Hematology Case Conference

11/26/02

Clinical History

- A 28-year-old man with a history of alcohol and intravenous drug use presented with delirium tremens, fever, and progressive anemia.
- Physical examination revealed marked pallor. No organomegaly was identified.

Laboratory Tests

- CBC: hemoglobin=10.3 g/dL; WBC= 0.8×10^9/L; and platelet count= 14×10^3/μL.
- WBC differential: 41% neutrophils; 48% lymphocytes; 6% monocytes; 4% eosinophils; and 1% basophils.
- The reticulocyte count was less than 0.1%.

Laboratory Tests (cont'd)

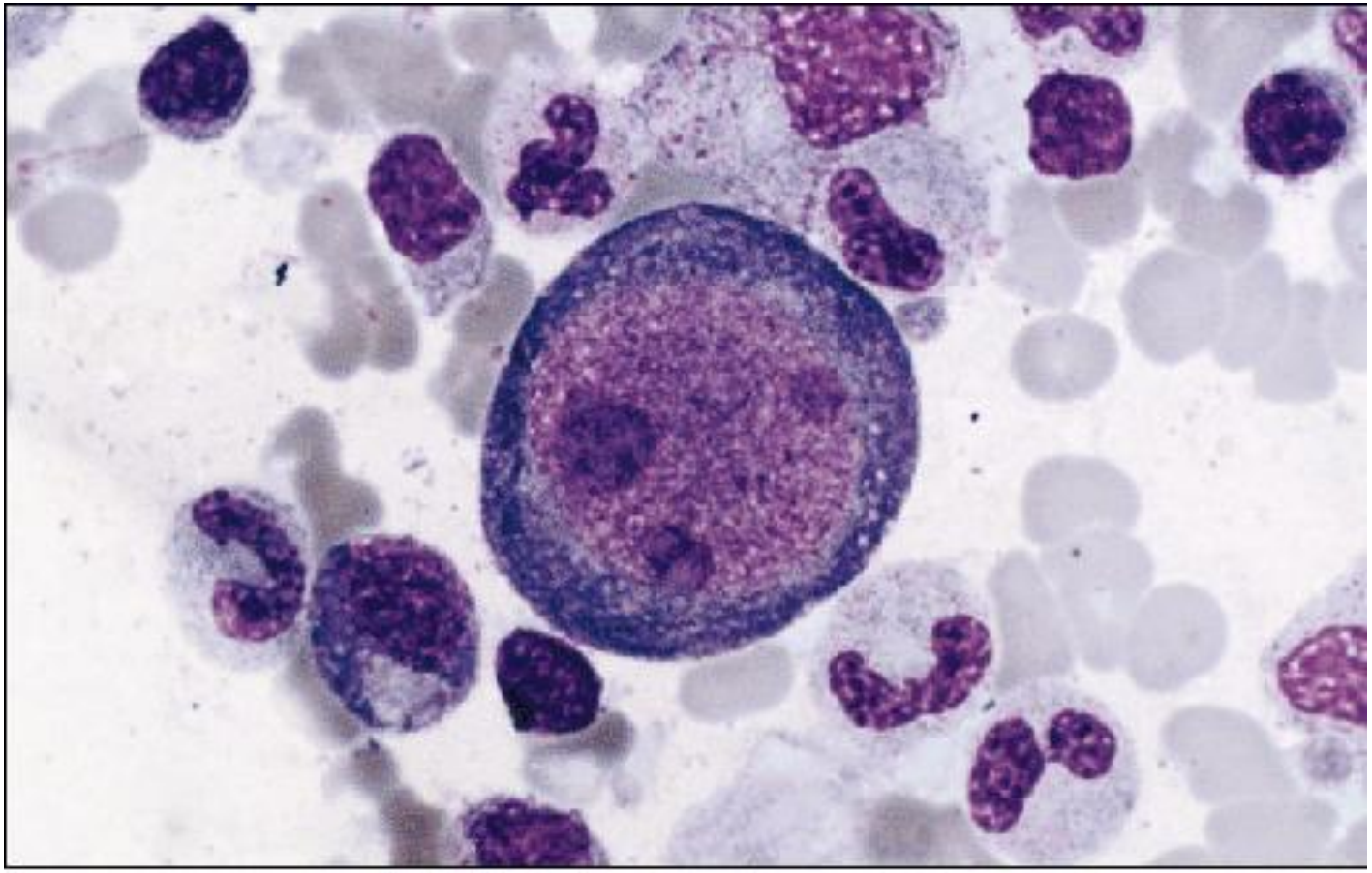
- Blood cultures were negative, HIV antibodies were negative.
- A bone marrow procedure was performed to evaluate the possible causes of pancytopenia. The marrow was hypocellular (30%) for the patient's age and showed a marked red cell aplasia

