# Unexpected aetiology of chronic thrombocytopaenia

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## CLINICAL QUESTION

An asymptomatic adult woman with no significant medical or family history was found to have splenomegaly during workup for chronic, mild thrombocytopaenia. A peripheral blood smear showed isolated thrombocytopaenia and was otherwise unremarkable. A bone marrow aspirate was essentially a dry-tap with normal flow cytometry and cytogenetics. Touch preparations and histological sections of the core biopsy demonstrated abundant histiocytes (figure 1). The background trilineage haematopoiesis was otherwise unremarkable.

Review the high-quality, interactive digital Aperio slide at http://virtualacp.com/JCPCases/jclinpath-2019-206289/ and consider your diagnosis.

Five differential diagnoses (including the correct answer) with options in alphabetical order

A. Crystal-storing histiocytosis.
B. Erdheim-Chester disease.
C. Gaucher disease.
D. Histoplasmosis.
E. Langerhans cell histiocytosis.

## DISCUSSION

Touch preparations of the core biopsy demonstrated abundant, bland histiocytes with expanded pale, blue-grey cytoplasm that had a crinkled texture, characteristic of classic 'Gaucher cells' (figure 1A–B). Histological sections of the core biopsy showed a diffuse infiltration of histiocytes among scattered islands of trilineage haematopoietic elements (figure 1C). The histiocyte cytoplasm had conspicuous striations imparting a crinkled or wavy appearance (figure 1D). While a hallmark of Gaucher disease, similar histiocytes can be seen in infectious diseases, histiocytic neoplasms and other lysosomal storage disorders.

Grocott's methenamine silver and Periodic acid-Schiff-diastase histochemical stains were negative for intracellular organisms such as dimorphic fungi and *Tropheryma whipplei*, respectively. By immunohistochemical staining, the histiocytes were negative for S100 and CD1a, excluding Langerhans cell histiocytosis. Erdheim-Chester clinically presents with orthopaedic symptoms and radiological abnormalities,[1] and will have xanthomatous and multinucleate histiocytes (Touton giant cells) on microscopy. Erdheim-Chester is also positive for the BRAFV600E mutation in 54% of cases,[2] so ancillary testing could be prudent in the appropriate clinical and morphological context. Crystal-storing histiocytosis describes the phenomenon of monoclonal immunoglobulin accumulation in histiocytes. These cells will stain positively for immunoglobulin light chain by immunohistochemistry and occur in the background of a lymphoplasmacytic neoplasm.

Gaucher disease, the most common lysosomal storage disorder, was confirmed in this case with markedly decreased beta-glucocerbrosidase activity in peripheral blood leucocytes. The chronic, non-neuropathic form, type I Gaucher disease, commonly presents as splenomegaly with thrombocytopaenia or anaemia in young adulthood.[3] Enzyme replacement therapy for Gaucher disease increases blood counts, decreases splenomegaly

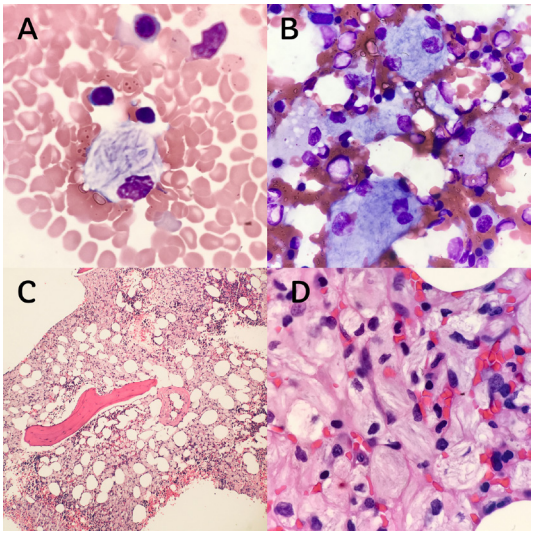


**Figure 1** Bone marrow aspirate and core biopsy. Histiocytes with characteristic 'Gaucher cell' features on touch preparations (A,B). Wright-Giemsa. Histological sections demonstrate diffuse infiltration of the bone marrow by histiocytes (C). High magnification shows bland histiocytes with voluminous cytoplasm with a lightly eosinophilic, striated appearance (D). H&E (C,D).

### Take home messages

- Type I Gaucher disease manifests as splenomegaly with chronic anaemia or thrombocytopaenia in young adults, in contrast to the aggressive infantile (type II) form of the disease.
- Bone marrow infiltration of 'wrinkled tissue paper'-appearing histiocytes is characteristic of Gaucher disease but is not pathognomonic.
- Infectious organisms, neoplastic disorders and lysosomal storage diseases should be carefully considered when Gaucher-like histiocytes are encountered.
- Reduced beta-glucocerebrosidase enzyme activity confirms Gauchers disease in the correct clinicopathological context but can also be seen in carriers of this autosomal recessive disease.



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and lengthens life span.[4] Additionally, normal sphingomyelinase activity excluded the attenuated, type B form of Niemann-Pick disease, which can clinically manifest similarly and is morphologically indistinguishable.[5]

## ANSWER

C. Gaucher disease

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