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Plasma Cell Leukemia Presents with Marked Plasmacytosis and *TP53* Mutation

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A 63-year-old woman developed IgG lambda-positive plasma cell myeloma. Conventional cytogenetic analysis showed a normal female karyotype. She presented with anemia (hemoglobin, 7.4g/dL), thrombocytopenia (platelet count, 43 x 10^9/L) and a normal white blood cell (WBC) count (8.3 x 10^9/L). No circulating plasma cells were identified. The patient was treated with cyclophosphamide, bortezomib and dexamethasone.

Two months later the patient developed marked leukocytosis (WBC 143.7 x 10^9/L) with 91% circulating plasma cells as well as persistent anemia (hemoglobin, 7.8 g/dL) and thrombocytopenia (platelet count, 14 x 10^9/L). A peripheral blood smear showed numerous plasma cells [Panels A-F] that were very pleomorphic. They were large with round to irregular, convoluted or lobulated nuclei, and some had a "flower cell" appearance [Panel B]. The cells had coarsely clumped chromatin with occasional distinct nucleoli and moderate to abundant basophilic cytoplasm. Many neoplastic cells had cytoplasmic vacuoles and inclusions. Flow cytometric immunophenotypic analysis confirmed that these cells were plasma cells, positive for CD38 (decreased), CD56 (partial), CD138 and cytoplasmic lambda light chain, and negative for CD19, CD27, CD45, CD81, CD117 and cytoplasmic kappa light chain. Bone marrow core biopsy showed sheets of neoplastic cells in diffuse and nested patterns [Panel G] with positive p53 expression by immunohistochemistry. Conventional karyotyping showed a complex karyotype: 43,X,-X,del(9)(p22),add(12)(q13),-13,add(14)(q32),del(14)(q31),-16,der(20)t(14;20)(q32;q11.2)[14]/42,idem,del(3)(p14),-22[1]/43,idem,t(4;5)(q31.1;q35)[1]/46,XX[4]. Molecular analysis showed a *TP53* mutation (NM_000546.5 c.772G>A p.E258K). The patient was diagnosed with plasma cell leukemia. She underwent leukapheresis and treatment with carfilizomib, hypercytoxan, and dexamethasone, but died 3 weeks later.

Plasma cell leukemia is defined as a plasma cell neoplasm in which monoclonal plasma cells constitute $\geq$20% of total leukocytes or the absolute plasma cell count is $\geq$2.0 x 10^9/L in the blood. It is rare and can arise *de novo* or as leukemic transformation of plasma cell myeloma. Compared with plasma cell myeloma, plasma cell leukemia carries a greater number of gene mutations and cytogenetic abnormalities, contributing to its aggressive clinical behavior and very poor prognosis. In the current case, the patient developed plasma cell leukemia two months after the diagnosis of plasma cell myeloma. This rapid leukemic transformation was associated with marked plasmacytosis, *TP53* mutation, and the emergence of a complex karyotype including a high risk translocation of t(14;20)(q32;q11.2) involving *MAFB* gene. Morphologically, plasma cells are very pleomorphic and some resemble monocytes or lymphoma cells. This anaplastic morphology may pose diagnostic challenges in the absence of clinical context and immunophenotypic analysis.

(**Received**: March 22, 2018 **Accepted**: April 1, 2018 **Published**: April 9, 2018)

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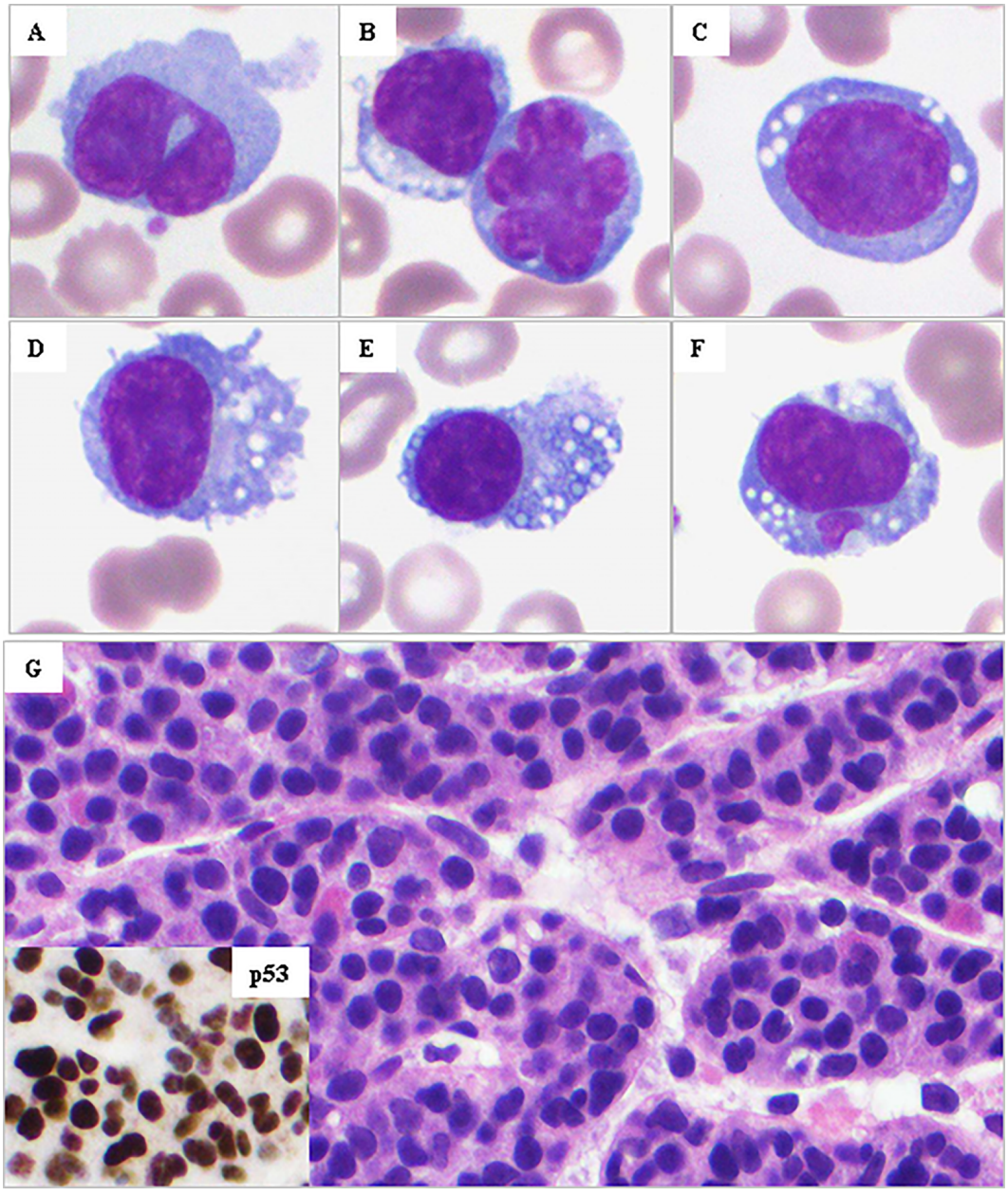
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