesion after 5 years from the initial radiotherapy treatment.

Radiotherapy is recommended to achieve locoregional disease control, with a dose of 40-45 Gy in 20-22 fractions if the tumour size is less than 2 cm and 50-55 Gy for larger tumours. The prognosis depends on the size of the lesion and nodal involvement at the time of presentation.

Bone marrow transplant is also a treatment option in plasma cell disorders with marrow involvement. 2 out of 32 cases underwent bone marrow transplant. Though rare, a case of spontaneous resolution of the plasmacytoma was also found in our review. Positron emission tomography CT is the gold standard investigation for clinical staging and evaluating suspected cases of relapse. EMPs have very good prognosis with a 10-year survival rate of 70-80%. Stage 2 and 3 disease, incomplete surgical clearance and resistance to chemo-radiotherapy worsen the prognosis[44,45].

Considering the relatively high rate of relapse or recurrence when compared with other benign lesions, patients diagnosed with EMP should be kept on regular follow-up.

PERSONAL EXPERIENCE

A 53-year-old male presented to the ENT outpatient department in March 2023 with complaints of left nasal blockage and difficulty breathing. He also reported experiencing on-and-off headaches. Diagnostic nasal endoscopic examination (DNE) of the patient revealed a pale pedunculated mass arising from the left middle turbinate, extending up to the anterior end of the middle and inferior turbinate (Figure 7). The rest of the physical examination revealed no additional details. Following this, a non-contrast computerized tomography of the nose and



Figure 7. Diagnostic nasal endoscopy showing a polypoidal mass arising from the left middle turbinate area, extending anteriorly.

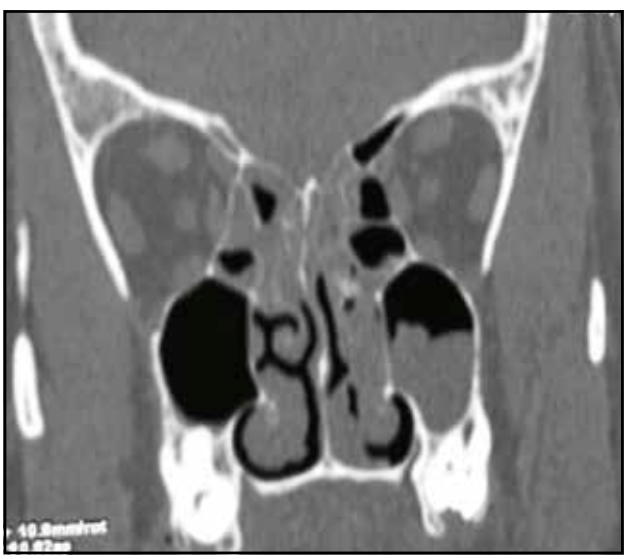


Figure 8. CT of the nose and paranasal sinuses, coronal section showing soft tissue lesion arising from the left middle turbinate, with extension to the maxillary sinus.

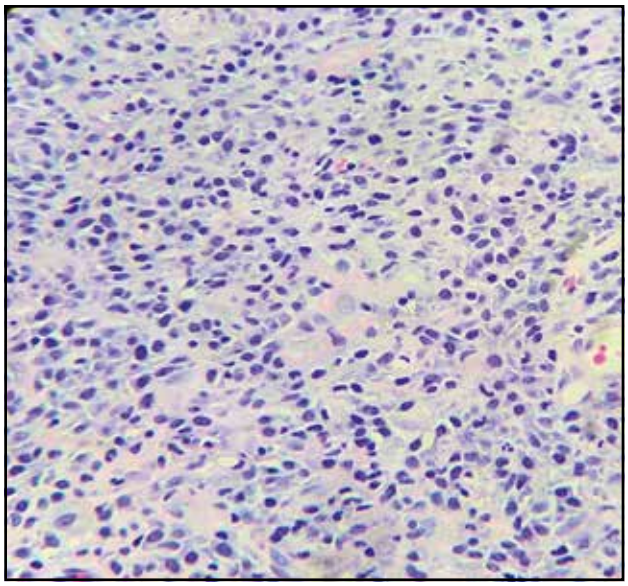


Figure 9. Histopathological examination with hematoxylin and eosin stain showing plasma cell proliferation.

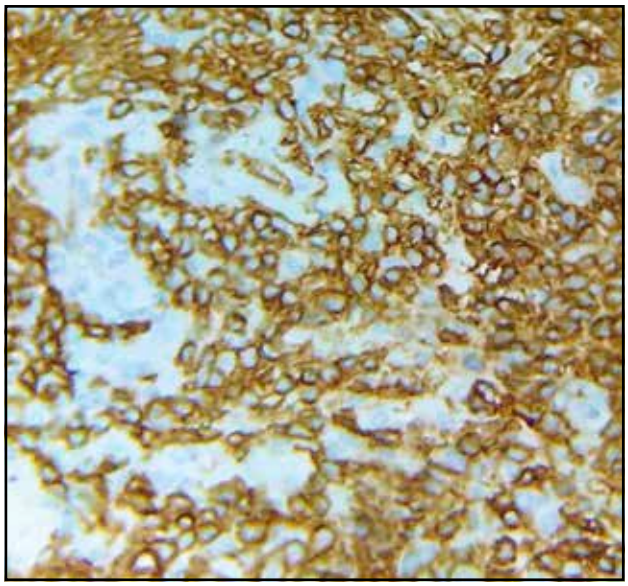


Figure 10. Immunohistochemistry showing CD138 positivity.

paranasal sinuses was performed, which showed soft tissue lesion involving the middle turbinate, extending anteriorly to the involved turbinate. The radiologist reported the scan as inverted papilloma (Figure 8). The patient underwent endoscopic excision biopsy with partial middle turbinectomy, inferior turbinectomy and middle meatal antrostomy on the 28th of March 2023. A retrospective staging was done according to the Wiltshaw et al.[39] criteria, and the patient was classified as having stage 1 EMP of the nasal cavity.

Histopathological examination showed diffuse sheets of atypical plasma cells. Occasional binucleate and multinucleate forms were also identified in the histological examination. Immunophenotyping showed CD138, MUM-1 and CD38 positivity with lambda light chain restriction (Figure 9, Figure 10). Radiological, haematological, biochemical, and bone marrow findings did not show any features of plasma cell myeloma and a diagnosis of extramedullary plasmacytoma of sinonasal origin was made.

The case was presented in the institutional tumour board meeting and the patient was referred to the Oncology Department for further management on postoperative day 10. In view of limited disease, chemotherapy was not included in the treatment plan. The patient received 40 Gy radiation therapy in 20 fractions over 4 weeks.

The patient has been on regular follow-up since receiving the last dose of radiation. Diagnostic nasal endoscopy and clinical examination of the neck are performed at each hospital visit, and the patient is currently free of any locoregional recurrence.

The patient consent was obtained for the inclusion of relevant images in the publication and the study has been conducted in accordance with the ethical standards outlined in the Declaration of Helsinki (2013 amendment).

CONCLUSIONS

Extramedullary plasmacytoma of the nasal cavity is a relatively uncommon condition, primarily observed in elderly males. It typically presents with non-specific symptoms such as nasal blockage, difficulty in nasal breathing, spontaneous self-limiting nasal bleeding, or facial pain. The clinical examination may not immediately point towards the diagnosis, as the appearance of the lesion is polypoidal. The evaluation in suspected cases includes radiological examination, and diagnosis is confirmed by tissue histopathology and immunohistochemistry. Treatment modalities include surgical intervention, radiation therapy and sometimes chemotherapy. Extramedullary plasmacytoma can progress to multiple myeloma over time.

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