



# Squash Cytology Diagnosing Plasmacytoma of Frontal Bone as First Presentation of Nonsecretory Multiple Myeloma

Vaishali B. Nagose<sup>1,2</sup> Swapnil B. Patil<sup>3</sup> Neha A. Mahajan<sup>2</sup>

<sup>1</sup> Department of Pathology, GMC Sindhudurg, Maharashtra, India

<sup>2</sup> Department of Pathology, DUPMCH, Jalgaon, Maharashtra, India

<sup>3</sup> Department of Surgery, DUPMCH, Jalgaon (Khurd), Maharashtra, India

Address for correspondence Vaishali B Nagose, MD, Flat No 306, B Wing, Gyan Chetna Residency, Opposite Godavari College of Engineering, Jalgaon, Maharashtra, 425001, India (e-mail: vaishali.nagose@gmail.com).

Asian J Neurosurg 2023;18:661–666.

## Abstract

Plasmacytoma of bone is one of the criteria for diagnosing plasma cell myeloma (multiple myeloma). A plasmacytoma involving a frontal bone is unusual, with only few being reported so far. Also, when typical clinical presentation is absent, diagnosis is usually not suspected clinicoradiologically. We report a rare case of frontal bone plasmacytoma presenting as a lump over the forehead, the squash cytology of which gave the diagnosis of neoplastic etiology. Thus, squash cytology helped in early and definitive diagnosis in this patient, hastening meticulous diagnostic investigations and appropriate management. With full workup, the final diagnosis of a nonsecretory multiple myeloma was made.

## Keywords

- ▶ plasmacytoma
- ▶ plasma cell neoplasm
- ▶ myeloma
- ▶ frontal bone
- ▶ squash cytology

## Key Messages

Intraoperative cytology (squash) can give the accurate diagnosis of the neoplastic process of plasma cells rather than as reactive plasmacytomas, so as to commence the battery of diagnostic tests of plasma cell neoplasms required in no time for correct final diagnosis paving the way for rapid management.

## Introduction

Multiple myeloma (plasma cell myeloma [PCM]) and solitary plasmacytoma are plasma cell neoplasms.<sup>1</sup> The rare nonsecretory subtype (nonsecretory myeloma [NSM]) of the latter (1–5% of PCM) does not have the diagnostic M band or raised serum-free light chains. Solitary plasmacytoma of bone (SPB) is a tumor localized in the bone, composed of monoclonal plasma cells without any clinical features of PCM and no physical or

radiographical evidence of additional plasma cell tumors. PCMs usually present with weakness, bone pain, infections, bleeding, and occasionally with neurological manifestations.<sup>1</sup> NSMs/PCMs and SPB presenting as a plasmacytoma are unusual as is cytology as the initial investigation for diagnosing plasmacytoma. Thus, the present case is unique in that plasmacytoma was diagnosed on squash cytology, which hastened full workup and confirmed the diagnosis of NSM in a short time.

## Case History

A 65-year-old male patient presented with a 1-year history of swelling over the right side of the forehead that gradually increased in size (▶ Fig. 1A). There was associated pain for the past 3 months with absence of neurological symptoms. On examination, the swelling was bony, 8 × 10 cm in size extending up to the vertex. There was no neurodeficit.

article published online  
September 27, 2023

DOI <https://doi.org/10.1055/s-0043-1774397>.  
ISSN 2248-9614.

© 2023. Asian Congress of Neurological Surgeons. All rights reserved.

