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Article type : Clinical Image

Title: Pure Erythroid Leukemia

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Key Clinical Message:

The diagnosis of pure erythroid leukemia (PEL) can be challenging. Prompt identification of CD45+, CD34-, CD71+, CD117+, E-cadherin+ erythroblasts is important. The differential diagnosis is broad and includes megaloblastic anemia.

Manuscript:

A 67-year-old gentleman presented with pancytopenia and 2% peripheral blasts. Bone marrow biopsy showed a hypercellular marrow, 90% proerythroblasts with high nuclear/cytoplasmic ratio, fine chromatin, distinct nucleoli and basophilic cytoplasm (Figures 1 and 2). The blasts exhibited CD45+, CD34-, CD71+, CD117+ by flow cytometry and E-cadherin+ by immunohistochemical staining (Figure 3). These findings were diagnostic of pure erythroid leukemia (PEL). Cytogenetics demonstrated a complex karyotype: 44,X,-Y,dic(9;16)(q13;p11.2),add(19)(p13)[11]/43,sl,add(15)(p13)[3]/44,sl,+6,der(12)t(12;14)(p13;q11.2),-14[cp6]/46,XY[1] (Figure 4). Sequencing studies demonstrated loss of function TP53 mutations (TP53p.E171_R174 52.1%; TP53p.P36fs 3.3%).

PEL is defined in the 2016 WHO classification system as a neoplastic proliferation of erythroid progenitors constituting >80% of bone marrow cellularity with ≥30% proerythroblasts, and without a significant myeloblastic component [1]. Diagnosis can be challenging due to its rarity (<1% of AML cases), CD34 negativity and absent erythroid-specific markers [2]. Megaloblastic

anemia related to B12/folate deficiency can have overlapping features with PEL including elevated erythroblasts. Other differential diagnoses include other acute leukemias, myelodysplastic syndrome, accelerated myeloproliferative disorders, and non-malignant etiologies including nutritional deficiencies and myelophthisis. PEL may be therapy-related or preceded by an antecedent myelodysplastic syndrome, is often associated with complex cytogenetics and *TP53* mutations, and has a poor prognosis with median survival of 3 months.

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Conflict of Interest: The authors of this manuscript have no conflicts of interest related to this article.

References:

1. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016;127(20):2391-2405.
2. Reinig EF, Greipp PT, Chiu A, Howard MT, Reichard KK. De novo pure erythroid leukemia: refining the clinicopathologic and cytogenetic characteristics of a rare entity. *Modern Pathology*. 2018;31(5):705-717. doi:10.1038/modpathol.2017.175

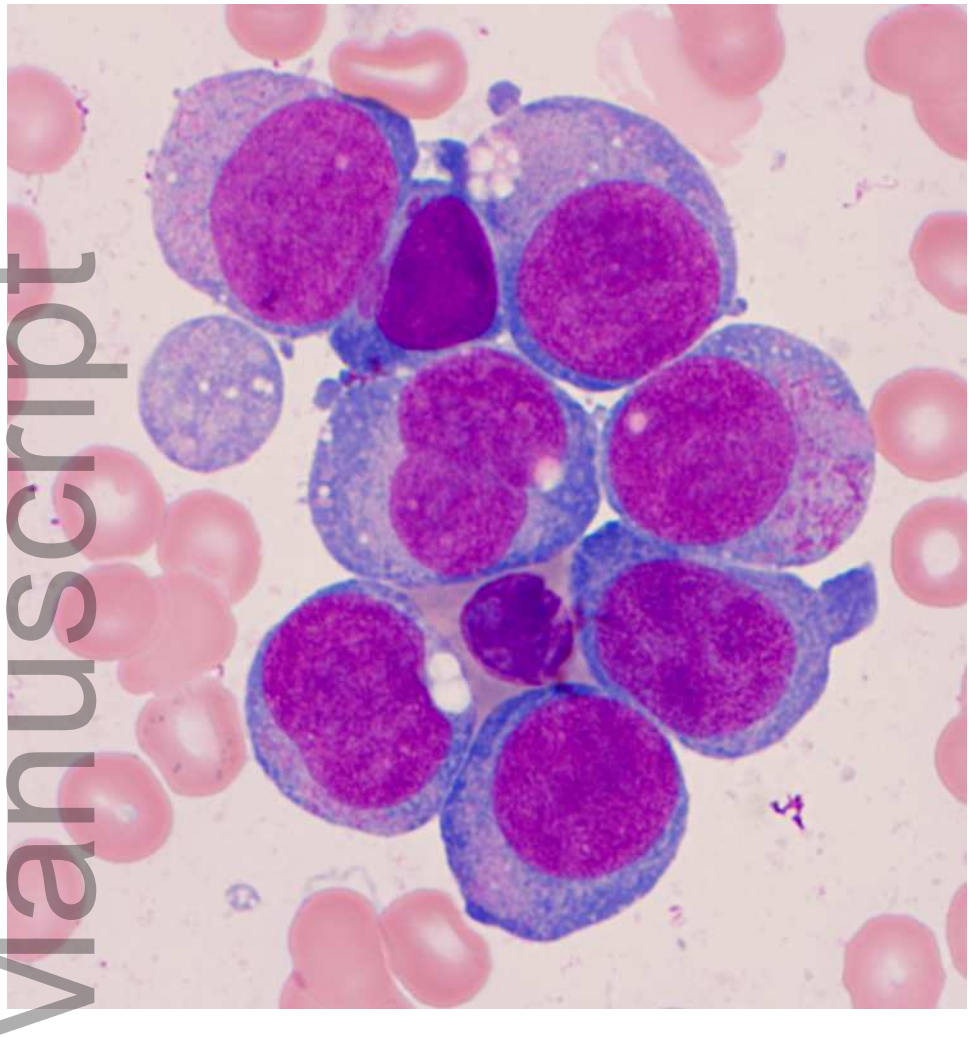
Figure Legends:

