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Short Communication

Proerythroblasts as the Maincomponent of Erythroid Dysplasia in Myelodysplastic Syndrome

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Abstract

We report an unusual case of Myelodysplastic Syndrome (MDS) in which proerythroblasts appeared as the main component of erythroid dysplasia. A 74-year-old man with pancytopenia underwent bone marrow examination that revealed 60% cellularity and immature cells with fine chromatin and vacuolization were found. The immunohistochemical stain revealed negative reactions to CD34, CD31, CD3, CD20, CD10, and CD117 and positive reactions to Periodic Acid-Schiff (PAS) and E-cadherin stains. We concluded that these immature cells were proerythroblasts, representing about 37% of all nucleated elements. A diagnosis of MDS with multilineage dysplasia was made. Proerythroblasts are not usually the main component in typical dyserythropoiesis. Based on the overall findings, this case may be a preleukemic state of pure erythroid leukemia. The cytogenetic analysis showed complex chromosomal abnormalities including del (5q), inv (17), add (19), and +8. A cancer panel by next-generation sequencing revealed TP53 (p.Met426Val, missense) and AXSL1 (p.Glu635fs, frame shift) mutations. This case demonstrates that proerythroblasts can manifest as the main component of erythroid dysplasia in MDS. Data collection of genetic abnormalities is needed to identify the molecular pathogenesis and clinical data of this entity compared to those of MDS and PEL.

Keywords: Proerythroblast; Myelodysplastic syndrome; Acute erythroblastic leukemia

Abbreviations

MDS: Myelodysplastic Syndrome; PAS: Periodic Acid-Schiff; E-cadherin: Epithelial Calcium-Dependent Adhesion Protein; PEL: Pure Erythroid Leukemia; WHO: World Health Organization; ANC: All Nucleated Cells; H & E: Hematoxylin and Eosin

Introduction

Here, we report an unusual case of Myelodysplastic Syndrome (MDS) in which proerythroblasts appeared as the main component of erythroid dysplasia. A 74-year-old man visited our hospital with general weakness and dizziness for several months. Work up revealed pancytopenia (hemoglobin 5.3 g/dL, white blood cell count 2.4 × 10^3/μL with an absolute neutrophil count 1.6 × 10^3/μL, and platelet count 24 × 10^3/μL). A bone marrow examination revealed 60% cellularity with a myeloid: erythroid ratio of 1.4:1. The granulocytic precursor revealed an usual maturation pattern: megakaryocytes were slightly decreased in number and revealed mild dysplasia including hypolobulation. In addition, immature cells with fine chromatin and vacuolization were found (Figure 1A). They reveal positive reaction as a granular pattern to Periodic Acid-Schiff (PAS) stain (Figure 1B). The pattern of PAS staining of erythroid precursors differs according to differentiation. Proerythroblasts stain as a granular pattern, and intermediate and mature erythroblasts stain as a diffuse pattern under PAS stain [1,2]. The present case revealed positivity to epithelial calcium-dependent adhesion protein (E-cadherin) stain (Figure 1C). E-cadherin is expressed on early erythroblasts and decreases gradually during cellular maturation [3]. Other specific markers for erythroid lineage, such as glycophorin, hemoglobin A, and CD36, usually are positive in mature forms and negative or weakly positive in the proerythroblast stage [2]. The immunohistochemical stain revealed negative reactions to CD34, CD31, CD3, CD20, CD10, and CD117 (Figure 1 D-F). In the present case, the immature cells were identified as erythroid dysplasia, arrested in the proerythroblasts stage.

In this case, the proerythroblasts were about 37% and the total erythroid precursors were about 42% of all nucleated elements. Some of the dysplastic erythroid precursors seemed like lymphoblasts with fine chromatin and a scant amount of cytoplasm, and some of them had light-blue-grey cytoplasm and nucleoli (Figure 1). Some of the erythroid precursors revealed large nuclei, moderate basophilic cytoplasm, and cytoplasmic blebs, like typical proerythroblasts. Morphologic overlap between lymphoblasts and small erythroblasts in Pure Erythroid Leukemia (PEL) was described in the World Health Organization (WHO) classification, although it is not described in erythroid dysplasia in MDS [4]. Other typical findings in erythroid dysplasia, such as multi-nuclearity and lobulated nuclei, were not found in this case, except nuclear chromatin clumping or megaloblastic change. By the diagnostic criteria, this case was diagnosed as MDS with multilineage dysplasia [4].

