

A new case of hemoglobin Chesapeake

When faced with polycythemia and normal erythropoietin (Epo) level, a search for an increased oxygen affinity of hemoglobin should be performed. We report a case of hemoglobin Chesapeake mimicking a myeloproliferative disorder.

A 58-year old man, native of Lille (North of France) with French and Flemish origins, presented in 1999 with a twenty-year history of erythrocytosis. He was a moderate smoker (3 cigarettes/day) and had never used anabolic steroids or erythropoietin (Epo). Monthly phlebotomies had been performed since 1997 for a supposed myeloproliferative disorder. At admission, physical examination showed facial erythema without splenomegaly. The white blood cell count was $9.22 \times 10^9/L$ (with 66.5% neutrophils, 21.2% lymphocytes, 5% monocytes, 3% eosinophils and 1% basophils), the red blood cell count was $6.80 \times 10^{12}/L$, hemoglobin concentration was 19.2 g/dL, hematocrit was 0.58, mean corpuscular volume was 85 fL, reticulocyte count was $96 \times 10^9/L$ and platelet count was $217 \times 10^9/L$. The erythrocyte sedimentation rate was 1 mm per hour. Total bilirubin concentration was 27 $\mu\text{mol}/L$ ($N < 17$) and ferritinemia was 10 ng/mL ($N 15-350$). The Epo level was 18 mU/mL ($N 10-25$), which did not support a diagnosis of polycythemia vera. Blood gas evaluation did not show hypoxemia. Investigations for an inappropriate secretion of Epo (renal tumor or cyst, hepatoma and cerebellar hemangioblastoma) were negative. The level of circulating transferrin receptor, obtained after multiple phlebotomies, was high (2.26 mg/L - $N 0.83-1.76$).

The presence of a high-oxygen-affinity hemoglobin was evoked and confirmed by a very low blood P50 value of 21 mmHg ($N 27.7 \pm 0.5$). High performance liquid chromatography revealed an abnormal hemoglobin component of 21%, which was also detected on cellulose acetate electrophoresis (pH = 9) and on isoelectrofocusing on agarose gel (pH = 6-8) (Figure 1). Polymerase chain reaction assay and structural analysis of the α -globin genes showed the presence of a mutation, characterized by a substitution from G to T at codon 92 of the $\alpha 2$ gene, typical of hemoglobin Chesapeake [$\alpha 92(\text{FG4Arg} \rightarrow \text{Leu})$].

Some mutations may produce hemoglobin molecules which do not release oxygen towards the tissues as readily as normal hemoglobin does. Such high-oxygen-affinity hemoglobin causes hypoxia and compensatory erythrocytosis. Hemoglobin Chesapeake, first described in 1966, is a rare very high-oxygen-affinity variant.¹ The mutation affects the amino acids involved in the $\alpha 1$ - $\beta 2$ chains' contact, and impairs the normal rotational transition from the deoxygenated low-affinity state to the oxygenated high-affinity state, tending to lock the hemoglobin into the high-affinity relaxed state.² In our case, the value of P50 – which is the oxygen tension at which hemoglobin is half saturated – was very low, related to an increased oxygen affinity of hemoglobin and to a shift to the left of the oxygen dissociation curve inducing a reactive polycythemia.

Until now, hemoglobin Chesapeake has only been described in a German and Irish family and in a Japanese one.³ Our case is the first described in a French family. In the heterozygous state, the quantity of abnormal component is 20-35% and patients present an erythrocytosis which may mimic a polycythemia vera.

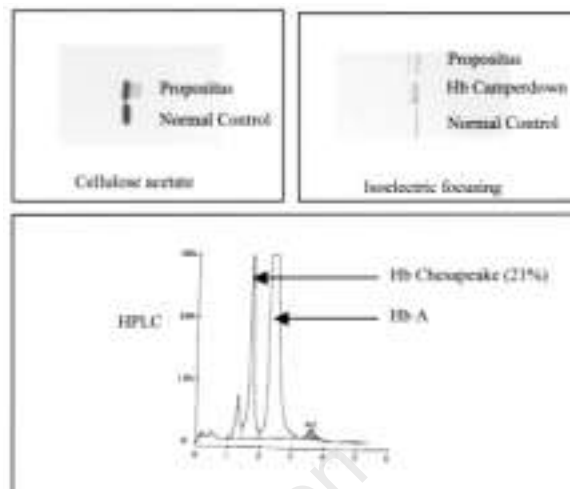


Figure 1. Cellulose acetate electrophoresis, isoelectrofocusing and HPLC (VariantTM System, Biorad, Hercules, CA, USA) showing the specific pattern of hemoglobin Chesapeake. Hb Camperdown is shown as an additional control.

This case underlines the importance of searching for a high-oxygen-affinity hemoglobin in patients suffering from chronic polycythemia, whether requiring or not phlebotomies.

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