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India



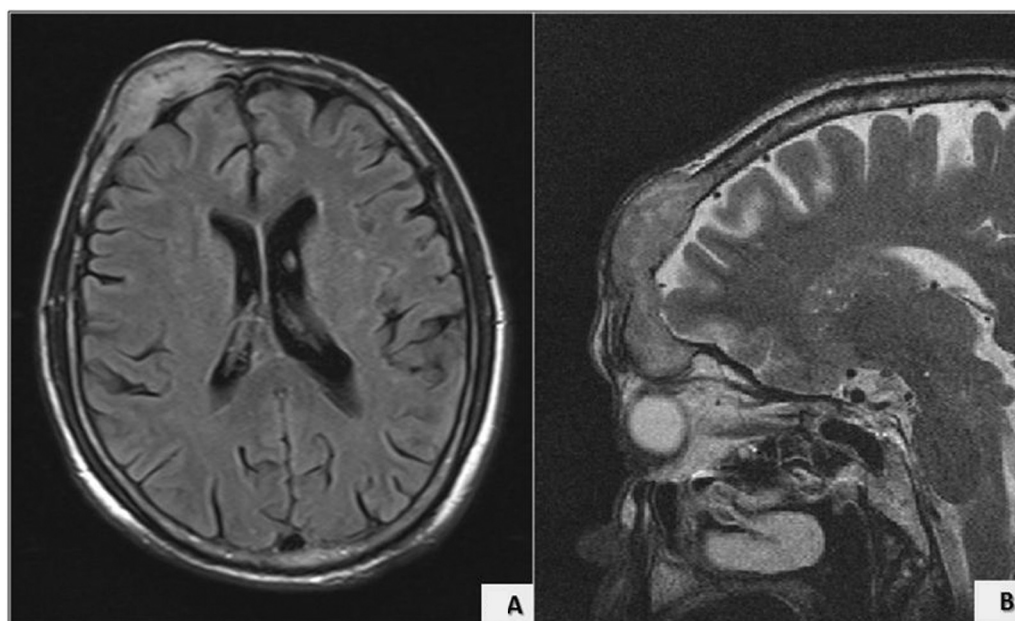
**Fig. 1** (A) Right-sided forehead swelling. (B) Intraoperative right frontal bone swelling.

Magnetic resonance imaging (MRI) of the brain showed an ill-defined extra-axial solid mass lesion (space occupying lesion [SOL]) in the right frontal region with both intracranial and extracranial extension, the former abutting the right frontal lobe and the latter causing thickening and expansion of the inner and outer tables of the right frontal bone (**Fig. 2**). Thus, the diagnosis of meningioma was made.

Right frontal craniotomy and near-complete excision of this frontal extra-axial SOL (intraoperatively found to be bony mass) was performed with a 2-cm bony margin circumferentially

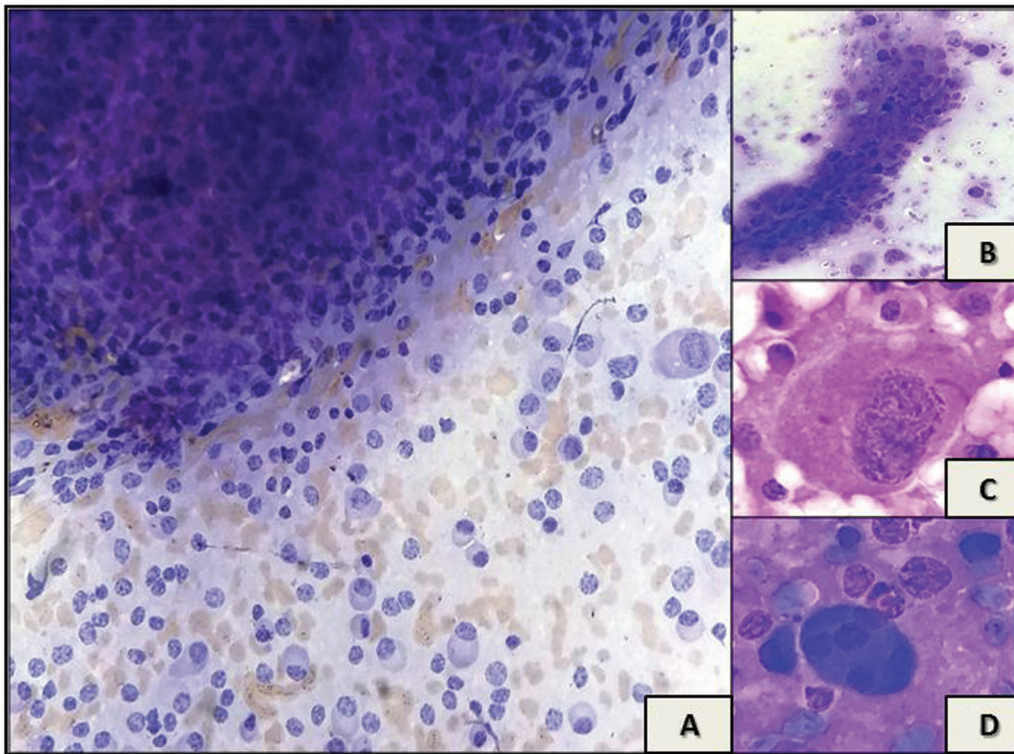
(**Fig. 1B**). The bony mass was found to be densely adhered to the underlying dura, and was thus excised along with it. The dural defect was repaired with the pericranium. Intraoperatively, a bit of the tumor was sent for squash cytology. The smears were hypercellular, consisting of plasma cells of mature, immature, pleomorphic, and blastemic morphology (**Fig. 3**). The tentative diagnosis of plasmacytoma of the frontal bone was conveyed.