Figure 1: A Wright-Giemsa stained bone marrow aspirate smear, original magnification x 1000.

Figure 2: An H&E stained bone marrow core section, original magnification x 800.

Figure 3: Immunohistochemical staining of a bone marrow core section for E-cadherin, original magnification x 800.

Figure 4: Metaphase karyotyping demonstrating a complex karyotype.



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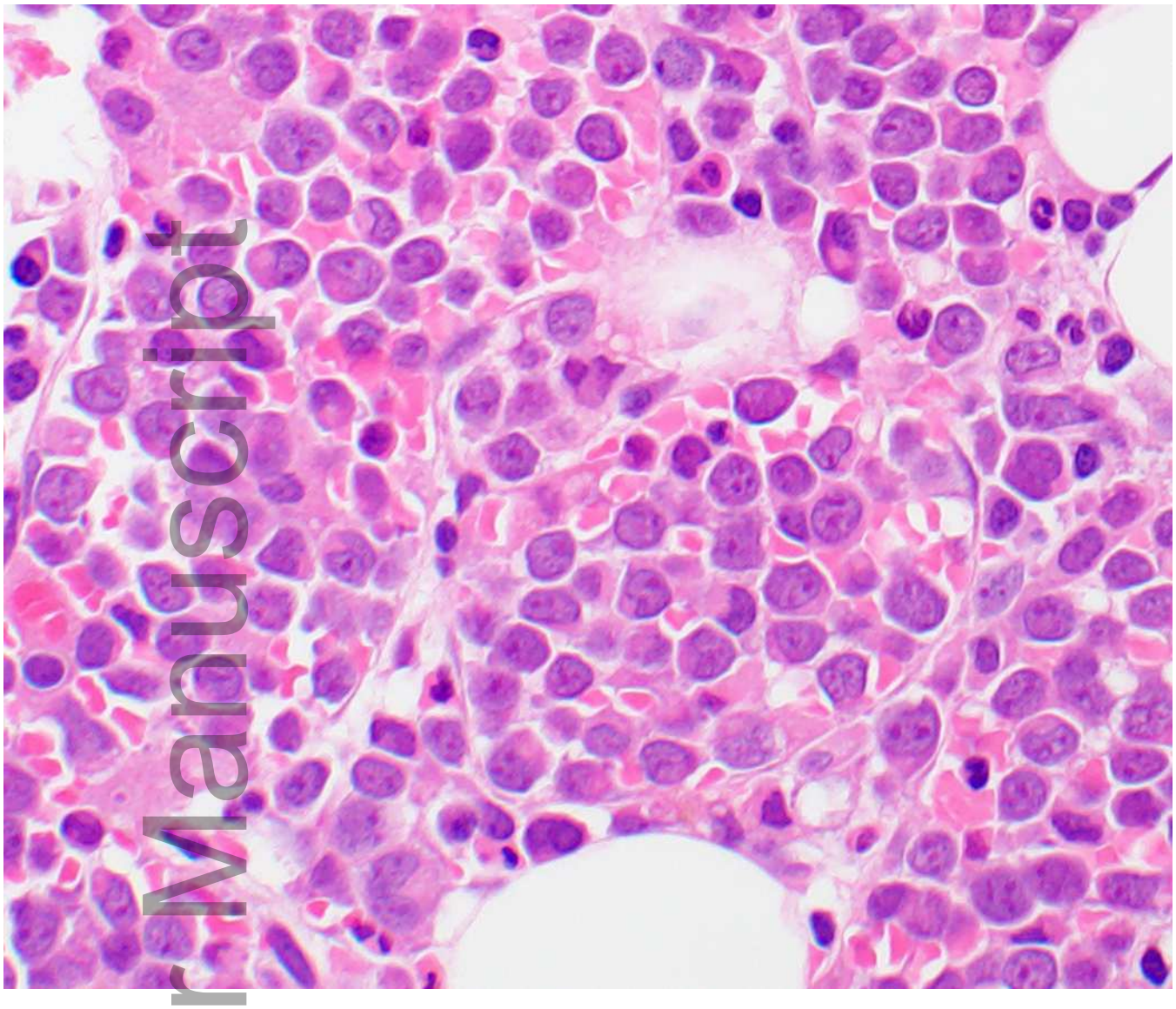

