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# A retrospective study of correlation of morphologic patterns, MIB1 proliferation index, and survival analysis in 134 cases of plasmacytoma

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ABSTRACT

Plasmacytoma classified into solitary plasmacytoma of bone (SPB) and extramedullary plasmacytoma (EMP) is characterized by infiltrate of plasma cells of diverse maturity and by their monoclonal immunoglobulin products. Both SPB and EMP represent different groups of neoplasm in terms of location, tumor progression, and overall survival rate. There is a need for features that indicate likelihood of myeloma in patients with plasmacytoma without other manifestations. This study was an attempt to study the morphologic patterns of plasmacytoma (SPB and EMP), MIB1 proliferation index, and correlation of these with clinicopathologic features and survival of the patients. The study group comprised of 134 cases of plasmacytoma (88 SPB and 46 EMP) over duration of 8 years and were graded as per Bartl's histologic grading system. Commonest site was vertebral body in SPB (36%) and upper aerodigestive tract in EMP (48%). On serum electrophoresis, overall M band was detected in 41% cases. Both SPB and EMP on histology revealed similar morphologic features. MIB1 proliferation index ranged from less than 1% to 80%. It was slightly higher in EMP in comparison with SPB ($P$ value = .002). Seventy percent of cases, which progressed to multiple myeloma (MM) showed MIB1 labeling index more than 10%; however, it was not statistically significant in predicting the disease progression. With the median follow-up of 19 months (range, 1-99 months), 10 SPB had disease progression of which 7 converted to MM, and 3 developed EMP, with a median interval of 21 months (range, 8-75 months) for the development of MM and 3 months (range, 3-9 months) for the progression to EMP. Five-year survival for EMP varied by site, with poorest survival in brain/central nervous system EMP as compared with EMP at other sites. To conclude, grade and MIB1 proliferation index help in predicting aggressive course in plasmacytoma.



## 1. Introduction

Plasmacytoma is characterized by infiltrate of plasma cells of diverse maturity and by their monoclonal immunoglobulin (Ig) products [1]. It comes under the common spectrum of plasma cell neoplasm that includes spectrum from clinically benign diseases like monoclonal gammopathy of uncertain significance and Castleman disease or heavy chain disease; indolent diseases like solitary plasmacytoma of bone (SPB) and extramedullary or extra-osseous plasmacytoma (EMP) and Waldenstrom macroglobulinemia, to the more common malignant disease like multiple myeloma (MM) and aggressive disease like plasma cell leukemia [2].

Plasmacytoma, classified into SPB and EMP, accounts for 5% to 10% of all plasma cell neoplasms, yielding the EMP: SPB: MM incidence ratio of approximately 1:2:40 [3-5]. Solitary plasmacytoma of bone accounts for 2% to 5% of all plasma cell neoplasms with predisposition for axial skeleton and thoracic vertebra being the most common site, followed by lumbar, sacral, and cervical vertebrae [6-11], whereas EMP comprising nearly 2% of all plasma cell neoplasms usually presents as a well-localized submucosal mass or swelling occurring commonly in the upper aerodigestive tract, especially in the nasal cavity [12]. Both SPB and EMP represent different groups of neoplasm in terms of location, tumor progression, and overall survival (OAS) rate. However, they share many of the biologic features of other plasma cell disorders including MM [6]. There is a need for determining the features that indicate likelihood of myeloma in patients with plasmacytoma without other manifestations.

Ki-67 is a labile, nonhistone nuclear protein expressed in G1, S, G2, and M phases of cell cycle, then rapidly catabolized at end of M phase and not detectable in G0 and early G1 cells [13]. MIB1, the Ig-G1 monoclonal antibody against Ki-67 antigen for formalin-fixed, paraffin-embedded tissue, is a marker of cell proliferation [13]. The rate of cell proliferation as assessed by MIB1 immunoreactivity has been studied as a prognostic indicator in numerous malignant neoplasms and shown to correlate with tumor grade and clinical course [14]. This study was an attempt to study the morphologic patterns of

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**Table 1**
Inclusion criteria of solitary plasmacytoma. All criteria must be met

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|---|
| Biopsy-proven plasmacytoma (SPB and EMP) with evidence of clonal plasma cells |
| Absence of osteolytic bone lesions in EMP and single area of bone destruction (site of lesion) in SPB |
| Bone marrow clonal plasma cell infiltration not exceeding 10% of all nucleated cells |
| Low serum and/or urine M-protein concentration (≤3 g/dL) |
| Absence of hypercalcemia or renal impairment |

plasmacytoma (SPB and EMP), MIB1 proliferation index, and correlation of these with clinicopathologic features and survival of the patients.

## 2. Materials and methods

This is a retrospective study of 216 cases of plasmacytoma over duration of 8 years (2002-2009). Of total 216 (SPB, 168 and EMP, 48) diagnosed cases of plasmacytoma, which were retrieved from the hospital information system and histopathology records, only 134 (SPB, 88 and EMP, 46) cases fulfilled the diagnostic criteria of plasmacytoma (Table 1), and, thus, the final study group is composed of 134 plasmacytoma cases. The details of the patients including routine and specialized diagnostic work-up, mode of treatment, progression, and survival details (wherever available) were obtained from the medical record section, electronic medical records, and by personal communication with the patients/relatives or their referring physicians.

