Hemoglobin Saint Etienne Found in a Chinese Family

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Dear Editor,

Hemoglobin Saint Etienne (Hb St. Etienne), also known as Hb Istanbul, is a rare inherited disease of hemoglobin which results in loss of heme from the β -globin chain. So far, Hb St. Etienne has only been described in 4 reports involving 6 patients, and all of them were European [1–4]. In this report, we for the first time identified a family with Hb St. Etienne in Zhejiang, which indicates that Hb St. Etienne also exists in Mainland China.

The proband (III 2) was a 33-month-boy who had mild anemia (Hb 87 g/L) with a significantly increased reticulocyte count (11.2%). Hemoglobin electrophoresis showed the presence of 6.9% hemoglobin S and C (HbS/HbC) and increased HbF, as well as HbA₂ (6 and 17.1%, respectively) (Table 1). It has been reported that his father (II 1) had more severe symptoms and clinical features with moderate anemia (Hb <90 g/L), thrombocyto-

penia, and splenomegaly before splenectomy 12 years previously (Table 2). The results from hemoglobin electrophoresis showed that the level of HbS/HbC was markedly higher in the proband's father (Fig. 1), and this difference may have been responsible for the difference in disease severity between the proband and his father.

To establish the molecular diagnosis of anemia in the proband, a hotspot mutation

Table 1. Summary of the clinical presentation and laboratory parameters of the patients with Hb St. Etienne reported in this study and in the literature

	This study		1972		2000		2009	
	III 2	II 1	#1	#2	#1	#2	#1	#2
Gender	M	M	M	M	F	M	M	F
Age, years	2.75	32	8	19	36	13	57	16
Hb, g/L	87	130	–	–	136	122	135	120
PLT, $\times 10^9/L$	121	382	–	–	–	–	–	–
Ret, %	11.2	31.5	–	–	4.9	16	–	–
MCV, fL	96.8	103.8	–	–	85.7	89	103	116
Splenomegaly	–	+	–	+	+	–	+	+
HbA, %	70	73.8	–	–	60.5	62.9	–	–
HbF, %	6	2.8	19	–	0.9	0.7	–	–
HbA ₂ , %	17.1	1.4	–	–	2.6	2.4	–	–
HbS/HbC, %	6.9	22	–	–	36	34	–	–

Hb, hemoglobin; PLT, platelet count; Ret, reticulocytes; MCV, mean corpuscular volume.

screening assay was performed, with a negative result. The exons of the *HBB* gene and their flank regions within 50 bp were amplified and sequenced with an ABI 3100 Dx (Thermo Fisher Scientific, USA) for the proband and his family members. It was shown that the proband as well as his father harbored a heterozygous variant (c.279C>A, p.H93Q), and the variation was segregated with the phenotype in this family (Fig. 2).

Thus, a diagnosis of Hb St. Etienne was finally established. To our knowledge, this is the first report of Hb St. Etienne in Mainland China; it could contribute to better understanding the prevalence and spectrum of *HBB* gene and related disorders in China. The prevalence of inherited hemoglobin disorders varies considerably with geographical location and ethnic group. In China, consider-

ing the cost-effectiveness of testing and other factors, it is common in clinical practice to perform hotspot mutation screening assays of *HBB* as well as *HBA1/2* in patients with anemia in Zhejiang as well as in other parts of China to rule out thalassemia and related disorders. The case of Hb St. Etienne described in this report could not have been confirmed if the *HBB* gene had not been analyzed via Sanger sequencing.

Fig. 1. Hemoglobin analysis and red blood cell morphology of the proband (III 2) and his father (II 1).

Table 2. Laboratory parameters of patient II 1 prior to and after splenectomy

	Prior to splenectomy	After splenectomy
WBC, ×10 ⁹ /L	7.3	6.2
N, %	63.2	61.8
HbC, ×10 ¹² /L	3.68	4.52
Hb, g/L	89	129
PLT, ×10 ⁹ /L	63	338

WBC, white blood cell count; N, neutrophils; PLT, platelet count.

Fig. 2. Hemoglobin Saint Etienne found in a Chinese family. **a** Family pedigree. **b** Chromatogram of *HBB* c.279C>A, p.H93Q, by Sanger sequencing.

We suggest that for patients clinically suspected of inherited hemoglobin disorders, whole-gene analysis by Sanger sequencing or target sequencing by next-generation sequencing should be applied, especially for patients with negative hotspot mutation screening results.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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