A bony tissue measuring  $6 \times 5 \times 2$  cm, having concave surface covered by the dura on one surface, was received in the histopathology department (**Fig. 4**). A grayish brown

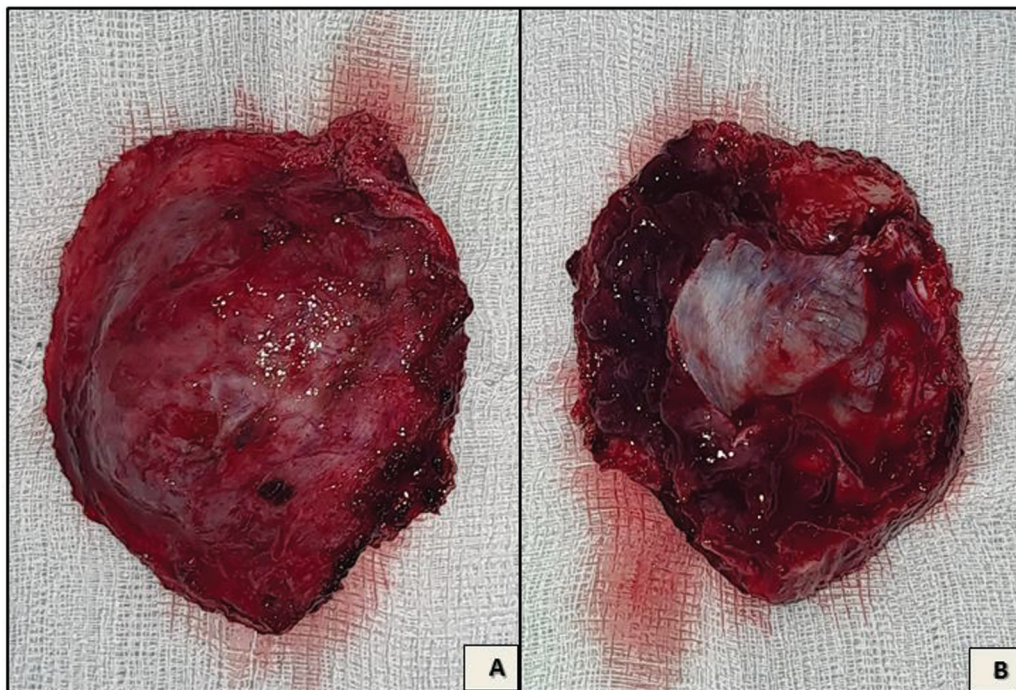


**Fig. 2** (A) Fluid-attenuated inversion recovery (FLAIR) image (plain magnetic resonance imaging [MRI] of the brain) and (B) Sagittal T2 MRI. A well-defined intraosseous mass in the right frontal bone with adherence to the underlying dura and abutting the right frontal lobe.