### 2.1. Histopathology

Hematoxylin and eosin (H & E)-stained slides of the cases were retrieved and were reviewed by 2 hematopathologists. We graded plasmacytoma according to the histologic grading criteria described by Alexiou et al [12] as the following:

a. Grade 1 (low grade): shows a marchalko type in which the neoplastic plasma cells are indistinguishable from normal plasma cells, with eccentric cartwheel nuclei, a perinuclear hof, and basophilic cytoplasm. Occasional mitotic figures can be seen (Fig. 1A and B).
b. Grade 2 (intermediate grade): is an asynchronous type in which there is marked discrepancy in nuclear and cytoplasmic maturation. At least 50% of all cells have enlarged nuclei with prominent nucleoli. The cytoplasm: nuclear ratio is low, but a small perinuclear hof usually is present (Fig. 1C).
c. Grade 3 (high grade): shows a plasmablastic type with large nuclei and very prominent, centrally located nucleoli. The cytoplasm is restricted to a fairly narrow rim. The perinuclear hof is inconspicuous or absent (Fig. 1D).

Other features studied were cellular pleomorphism, mitosis, necrosis, and amyloid deposition. The presence of intralesional amyloid was determined with the Congo red stain and polarizing lens.

Immunohistochemical (IHC) analysis slides (CD138, κ, λ, CD56, cyclin D1, and MIB1), wherever available, were reviewed in all cases. The proliferation index was assessed with the monoclonal antibody against the Ki-67 antigen. In cases in which MIB1 was not available, MIB1 was done according to the manufacturer's protocols. A grid ocular objective was used to count 500 cells over 5 high-power fields (×400), and the percentage of positive cells was reported as 0% to 100%. Immunohistochemical for Epstein-Barr virus–latent membrane protein was performed in cases of high-grade tumors with plasmablastic morphology to differentiate it from other high-grade tumors.

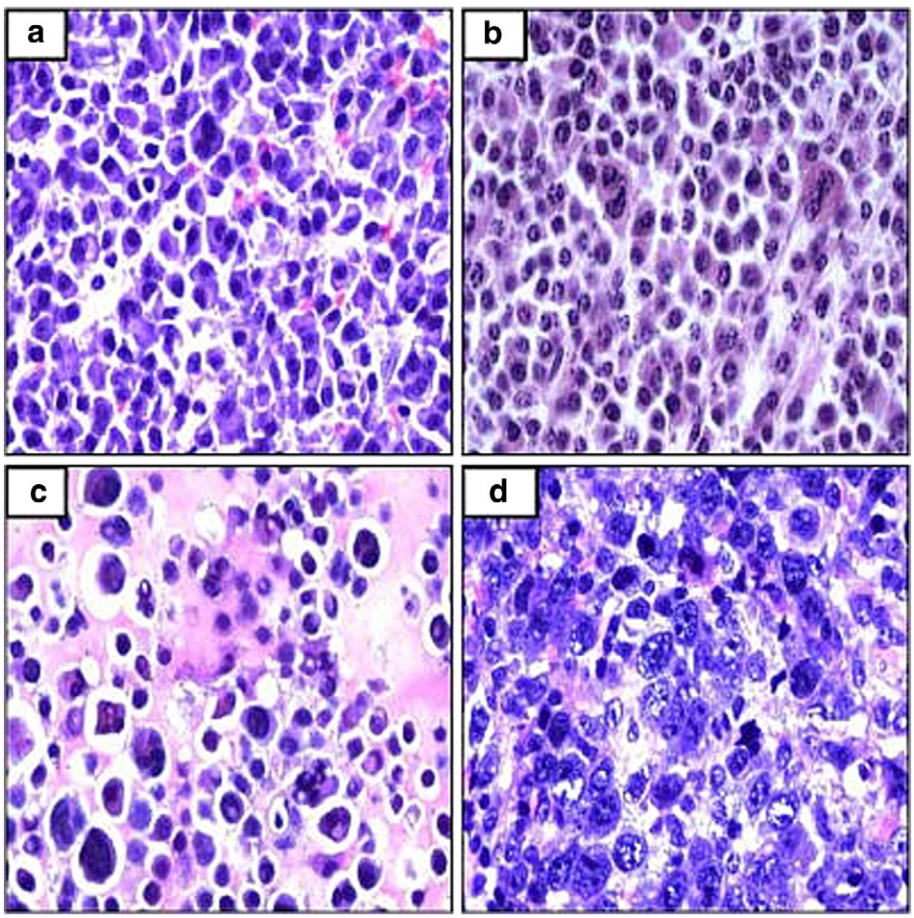


**Fig. 1.** Grade 1 morphology with plasma cells arranged in sheets (H & E, ×200) (A and B); grade 2 morphology (H & E, ×400) (C); and grade 3, plasmablastic morphology (H & E, ×400) (D).