

## Paravertebral extramedullary hematopoiesis due to pyruvate kinase deficiency

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Hematopoiesis occurs during fetal development mainly in liver and spleen. By week 24-25 and until birth bone marrow becomes progressively more important, being the only site of hematopoiesis in adult life. For this reason, the presence and proliferation of hematological precursors outside the bone marrow in an adult is considered as an abnormal finding called extramedullary hematopoiesis (EMH). In most instances EMH develops in liver and spleen, representing about 95% of cases in some series.<sup>1</sup> Non hepatosplenic EMH typically appears as a solid homogeneous mass in the mediastinum surrounding the thoracic vertebral column, as in our case.<sup>2</sup> Other reported sites of involvement are central nervous system, lymph nodes, lung and pleura,<sup>3</sup> myocardium,<sup>4</sup> and other. EMH often appears as a compensatory phenomenon in patients with deficient bone marrow hematopoiesis secondary to peripheral red cell destruction or ineffective central production. Nearly always EMH presents with an associated disease that has an important etiopathogenic role. The most common associated diseases are myelofibrosis with myeloid metaplasia and thalassemia, being others entities very unusual. We report a case of EMH in a patient with pyruvate kinase (PK) deficiency. A 53-year-old woman was admitted in our hospital because of a paravertebral mass diagnosed by a chest X-ray made during a respiratory process. Twenty-five years before she was diagnosed of PK deficiency with compensated hemolytic anemia. Pyruvate Kinase activity was 2.69 IU/gHb (normal 7.2-15.6). At the moment of the initial diagnosis other hereditary red cell defects were excluded: hemoglobin electrophoresis did not disclose any abnormal Hb fraction, HbA2 concentration was 2.5% (normal <3.5%) and the osmotic fragility tests gave normal results. The patient never required transfusions nor underwent splenectomy. The physical examination was normal. The main hematological parameters were: hemoglobin 116 g/L, reticulocytes  $139.5 \times 10^9/L$ , white blood cell count  $4.3 \times 10^9/L$  (63% neutrophils, 26% lymphocytes, 7% monocytes, 4% eosinophils) and platelet count  $211 \times 10^9/L$ . Red blood cell indices were normal (Table 1). Total bilirubin serum level was 28.1  $\mu\text{mol/L}$ . Lactate dehydrogenase concentration was 180 U/L. Bone marrow aspirate and biopsy showed only erythroid hyperplasia. The cytogenetic study was 46 XX.<sup>25</sup> Iron deficiency was evident with Perls stain in marrow aspirate. This iron deficiency was secondary to hypermenorrhea due to multiple uterine leiomyoma. X-Ray showed no condensations in the lungs. As an incidental finding, a widening in mediastinum was evident at D8-D11 level. Further investigation with computed tomographic scan (CT) and nuclear magnetic resonance revealed bilateral paravertebral soft tissue masses from T9 to T11. A radionuclide scan showed hypercapitation of transferrin in the paravertebral masses. A computed tomographic scan-guided fine needle aspiration was performed, and the cytological study showed the presence of cellular precursors of all three blood cell lineages. The general aspect of the sample was that of a bone marrow aspirate with erythroid hyperplasia. The patient was discharged from the hospital with oral iron and folic acid. Follow-up CT studies showed no changes in size and appearance of the mass for three years.



Figure 1.

Table 1.

	6 months before	3 months before	EMH Diagnosis	6 months later	4 years later
Haemoglobin (g/L)	112	112	116	105	119
MCV (fL)	94,4	95,5	94,9	95,1	93,7
MCH (pg)	31,8	31,1	31,4	31,4	31,4
MCHC (g/L)	337	326	331	330	335
RDW (%)	12,8	12,5	12,2	12,6	12,8
Reticulocytes ( $\times 10^9$ )	158,9		139,5		135,3
Haptoglobin (g/L)	0,02		0,05		
Ferritin (ng/mL)	10,4		24	102	216
Leucocytes ( $\times 10^9$ )	4,4	4,5	4,3	4,3	4,2
Platelets ( $\times 10^9$ )	204	208	211	191	209

As far as we know, only two cases of EMH associated with pyruvate kinase deficiency have been previously reported in the literature. In one case EMH affected exclusively the spleen and could be evidenced only after cytometric analysis of homogenized splenic tissue.<sup>5</sup> The other case presented as a paraspinal mass in a patient with PK deficiency and anemia who needed blood transfusions.<sup>1</sup> Instead, in the case we report, the paravertebral mass was clearly observed in a plain X-Ray film, in an otherwise asymptomatic patient that received a diagnosis of PK deficiency 25 years before, and whose clinical course was uneventful.

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## References

- Koch Ca, Li CY, Mesa RA, Tefferi A. Nonhepatosplenic extramedullary hematopoiesis: associated diseases, pathology, clinical course and treatment. *Mayo Clin Proc.* 2003;78:1223-1233.
- Moran CA, Suster S, Fishback N and Koss MN. Extramedullary Hematopoiesis presenting as posterior mediastinal mass: a study of four cases. *Mod Pathol.* 1995;8(3): 249-251.
- García-Riego A, Cuiñas C, Vilanova JJ, Ibarrola R. Extramedullary hematopoietic effusions. *Acta Cytol.* 1998;42(5):1116-1120.
- Hill DA, Swanson PE. Myocardial extramedullary hematopoiesis: a clinicopathologic study. *Mod Pathol.* 2000;13(7):779-787.
- Aizawa S, Kohdera U, Hiramoto M, Kawakami Y, Aisaki K, Kobayashi Y, Miwa S, Fujii, H, Kanno H. (2003). Ineffective erythropoiesis in the spleen of a patient with pyruvate kinase deficiency. *Am J Hematol.* 2003;74: 68-72.