  (myeloid/erythroid ratio of 11:1).

Bone Marrow Aspirate

- Giant proerythroblasts were present in the aspirate, with a high nuclear/cytoplasmic ratio; a narrow rim of intensely blue, vacuolated cytoplasm; fine nuclear chromatin pattern; and multiple, distinct, large purple inclusions in the nucleus.

Bone Marrow Aspirate (cont'd)

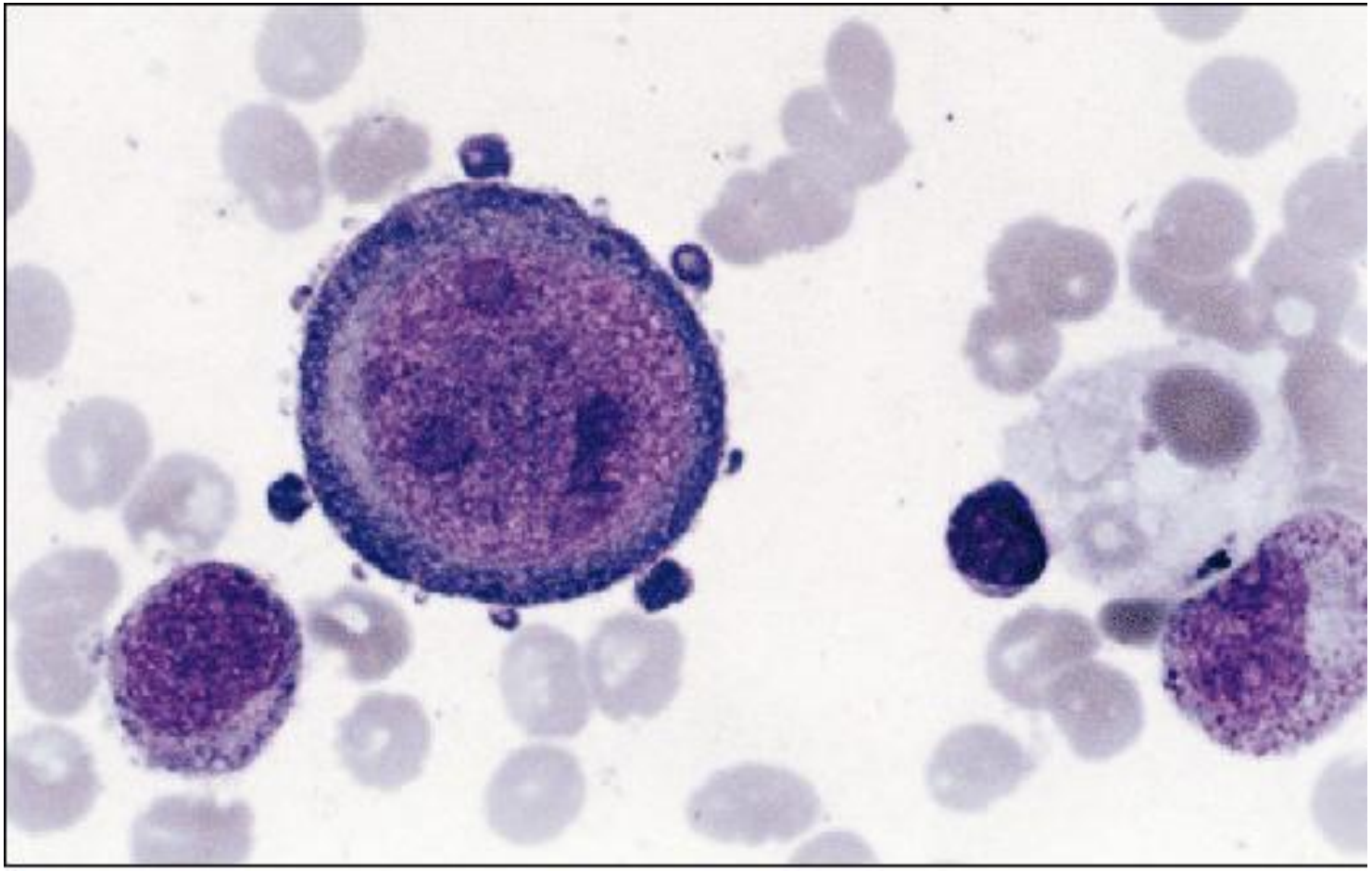


[11] Giant proerythroblast with intensely blue, vacuolated cytoplasm; compact nuclear chromatin pattern; and multiple, distinct, large purple inclusions in the nucleus (Wright-Giemsa, oil immersion, ×1,000).

Bone Marrow Aspirate (cont'd)

- The large size of the proerythroblasts could be appreciated by comparison with adjacent neutrophils.
- Some of the giant proerythroblasts showed multiple small cytoplasmic projections called "pseudopodia" or "dog ears"

Bone Marrow Aspirate (cont'd)