**Fig. 3** Squash cytology. (A) Tumor mass composed of pleomorphic immature plasma cells (large nuclei with open chromatin and at places prominent nucleoli; Giemsa, 400x). (B) Tissue fragment (papillary; Giemsa, 400x). (C) Gigantic immature plasma cell (Giemsa, 400x). (D) Multinucleated plasma cell (Giemsa, 400x).



**Fig. 4** Gross specimen. (A) Outer convex surface. (B) Inner concave surface showing removed adherent part of the dura and grayish brown tumor on bone table.



tumor measuring  $5.5 \times 2 \times 4.5$  cm was present in the bone table. On the cut section, a friable, soft tumor with areas of hemorrhage attached to both the dura and the bone was noted.

Microscopically a neoplasm composed of mature, immature, plasmablastic, or anaplastic plasma cells arranged in sheets, eroding adjacent bone, and infiltrating dura at places was seen (**Fig. 5A**). The mitotic count was 5 to 6/10 high power field. Thus, histopathologically plasmacytoma of the bone was confirmed. As there was absence of clinical features of PCM and physical evidence of additional plasma cell tumors, radiographical studies—skeletal survey including MRI and computed tomography (CT)—were advised soon after the operative procedure (day 1). No other bone lesions were found.

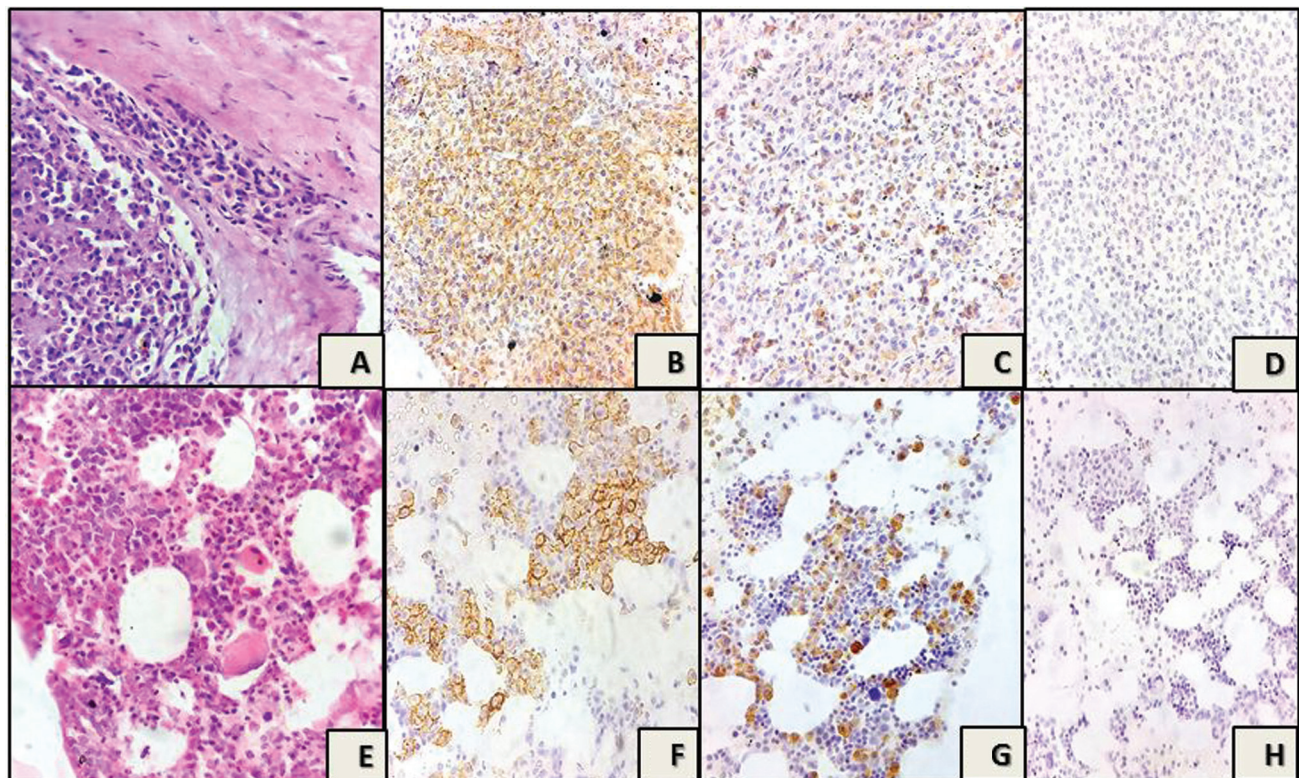
The preoperative workup had showed hemogram with low hemoglobin (10 g/dL,  $>2$  g/dL below the normal lower limit). Peripheral blood smear showed normocytic anemia. Postoperatively bone marrow aspiration (BMA) and bone marrow biopsy (BMB) were done. The bone marrow plasma cell percentage was 12%. The immunohistochemistry of the BMB as well as the frontal plasmacytoma proved the monoclonality of the proliferating plasma cells. They were immunopositive for CD138 with expression of only lambda light chains and immunonegative for kappa light chain (**Fig. 5**). Bone marrow iron stores were normal. M band was not detected on serum electrophoresis (no evidence of

