Psuedo Chediak Higashi anomaly in case of hypogranular variant of acute promyelocytic leukemia (AML-M3v): A morphologic enigma

Sir,

A 50-year-old lady, labourer by occupation, presented to our hospital with fever, pain in abdomen and increased frequency of micturition of 15 days duration, along with recent onset of breathlessness and chest pain for the past three days. She also gave a history of being treated outside for urinary tract infection (UTI) with norfloxacin.

On examination, she was febrile (100°F) with a pulse of 100/min, blood pressure of 110/80 mm of Hg, and respiratory rate of 28/min. Patient was pale, poorly hydrated and had oral candidiasis. Respiratory examination revealed bilateral basal crepitations with spO_2 of 82% at room air. Rest of the examination was within normal limits and the patient was admitted to High Dependency Unit with a provisional diagnosis of sepsis with Acute Respiratory Distress Syndrome (ARDS).

Investigations revealed hypokalemia (serum K^+ level of 1.9 mEq/l) and respiratory alkalosis (pH - 7.6 pH units, pO2 - 49.1 mm Hg, pCO2 - 29 mm Hg and HCO3 - 30.3 mEq/l). Chest X- ray showed changes of early ARDS and urine culture grew E. Coli which was sensitive to amikacin and doxycycline but resistant to norfloxacin and ampicillin.

Hematologic examination at this stage revealed hemoglobin 6.7 gm%, total leukocyte count 52,700/cumm and platelet count 1,13,000/cumm. Differential count revealed 54 atypical promyelocyte count, 07 myelocyte, 30 neutrophils and 09 lymphocytes. These atypical promyelocytes were large with bilobed nuclei and three to four nucleoli. These cells had moderate amount of basophilic cytoplasm which was hypogranular with occasional Auer rods. About 2% of these atypical cells showed round to oval, azurophilic intracytoplasmic granules with size ranging from 1-3 μm [Figures 1and 2]. These granules were not seen in any other cell. The atypical promyelocytes showed strong Myeloperoxidase (MPO) positivity as did these giant

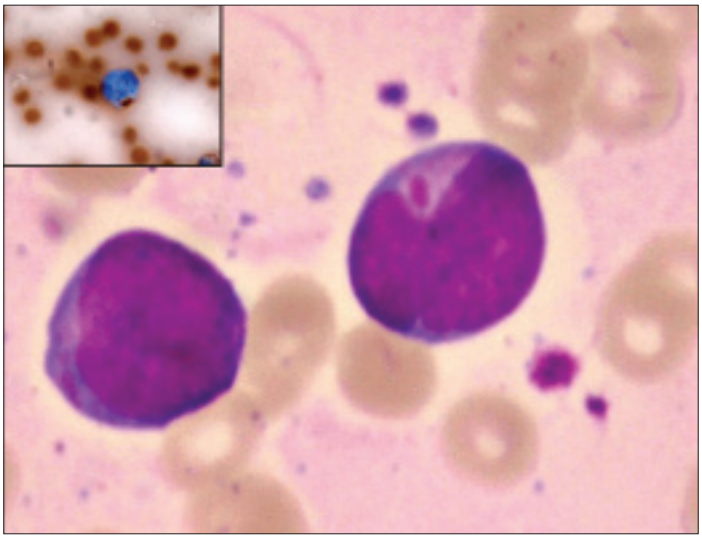

Figure 1: Photomicrograph showing one atypical promyelocyte with pseudo Chediak Higashi granule and another one showing Auer rod (Leishman's stain, x1000). Inset shows peroxidase positivity of these granules (MPO stain, x1000)

granules. Periodic Acid Schiff (PAS) stain was also done which was found to be negative. Based on the above findings, a final diagnosis of Acute Myelogenous Leukemia M3 variant (AML-M3v) with Pseudo Chediak Higashi anomaly (PCHA) was offered. Bone marrow examination was scheduled and patient was offered treatment, however, the patient left against medical advice.

Chediak-Higashi syndrome is characterized by presence of giant granules in the cytoplasm of neutrophils, lymphocytes and monocytes. Similar granules are seen albeit rarely in various myeloid disorders like AML and its subtypes, chronic myeloid leukemia and myelodysplastic syndrome and have been described as PCHA.[1] Didisheim *et al*. described PCHA for the first time in 1964 and since then a number of cases have been described and studied morphologically, cytochemicaly and ultrastructurally.[1-3] However, to our knowledge, no case of PCHA has been previously described in hypogranular variant of Acute promyelocytic Leukemia (AML- M3v).

Electron microscopic studies have revealed that the granules in PCHA arise from fusion of azurophilic granules in contrast to lysosomal origin of the inclusions seen in Chediak- Higashi syndrome.[3,4] The size of these granules ranges from 1-7 μm and are represented in only a small proportion of leukemic cells i.e., <10% in most of the reported series.[4,5] Majority of the reports describe them to be azurophoilic and purple in colour with few studies describing them as pink.[1,2,4,5] In most of the cases, they have been reported to be round to oval in shape as in our case, however some reports have described irregular granules with some present within vacuoles.[1,2,4,5] Cytochemical analysis have been done extensively and the PCHA granules have been found to be MPO positive in all but one case.[4] Other stains have been done less often and have revealed inconsistent results with Sudan Black B, PAS, Chloroacetate esterase and acid phosphatase being positive

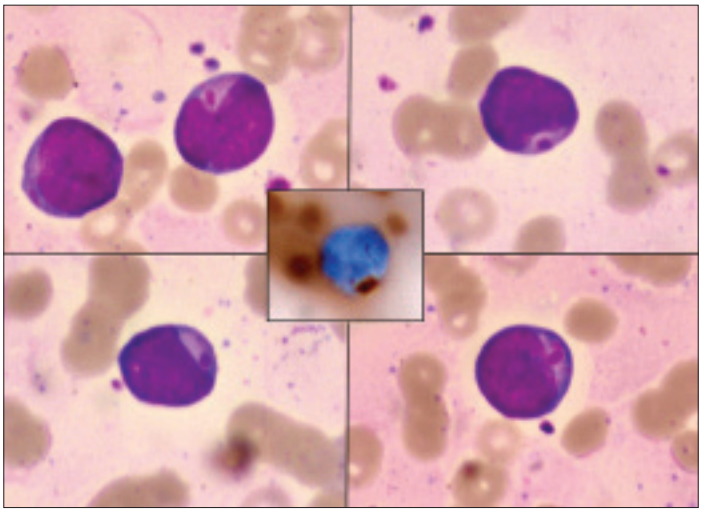

Figure 2: Composite photomicrograph showing myeloblasts with pseudo Chediak Higashi granules (Leishman's stain, x1000) at the four corners with the central photomicrograph showing peroxidase positivity of these granules (MPO stain, x1000)

while α- naphthyl acetate esterase being negative in most cases.[1,4,5]

The clinical significance of the granules is controversial; however, most of the cases have reported short survival due to either fulminant infection or disseminated intravascular coagulation.[4,5] To conclude, PCHA is a rare, aberrant but an interesting morphologic finding in acute leukaemia, the clinical significance of which needs further validation.

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