Dyserythropoiesis in a Patient with Ellis-van Creveld Syndrome: A Novel Syndrome Association

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A patient with Ellis-van Creveld (EVC) syndrome

- 4 year-old Hispanic male with EVC syndrome; his sister 13 months older with similar features. Pathological findings are from autopsy and bone marrow (pre-mortem).
- EVC [1-5] is a rare autosomal-recessive disorder characterized classically by the tetrad :
  1. Chondrodysplasia: short-limb dwarfism, length < 5th percentile
  2. Bilateral post-axial polydactyly
  3. Ectodermal dysplasia: hypoplastic spoon-shaped nails, multiple frenula with gum abnormalities, supernumerary upper teeth including one conical
  4. Cardiac malformation: cor triatriatum, ostium primum and secundum atrial septal defects

Fig. 1. Polydactyly with dysplastic nails

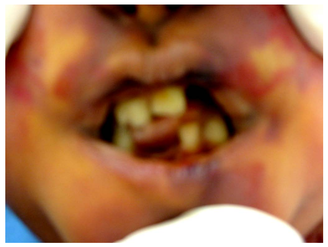

Fig. 2. Dysplastic teeth with gingival abnormalities

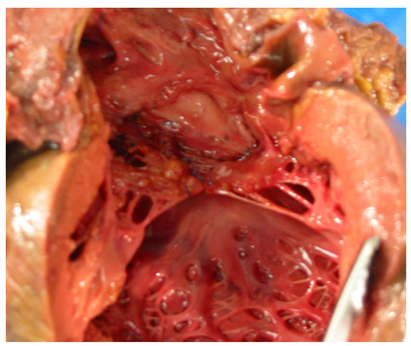

Fig. 3. Cardiac anomalies. a partial AV canal defect with ostium primum and secundum defects, and a cleft in the mitral valve.

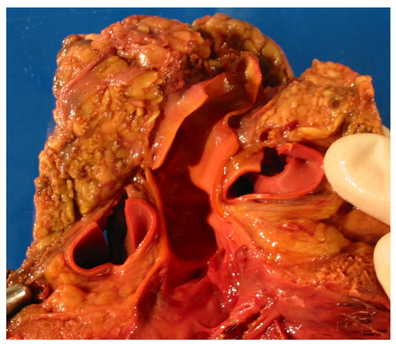

Fig. 4. “Gooseneck deformity”: left ventricle outflow tract is narrow and elongated

Reported instances of hematologic abnormalities in EVC syndrome are extremely rare
A single case report from 1969 describes a neonate with a possible variant of EVC syndrome with acute myeloblastic leukemia [6].

HEMATOLOGIC FINDINGS

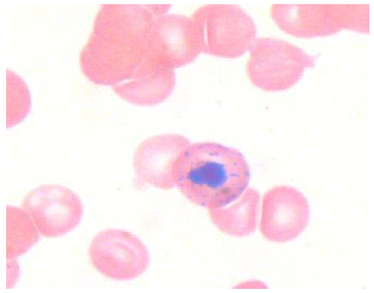

Fig. 5. Peripheral Blood: nucleated RBCs with basophilic stippling

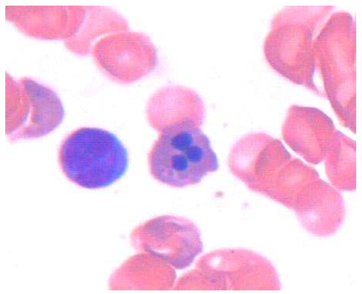

Fig. 6. Bone marrow aspirate: marked dyserythropoiesis

Peripheral blood examination
- Normochromic microcytic RBCs
  Hgb 13.9 g/dl
  Hct 40.8%
- Anisopoikilocytosis
- Many nucleated RBCs
- Leukocytosis (47,900/mm3) with left shift
  -54% neutrophils
  -14% band forms
  -10% lymphocytes
  -1% monocytes
  -18% metamyelocytes
  -3% myelocytes.
  -Granulocytes without dysplastic changes
  -Decreased platelets (73,000/mm^3) with a few large forms

Bone marrow aspirate and biopsy
- Erythroid hyperplasia (M:E ratio 0.9:1) with numerous dysplastic forms
- Normal granulopoiesis and megakaryopoiesis
- Decreased iron stores

DISCUSSION

Myelodysplastic syndromes (MDS) are clonal hematopoietic disorders associated with dysplasia in one or more myeloid cell lines [7]. MDS may develop as primary disorders with no known etiology or as therapy-related secondary disorders. Secondary MDS have been associated with chemotherapeutic agents and radiotherapy. The patient presented had no known exposure to such agents. MDS typically affect older adults (median age: 70 years) and are uncommonly encountered in the pediatric population.

However, MDS in pediatric patients with predisposing genetic abnormalities such as Down’s syndrome is a well-recognized association [8].

The dyserythropoiesis identified in this child with EVC syndrome may signify a unilineage myelodysplastic change or a primary myelodysplastic syndrome. In either event, the dyserythropoiesis may be a coincidental occurrence or may represent an unusual EVC syndrome association. Patients with EVC syndrome that present with unexplained hematologic findings may warrant evaluation for possible myelodysplastic change or MDS.

References

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