

Xanthomatous macrophages in bone marrow biopsies: systemic manifestation of mycobacterioses

Cristiano Claudino Oliveira¹ · Lígia Niéro-Melo² ·
Maria Aparecida Custódio Domingues¹

Received: 2 April 2017 / Accepted: 3 May 2017 / Published online: 16 May 2017
© Springer-Verlag Berlin Heidelberg 2017

Dear Editor,

Systemic mycobacterioses, such as tuberculosis and leprosy, have lymphoproliferative diseases as a differential diagnosis [1, 2]. This is especially true when the infectious diseases present with a disseminated form, which represents a diagnostic challenge for medical teams [3].

In this context, bone marrow biopsy is a diagnostic method used for investigation. In patients with systemic mycobacterioses, bone marrow biopsies exhibit a reactional pattern with numerous xanthomatous macrophage clusters, usually with an increase in the reticuline frame in these areas. Faced with this morphological pattern, special staining is essential for the research of acid-alcohol resistant bacilli and fungi [3].

Images presented in Fig. 1(a–b) are from a 36-year-old woman with pancytopenia and clinical-pathological diagnosis of lepromatous or Vichowian leprosy in the skin. The patient was submitted to bone marrow biopsy to investigate her pancytopenia. She did not have any immunosuppression causes detected by laboratorial exams.

Figure 1a and b demonstrates clustered cells with light cytoplasm, adjacent to the trabecular bone, in a bone marrow biopsy. Figure 1c is a representation of these cells in higher observation. These cells are xanthomatous macrophages. Figure 1d indicates infection from acid-alcohol resistant bacilli using the Fite-Faraco technique. The Ziehl-Neelsen histochemical technique was also positive in our case.

The histochemical positivity for these infectious agents imposes clinical, laboratory and radiological investigation of possible lesions that justify a systemic picture. In general, when bone marrow is involved, other organs of the reticulo-endothelial system may also be involved, indicating severity of the disease [3, 4].

In general, morphological situations such as these indicate tuberculosis as an important diagnostic hypothesis. However, the skin should be carefully evaluated, since leprosy may also exhibit this pathological pattern [4]. Our patient has skin lesions whose histopathological analysis showed nerves surrounded by numerous xanthomatous macrophages, similar to those seen in bone marrow biopsies, which contain acid-alcohol resistant bacilli, which tested positive using Ziehl-Neelsen and Fite-Faraco techniques.

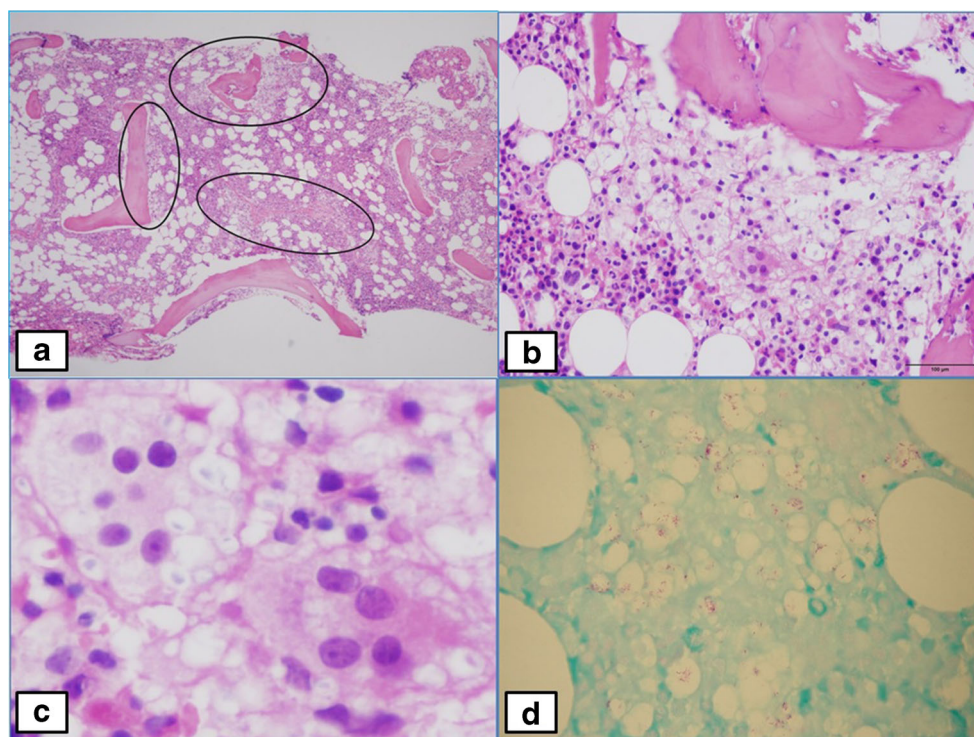
Leprosy with systemic dissemination represents the multibacillary Virchowian form (or lepromatous) of this disease. Reports of the disseminated clinical form as the first manifestation of the condition have been published since the 1970s, always with lymphoproliferative diseases as a differential diagnosis. Bone marrow biopsy is a diagnostic tool for these cases [1–3]. Bone marrow