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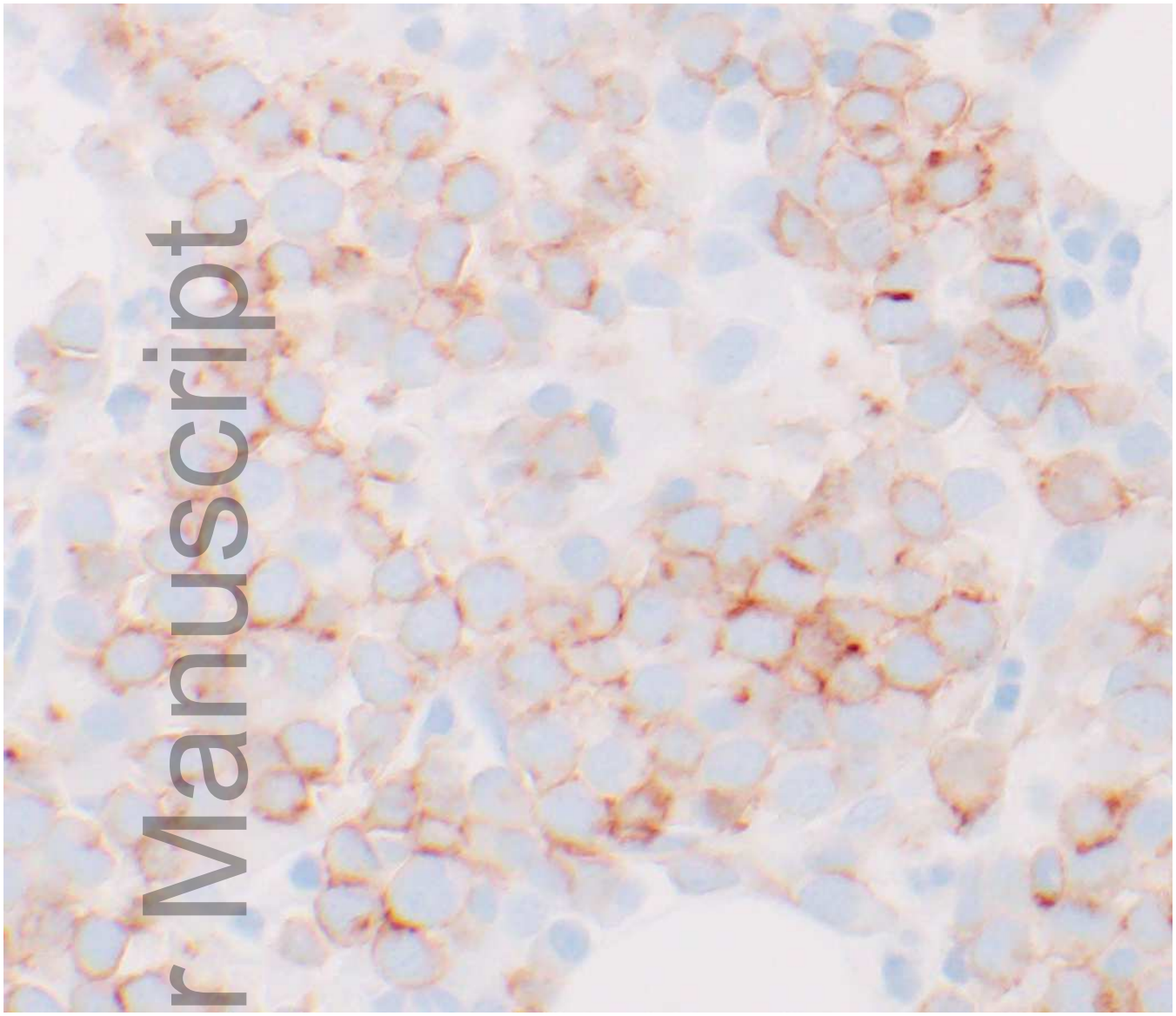