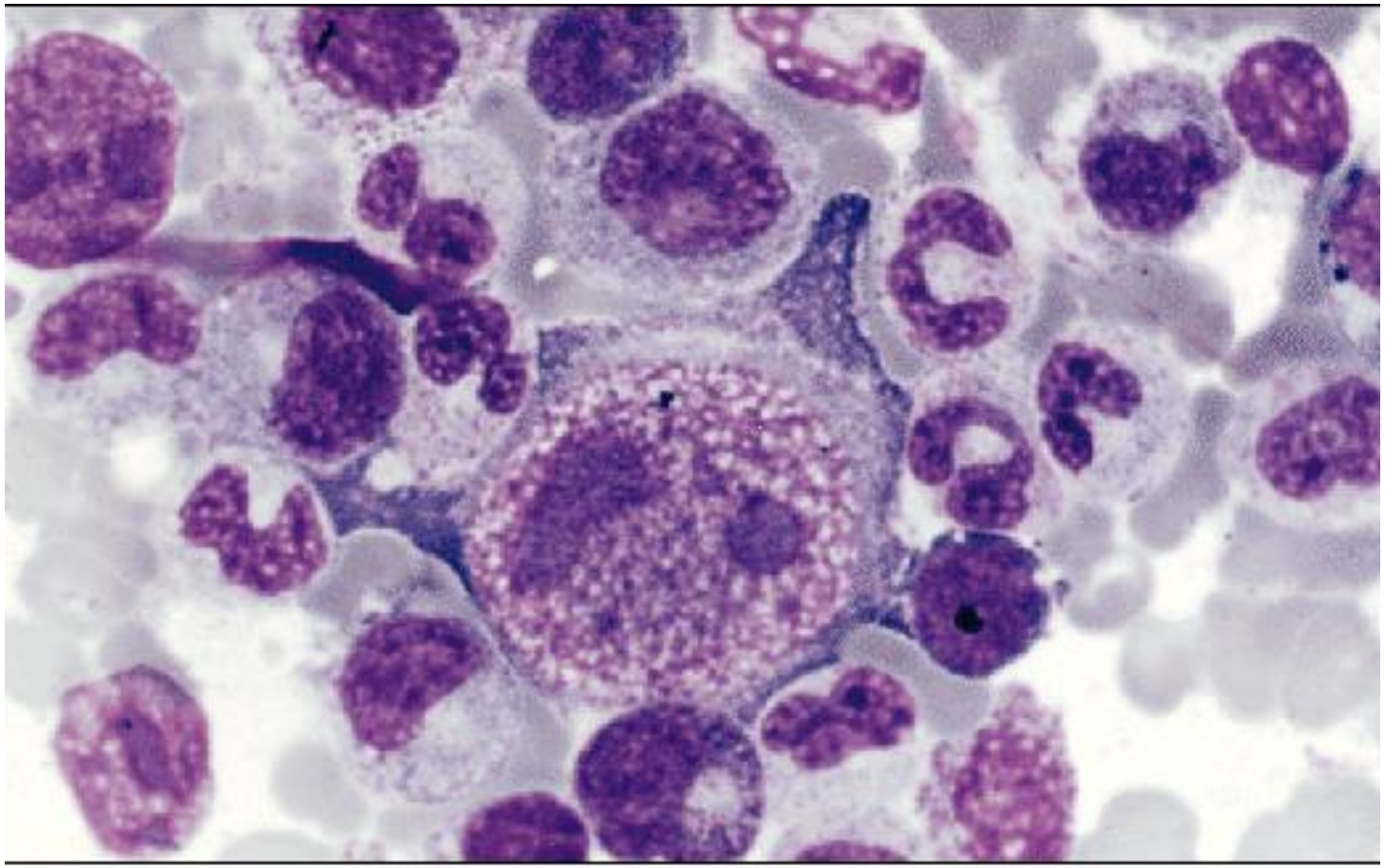


[12] Early giant proerythroblasts showing multiple small cytoplasmic projections called "pseudopodia" or "dog ears" (Wright-Giemsa, oil immersion, ×1,000).

Bone Marrow Aspirate (cont'd)

- Giant proerythroblasts having frayed cytoplasm with decreased basophilia and coarse nuclear chromatin with very large inclusion were also identified.

Bone Marrow Aspirate



[13] Intermediate giant proerythroblasts with frayed cytoplasm with decreased basophilia and coarse nuclear chromatin with a large inclusion (Wright-Giemsa, oil immersion, ×1,000).

Diagnosis & Follow-up

- In combination with red cell aplasia, these changes in erythroid precursors are consistent with infection by parvovirus B19
- DNA analysis using PCR for parvovirus B19 DNA was performed, and the result was positive. However, the IgG and IgM results for parvovirus B19 were negative.
- The patient received intravenous immunoglobulins for parvovirus B19. He left against medical advice 3 days later.

Parvovivrus B19

- Parvovirus B19 is a small, nonenveloped, single-stranded DNA virus, classified in the family Parvoviridae, the subfamily Parvovirinae, and genus Erythrovirus.
- Parvovirus B19 is known to cause erythema infectiosum (fifth disease), polyarthritis, aplastic crisis in various hemolytic anemias, prolonged erythroid suppression in immunodeficient patients, and fetal death in many cases of vertical transmission.

Parvovivrus B19 (cont'd)

- It is cytotoxic to erythroid progenitor cells in vivo and in vitro. It is known to enter the red cell precursors through the blood group P antigen.
