“Cup-like” blasts and *NPM1* and *FLT3 (ITD)* mutations in acute myeloid leukemia (AML)

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A 68-year-old male presented with progressive fatigue, weakness and respiratory infections since last few days. A complete blood cell count showed anemia (hemoglobin 9 g/dL), hyperleukocytosis (139.3K/ μ L) and low platelets (50K/ μ L) with 95 % blasts in peripheral blood. Bone marrow aspirate demonstrated 93 % blasts which were positive for myeloperoxidase and showed normal male (46, XY) karyotype. These blasts were intermediate in size with folded nuclei (Fig. 1a; 500 $\times$ magnification), many with a nuclear invagination giving a cup-like nuclear indentation (see arrows), or “fish-mouth” appearance. Auer rods were not seen. Figure 1b from bone marrow aspirate smear demonstrates high resolution (1000 $\times$ magnification) of these “cup-like” blasts. Flow cytometry studies demonstrate that the blasts were positive for CD33, CD13, CD117 and MPO confirming the diagnosis of acute myeloid leukemia (AML). The unusual morphology of blasts with cup-like nuclear indentation, also known as a fish-mouth shape, has been described in a subset of AML with *NPM1* and *FLT3 (ITD)* mutations. Altered nucleocytoplasmic shuttling and accumulation of mitochondria due to increased flexibility of nuclear envelope in *NPM1* mutations is proposed to be responsible for this alteration in the morphology of blasts.

Fig. 1 a, b Bone marrow aspirate showing blasts with cup like indentation and “Fish mouth nuclei” (see arrows)

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