

Commentary: Extramedullary hematopoiesis in the facial sinus, is it the time to search actively for it in some patients with thalassemia intermedia?

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I read with great interest the case of Talarico et al¹. Briefly, they reported a rare localization of extramedullary hematopoietic (EMH) tissue developed in the paranasal sinuses in a patient homozygous for Hemoglobin Lepore. Unluckily, data regarding spleen status and parameters of erythron expansion, such as erythropoietin (EPO), nucleated RBC count (NRBC), as well as soluble transferrin receptor (sTfR), were not reported. However, the case is well described and handled and may lead to discuss several aspects in the pathophysiology and in the management of patients with thalassemia intermedia (TI). In our Center, from 2003 to 2004, 28 patients with TI underwent MRI to search EMH both at paraspinal and cranial level; we found that 46% of the patients were affected by paraspinal localization and one patient had also sinus involvement but was asymptomatic². He was heterozygous for $\beta 0$ 39 nonsense C \rightarrow T mutation along with the $\delta\beta$ -thalassemia allele; he was splenectomized in 1994. However, due to the co-existence of paraspinal EMH, to the radiologist expertise with EMH detection and diagnosis and/or to the more characteristic MRI appearance of the lesion, biopsy was not required. In 2004, to ameliorate anemia and treat the progression of extramedullary erythropoietic masses previously diagnosed, the patient was started on hydroxyurea (HU) therapy. His hemoglobin increased by approximately 1.5 g/dL, and the lesion, despite not disappearing, never progressed until today. He had both high nucleated red blood cell count and level of sTfR ($650\text{-}750 \times 10^9/\text{L}$ and 12 mg/L, respectively).

In 2012, in a larger series, we found that EMH involved 39% of TI patients, particularly, those splenectomized. We established a useful relationship between the level of sTfR and the presence of EMH at paraspinal level^{3,4}. More recently,

we described the clinical and hematological features of patients carrying the hemoglobin (Hb) Lepore variant in homozygous or in association with other hemoglobinopathies⁵. Our six cases of homozygotes were all splenectomized and, apart one case, were more similar to thalassemia patients and were not affected by EMH probably because chronically transfused. However, despite the current optimal transfusion regimen, they maintained an increased level of sTfR.

As authors correctly stated, few cases of sinus involvement have been reported and, as per our case, a genotype-phenotype relationship seemed to be at least improbable. There are no guidelines or specific protocol for search for EMH in TI patients, which could be detected in almost all body sites; however, only paraspinal involvement received special attention in NTD guidelines due to potential spinal compression occurring in less than 20% of cases⁶. Therefore, most of the masses of EMH are usually incidentally discovered by radiologic techniques unless they are not regularly screened with adequate methodology or become symptomatic because of compressive effect. So, cases presented here, like this one, remain anecdotic and/or underdiagnosed. In patients with TI, EMH is a rising phenomenon linked to aging⁷ and to some extent it could be appropriate to say, "the more you search it, the more you find it". As a consequence, in TI patients, it seems proper to regularly search EMH and monitor its activity by MRI at least at paraspinal level, particularly, in those presenting risk factors that were already recognized, such as the splenectomy status and increase in markers of expanded erythropoiesis. Probably, this would lead to more appropriate management of the patients, owing to the prevention of spinal compression and to a timely recognition to start a regular transfusion regimen⁸.

Ideally, in patients already affected by paraspinous EMH, at least once in their life, a cranial and a whole-body scan could be recommended. It would contribute to better detect and treat unconventional site of EMH localization. The availability of genetic, biochemical, clinical and radiological data may lead also to create useful algorithm to avoid invasive biopsy. However, these are considerations that should be accurately discussed by a consensus group of experts, including radiologists and hematologists.

Conflict of Interest

The author declare that he has no conflict of interests.

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