✉ Cristiano Claudino Oliveira
cristiano_c_oliveira@hotmail.com

¹ Department of Pathology, Botucatu School of Medicine, São Paulo State University, Distrito de Rubião Junior, s^o 9, Botucatu, São Paulo 18618-970, Brazil

² Department of Internal Medicine, Botucatu School of Medicine, São Paulo State University, Botucatu, São Paulo, Brazil

Fig. 1 Bone marrow biopsy. **a** H&E, $\times 100$ and **b** H&E, $\times 200$: cluster of cells with light cytoplasm, adjacent to the trabecular bone, in a bone marrow biopsy. **c** H&E, $\times 400$: these cells are xanthomatous macrophages, note the light cytoplasm with vacuolated aspect. **d** Fite-Faraco, $\times 1000$: infection from acid-alcohol resistant bacilli using the Fite-Faraco technique



leprosy is an infrequent situation and represents an evidence of systemic disease, what is documented in Virchowian form. Pathologists must pay attention to the presence of xanthomatous macrophages, mainly when it is the leprosy diagnosis not defined. Even after some years of treatment, bone marrow biopsies may reveal histiocytic clusters without bacilli [4, 5].

Global hypercellularity, granulocytic hyperplasia, eventual plasmacytosis and clusters of these macrophages characterize the morphological pattern observed in a leprosy reactional bone marrow. The xanthomatous aspect of the histiocytic cytoplasm is due to the high concentration of bacteria that have, in the constitution of their high wall, lipid concentration [4, 5]. The use of the Fite-Faraco technique was diffused due to the increased sensitivity in the specific detection of this microorganism, since it uses lipophilic substance prior to the application of lipofuscin. As happened in our case, the Ziehl-Neelsen staining may also be positive, but is not usually. The Ziehl-Neelsen negativity can be a false negative test, so, when we have the hypothesis of leprosy, we must use Fite-Faraco for bacilli detection. A positive Fite-Faraco test is sufficient for the diagnosis and molecular exams are not necessary. Molecular assessments are useful when we have drug resistance or maintenance of systemic disease [5].

Brazil and India have the largest number of leprosy cases in the world. It is a disease with increasing relevance in the

current geopolitical scenario, with the accentuation of migratory flows, especially in European countries, where epidemiologically this disease is less frequent [4, 6, 7].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Lawrence C, Schreiber AJ (1979) Leprosy's footprints in bone marrow histiocytes. *N Engl J Med* 300(12):834–835
2. Azulay RD (1987) Primary visceral virchowian (lepromatous) Hanseniasis. *Int J Lepr Other Mycobact Dis* 55(3):450–453
3. Velasco C, Lozano S, Villarúbia J (2013) Leprosy diagnosed by bone marrow aspiration. *Br J Hematol* 160:121
4. Scollard DM, Dasco MM, Abad-Venida ML (2015) Tuberculosis and leprosy classical granulomatous diseases in the twenty first century. *Dermatol Clin* 33:541–562
5. Faria JL (1949) Valor do método de Faraco para coloração do bacilo de Hasen em cortes. *Rev Bras de leprologia* 1:18–26
6. Singh N, Bhatie AL, Arora VK, Bhattacharya NS (2006) Comparative cytomorphology of skin, lymph node, liver and bone marrow in patients with lepromatous leprosy. *Cytopathology* 17: 257–261
7. Suster S, Cabello-Inchausti B, Robinson MJ (1989) Nongranulomatous involvement of the bone marrow in lepromatous leprosy. *Am J Clin Pathol* 92(6):797–780