monoclonal gammopathy) and serum-free light chain was not increased by immunofixation and electrophoresis. Urinary Bence Jones proteins were positive and 24-hour urinary proteins were 772.5 mg/d. Kidney function test including serum creatinine and serum calcium levels were normal. Final diagnosis of nonsecretory PCM, that is, nonsecretory multiple myeloma was made.

The patient was advised postoperative irradiation and systemic chemotherapy (12 cycles of bortezomib, cyclophosphamide, and dexamethasone [VCD] regimen weekly). He completed his chemotherapy without any recurrence of the frontal swelling or any new complaint to date.

## Discussion

Plasma cell neoplasms consist of plasmacytoma (localized tumors consisting of monoclonal plasma cells), PCM (multiple myeloma), monoclonal immunoglobulin deposition diseases, and plasma cell neoplasms with associated paraneoplastic syndrome. The NSM is a rare variant of PCM ( $<2\%$  of PCM). In PCM, mass disease or organomegaly may be present on examination in 10% of patients due to extramedullary plasmacytomas or amyloidosis. However, initial diagnosis with cytology is quite uncommon, with only few such cases being reported.<sup>2-4</sup> All of them are done by fine-needle aspiration (FNA) cytology. As there is cortical bone destruction in bony lesions of PCM, they are amenable by



**Fig. 5** Forehead mass biopsy (upper A–D) versus bone marrow biopsy (lower E–H). Both show (A,E) diffuse plasma cells infiltrate the monoclonality that was proven by the expression of (B,F) CD138, (C,G) the lambda light chain, and (D,H) negative for the kappa light chain.

FNA with a rich cell yield. However, the present case was diagnosed on squash cytology as FNA was not possible here.

Solitary plasmacytomas including solitary bone plasmacytoma and solitary extramedullary plasmacytoma are diagnosed only after excluding systemic disease by skeletal survey, the plasma cell infiltration lower than 10% of the bone marrow by BMA and BMB, and lack of myeloma-related organ dysfunction.