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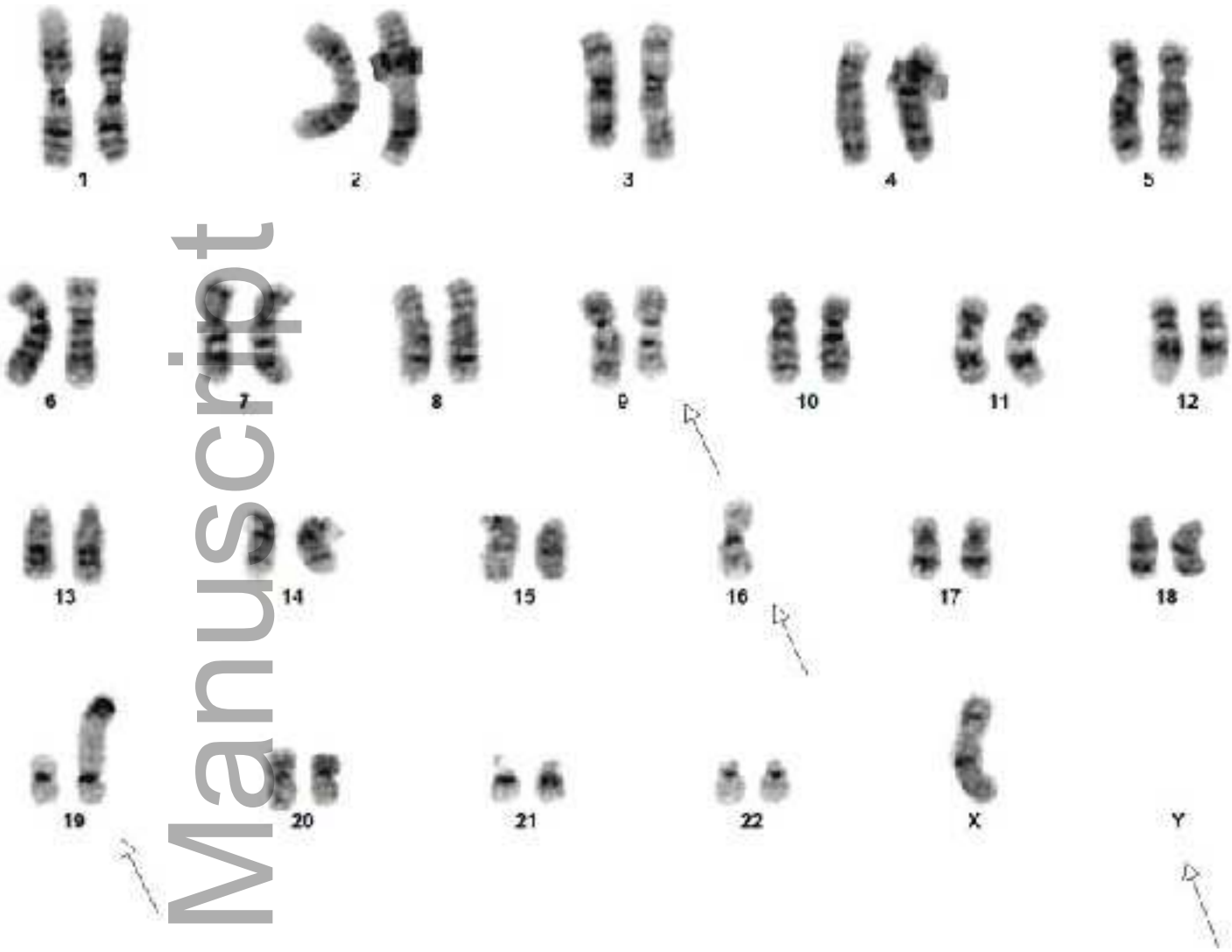

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