Mazzella and colleges suggested the concept of acute erythroleukemia subtypes, and the present case can be classified into the M6B subtype, which is defined by ≥ 30% erythroblasts of All

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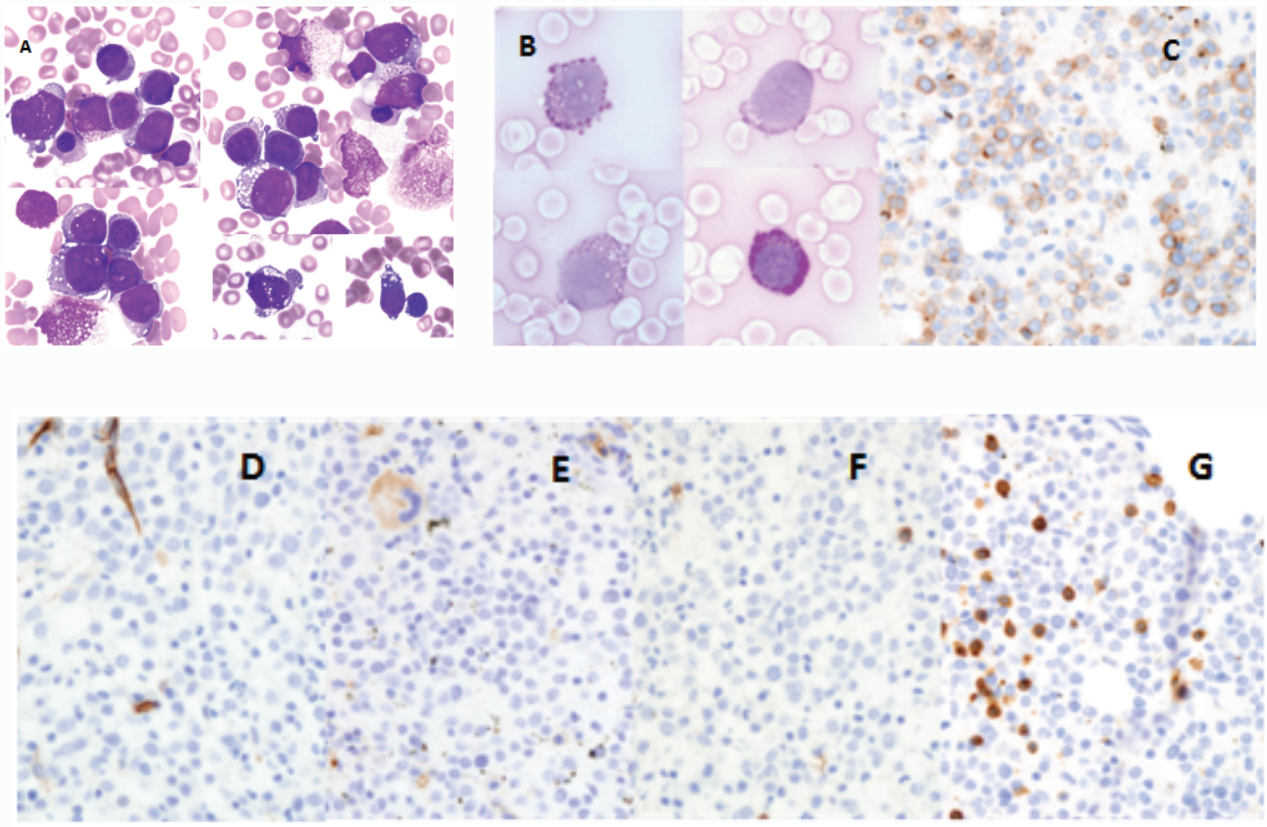

Figure 1: Morphologic findings from bone marrow aspirates (A-B) and clot section (C-G). (A) H & E stain (×1000). Small-to-large immature erythroid precursors (proerythroblasts) with fine chromatin and vacuoles with blue-grey or basophilic cytoplasm. These cells reveal a fine or punctate granular pattern with periodic acid-Schiff (PAS) stain (B) (×1000) and positivity for E-Cadherin (C) (×400). (D) CD34, (E) CD31, (F) CD20, and (G) CD3 (×400) immunohistochemical stains were negative.

Nucleated Cells (ANC) without increased myeloblasts [5]. However all acute erythroleukemia subtypes can be diagnosed basically over ≥ 50% of erythroid precursors of ANC in Mazzella and college's report and WHO classifications. Therefore, this case is categorized as MDS under all previous and current criteria. Proerythroblasts are not usually the main component in typical dyserythropoiesis [6]. Based on the overall findings, this case might be a preleukemic state of PEL.

The cytogenetic analysis showed complex chromosomal abnormalities of 46~47,XY,del(5)(q13),+8,-15,inv(17)(p13q11.2),der(19)hsr(19)(p13.3)add(19)(p13.3),-22,+1~2mar[cp8]. The International Prognostic Scoring System for MDS risk score was 1.5, corresponding to intermediate-2 risk. A cancer mutation panel by next-generation sequencing revealed *TP53* (p.Met426Val, missense) and AXSL1 (p.Glu635fs, frame shift) mutations, known mutations in MDS. The known specific mutations in PEL have not been defined, and *TP53* and AXSL1 mutations were reported in cases of PEL [2]. Considering his old age, the present patient was treated with 20 mg/m^2 decitabine for days 1-5 every 4 weeks, and his symptoms including general weakness and fatigue were alleviated quickly. He experienced no adverse events related to decitabine except myelosuppression, and he continued to receive chemotherapy.

Erythroid dysplasia with maturation arrest at the proerythroblastic stage without other typical dysplastic changesis rare as the main component of MDS. In such cases, PAS or other immunohistochemical stains are helpful for rapid differentiation. Data collection of genetic abnormalities is needed to identify the molecular pathogenesis and clinical data of this entity, in order to identify molecular characteristic of this phenotype is closed to either MDS or/and PEL.

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