Any kind of systemic involvement in a case of plasmacytoma confirms PCM.<sup>1</sup> However, the presence of more than 10% clonal bone marrow plasma cells with biopsy-proven bony or extramedullary plasmacytoma is diagnostic of PCM and here the absence of the myeloma defining events (MDEs) makes no difference. In the present case, there was clonal proliferation of plasma cells both in the bone marrow (12%) and in the frontal plasmacytoma. Systemic involvement was evident from hemoglobin >2 g/dL below the normal lower limit, and positive urinary Bence Jones proteins and elevated 24-hour urinary proteins (772.5 mg/d) were also present. However, the urinary Bence Jones proteins and elevated 24-hour urinary proteins are not included in the criteria for diagnosis of PCM, although they support the diagnosis. Anemia in these cases results from bone marrow replacement and renal damage. The absence of M band and raised serum-free light chains have to be confirmed by a serum protein electrophoresis (SPEP), serum immunofixation, and serum-free light chain (FLC) assay. The true nonsecretory disease patients have no evidence of an M protein on any of the above studies, similar to the present case, which constituted less than 2% of PCM patients. Clinically, the NSM cases have a lower incidence of renal insufficiency and hypercalcemia as compared to other PCMs.

Plasmacytomas are usually present in the vertebrae and ribs. The solitary frontal bone involvement without other bony lesions or bone pain is quite unusual.<sup>5</sup> This patient presented with forehead swelling for more than 1 year, but local pain was presented only from the past 3 months.

Clinically, the differential diagnosis of nontraumatic scalp masses associated with bone lesions includes hematological malignancies: Langerhans cell histiocytosis and lymphoma, and others like intraosseous hemangioma, atypical and malignant meningioma, and metastases.<sup>6</sup> Plasmacytoma, rare in this site, may arise as a primary from the skull bone or intracranial extramedullary lesion arising from the dura and brain.<sup>5</sup> The neurological abnormalities at presentation may be headache, nausea, vomiting, visual disturbances, etc., resulting from raised intracranial tension.

Radiologically, the intracranial ones manifest as dura-based hyperintense lesions on both CT and T2-weighted MRI scans. Uniform enhancement is seen on contrast CT and variable enhancement is seen on MRI after gadolinium. Dural involvement with expansion of the bone table in this case gave rise to the radiological diagnosis of meningioma.

The squash cytology, however, showed the mass was composed of plasma cells. Features of immaturity such as open or more dispersed nuclear chromatin, a higher nuclear-

to-cytoplasmic ratio, and frequent prominent nucleoli were present. Multinucleated and pleomorphic plasma cells were also seen (►Fig. 3C, D). Nuclear immaturity and pleomorphism correctly indicated neoplastic proliferation of these cells and not reactive. These features are the same as seen in cytology by FNA. Both squash cytology and frozen sections (FSs) are able to distinguish plasma cell tumors easily. However, on FSs, distinguishing plasmacytomas from metastatic carcinoma may not be readily possible sometimes. Occasionally, on FS, the morphology of the plasma cells may not be plasmacytoid, and freezing artefacts/icy crystals may complicate it further.<sup>7</sup> Squash cytology is helpful here as the plasmacytoma shows the absence of sheets and aggregates of neoplastic cells unlike metastatic carcinoma. Also, when such cohesive plates and three-dimensional groups of metastatic cells are found in smears, these cluster edges are sharp and well defined.<sup>8</sup> There might be difficulty in squash smear preparation due to the rubbery consistency of plasmacytomas in the form of crush artefacts, which will be absent in ideal smear preparations revealing the plasmacytoid nature of these lesions.

Intraoperative investigations such as squash cytology and FS on cryostat have the advantage of rapid diagnosis with diagnostic accuracy of squash cytology being 74 to 95% and FS being 75 to 99%.<sup>9,10</sup> The role of inexpensive and simpler intraoperative cytology—squash cytology<sup>9</sup>—in rapid diagnosis and guiding the management, especially in resource-limited settings (in the absence of cryostat for FS) was yet again proved here as it paved the way for hastening the battery of tests required for accurate diagnosis of NSM in this case. This can lead to a reduction in the length of hospital stay. On post-op day 1 itself full-body scan was advised, as were kidney function tests, serum calcium, 24-hour urine proteins, Bence Jones urine test, and serum electrophoresis for M band, which were done quickly. On post-op day 5, BMA and BMB were done. BMA and BMB showed plasma cells scattered interstitially, with normal hematopoiesis being evident (►Fig. 5D). The cytological features of immaturity and pleomorphism in plasma cells were observed again. In absence of the M band, IHC was advised on plasmacytoma and BMB to confirm the clonality of the plasma cells. Both tissues showed positive staining for CD138 and lambda in absence of kappa light chain (►Fig. 5), thus proving clonality and ruling out other neoplasms including lymphomas with marked plasma cell differentiation.<sup>11,12</sup>

