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Pleomorphic multinucleated plasma cells simulating megakaryocytes in anaplastic variant of myeloma

Running title – Anaplastic myeloma simulating megakaryocytes

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To the editor,

Myeloma cells are notorious for their morphological variations which range from mature appearing plasma cells to other poorly differentiated forms. The pleomorphic or anaplastic variants are its uncommon rare variants which in may pose diagnostic dilemma in unprecedented cases. These anaplastic variants may mimic high grade lymphomas, leukemia or even metastatic carcinomas [1, 2]. Anaplastic plasma cells may be seen at diagnosis or evolve during the terminal phase of the disease [3]. The correlation of this morphological variant with treatment outcome is controversial, but it is believed to be a harbinger of aggressive disease [4, 5]. Herein we report the case of an unsuspected multiple myeloma, where bone marrow examination revealed the presence of bizarre plasma cells simulating megakaryocytes.

Asymptomatic 65-years-old diabetic male presented with bicytopenia. Complete blood count analysis showed hemoglobin of 7 g/dl, total leucocyte count of 6.3 x10^9/l and 51 x10^9/l platelets. Peripheral smear showed presence of occasional circulating plasma cell (inset, figure 1 A) with minimal rouleaux formation. Bone marrow examination revealed proliferation of highly pleomorphic cells with multinucleation, simulating megakaryocytes. Cells had moderate to abundant basophilic cytoplasm, while nuclei were multilobulated, with opened up chromatin and prominent nucleoli, along with a few intra-nuclear basophilic inclusions (Figure 1A). Serum protein electrophoresis revealed a monoclonal protein of 0.19 g/dl, which was confirmed to be IgA kappa on immunofixation (Figure 1B). Kappa/ lambda ratio was 427.6 and β2 microglobulin levels were 21.9 mg/l. Immunophenotypically, the cells expressed CD38, CD138, CD56 and CD200 (Figure 1C-E). FISH analysis performed after magnetic bead enrichment of plasma cells, showed the presence of del(13q14.3). The patient was unfortunately lost to follow-up.

Anaplastic multiple myeloma (AMM) is a rare morphological variant of multiple myeloma, the true incidence of which is largely unknown [1, 2, 6, 7]. In the early 1990s, Allen et al, reviewed one hundred eight cases of anaplastic myeloma, 68 of which showed presence of extramedullary disease [3]. Other salient characteristics of anaplastic MM, which have been observed by other authors too include a younger age of presentation, cytopenias, predilection with IgA myelomas and an aggressive clinical course [4, 7-9]. Bahmanyar et al reviewed the genetic features of 11 cases of AMM for the presence of myeloma associated genetic abnormalities and compared them with 188 newly diagnosed non-anaplastic variants of MM. They observed a significantly higher frequency of higher prevalence of 1q21 amplification, 17p(p53) deletion and t(4,14). Additionally presence of complex karyotype, del(13q14.3), t(1;19) and near tetraploidy has also been reported [8-10]. The treatment outcome of this variant is considered poor as per the older literature, however patients treated with triple drug chemotherapeutic agents in the modern era have shown sustained responses [1, 5, 9].

To conclude, awareness of these variants in myeloma is important for an accurate diagnosis. In cases where myeloma cells show extreme ‘de-differentiation’, a multidisciplinary approach with the addition of immunophenotyping in the diagnostic armamentarium is recommended. With the advent of triple drug regimens in myeloma therapy and autologous bone marrow transplantation, the outcome of this variant needs to be re-addressed by larger studies.
References


Figure 1. Panel of photomicrographs, A, May Grunwald Giemsa stained bone marrow aspirate smear (100 x) showing pleomorphic cells, with multinobation and multinuclearity, with prominent inclusions (red arrows) and abundant basophilic cytoplasm, and absence of perinuclear hof. B, serum immunofixation highlighting presence of IgA kappa monoclonal protein, C, D, E panel of dot plots documenting these atypical plasma cells to be positive for CD38, CD138, CD200, CD56 and negative for CD45.