- The presence of red cell aplasia and full spectrum of characteristic giant proerythroblasts in the bone marrow are pathognomonic of parvovirus B19 infection.
- The pathogenesis of the giant proerythroblasts and mechanism of erythroid hypoplasia in parvovirus B19 infection are not fully understood. Induction of apoptosis has been suggested due to the presence of cytoplasmic blebs; a direct cytopathogenic lytic effect of the virus on erythroid precursors has also been suggested.

Parvovivrus B19 (cont'd)

- In immunocompetent patients, the infection typically resolves in 2 to 3 weeks with the production of IgG that neutralizes the virus infectivity for erythroid host cells.
- Persistent or recurrent parvovirus B19 infection can be associated with suppressed serologic response.
- By the age of 30 years, 30% to 60% of the normal adult population is estimated to have IgG antibodies against parvovirus B19.
- Immunocompetent hosts rarely remain ill due to this viral infection, but in immunodeficient patients, the virus usually persists for prolonged periods and can lead to chronic anemia.

Parvivirus Infection in This Patient

- Diagnostic data from: bone marrow aspirate, DNA test by PCR.
- Negative serology (IgG and IgM): due to
  1. immunosupressed ?
  2. persistent infection with suppressed serologic response ?

Images shown in this case

- The images shown in this file are taken from a published journal article which covers the case under discussion:

  “Gupta, D., Wu, S.L., **Nguyen, A.N.D.**: Human Parvovirus B19 in the bone marrow with negative viral serologic results. Laboratory Medicine. Aug 2001; no 8, vol 32, 429-431”