The treatment of NSM is the same as the standard treatment for PCM, although there is difficulty in monitoring the response. The prognosis of NSM is similar to other PCMs. Survival is better for patients with normal free light chain ratio than those with an abnormal ratio.

## Conclusion

To conclude, present case proves the importance of intraoperative cytology yet again in the accurate diagnosis of neoplastic process of plasma cells, so as to commence the battery of diagnostic tests required in no time.

**Author Contributions**

Nagose VB has contributed in concept, design, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, manuscript preparation, editing, review and is acting as guarantor. Patil SB has contributed to concept, design, definition of intellectual content, clinical studies, data acquisition, manuscript editing and review. Mahajan NA has contributed to concept, clinical studies, data acquisition, manuscript editing and review.

**Funding**

None.

**Conflicting Interest**

None declared.

**References**

- 1 Rajkumar SV. Multiple myeloma: 2022 update on diagnosis, risk stratification, and management. *Am J Hematol* 2022;97(08):1086–1107
- 2 Gargava A, Vaidya S, Sharma JK. Solitary plasmacytoma of frontal bone: a case report. *Indian J Otolaryngol Head Neck Surg* 2019;71 (Suppl 3):1944–1947
- 3 Sahu KK, Kumar PDA, Yanamandra U, Malhotra P. Macrofocal multiple myeloma with frontal plasmacytoma. *BMJ Case Rep* 2015;2015:bcr2015210759
- 4 Saksena A, Mahajan N, Agarwal S, Jain S. Solitary bone plasmacytoma: an interesting case report with unusual clinico-cytological features. *J Cytol* 2014;31(03):158–160
- 5 Peker BC, Ataizi ZS, Ozbek Z. Solitary plasmacytoma of the frontal bone. *J Korean Neurosurg Soc* 2021;64(02):316
- 6 Trejos T AM, Cuartas M MC, Korenfeld K Y, Cardona Q R. Giant forehead plasmacytoma as a growing lump in a patient with multiple myeloma. *Radiol Case Rep* 2020;15(12):2589–2593
- 7 Liu Y, Qiu J. Solitary intracranial plasmacytoma located in the clivus: a diagnostic and therapeutic challenge. *N Am J Med Sci (Boston)* 2012;5(04):232–234
- 8 Acharya S, Azad S, Kishore S, Kumar R, Arora P. Squash smear cytology, CNS lesions –strengths and limitations. *Natl J Lab Med.* 2016;5:1–7
- 9 Jain S, Kaushal M, Choudhary A, Bhardwaj M. Comparative evaluation of squash smear and frozen section in the intraoperative diagnosis of central nervous system tumours. *Cytopathology* 2022;33(01):107–113
- 10 Nanarng V, Jacob S, Mahapatra D, Mathew JE. Intraoperative diagnosis of central nervous system lesions: comparison of squash smear, touch imprint, and frozen section. *J Cytol* 2015;32(03):153–158
- 11 Bataille R, Jégo G, Robillard N, et al. The phenotype of normal, reactive and malignant plasma cells. Identification of “many and multiple myelomas” and of new targets for myeloma therapy. *Haematologica* 2006;91(09):1234–1240
- 12 Ocqueteau M, Orfao A, Almeida J, et al. Immunophenotypic characterization of plasma cells from monoclonal gammopathy of undetermined significance patients. Implications for the differential diagnosis between MGUS and multiple myeloma. *Am J Pathol* 1998;152(06):1655–1665