

## Unusual Presentation of a Patient with Hemoglobin Constant Spring and Immune Hemolytic Anemia

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### Abstract

#### Introduction:

Hemoglobin Constant Spring (Hb CS), an abnormal Hb characterized by elongated  $\alpha$ -globin chain resulting from mutations of the termination codon in the  $\alpha 2$ -globin gene, is the most common nondeletional  $\alpha$ -thalassemic mutation and is an important cause of HbH like disease in Southeast Asia.

#### Case Report:

A 9-year-old female with immune hemolytic anemia and splenomegaly and abnormal hemoglobin in Hb electrophoresis is reported.

#### Results:

The first presentation of our patient was weakness and dark urine. She had a hemolytic anemia with normal MCV and positive direct coombs. In Hb electrophoresis, she had abnormal hemoglobin near the A2 region and slow moving component. PCR testing showed homozygous mutation in codon 142. Hb CS-containing RBCs have membrane pathology and these pathology lead to destruction of her RBCs in reticuloendothelial system and she had a RBC sick syndrome resemble thalassemia intermedia.

#### Conclusion:

Our study showed that the five-day massage therapy is a safe technique mothers can perform for stable preterm infants to facilitate weight gain in neonate.

#### Keywords:

Constant Spring, Hemoglobin, Hemolysis Anemia, Immune.

### Introduction

Hemoglobin Constant Spring (HbCS) is the most common nondeletional  $\alpha$ -thalassemic mutation and is an important cause of HbH like disease in Southeast Asia. HbCS variants have an almost normal mean cell volume (MCV) and the anemia is more

severe when compared with other  $\alpha$ -thalassemic variants (1). Hemoglobin Constant Spring (CS) is characterized by an elongated  $\alpha$  chain due to T-C transition of codon 142 of the  $\alpha 2$ -globin gene. Heterozygosity for this mutation is usually associated with mild anemia (2).

The simple heterozygous form of Hb CS is minimally anemic; however, patients with homozygous Hb CS or combined heterozygous with  $\alpha^0$ -thalassemia may

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develop more severe clinical features. The homozygous Hb CS is associated with mild thalassemia intermediate with variable Hb, Hct and MCV levels. RBC morphology shows marked anisocytosis, hypochromia and basophilic stippling (3). To understand the cellular events that may contribute to differences in HbCS disease severity and state of hydration, a series of biophysical and biochemical analyses on erythrocytes obtained from patients with severe HbH disease, HbH/CS, HbCS/CS, HbCS trait and  $\alpha$ -thalassemia discovered that the membrane pathology of HbCS variants, which includes increased membrane rigidity and altered cell hydration, is the result of perturbations induced by association of oxidized  $\alpha^{CS}$  with the membrane (1).

### Case Report

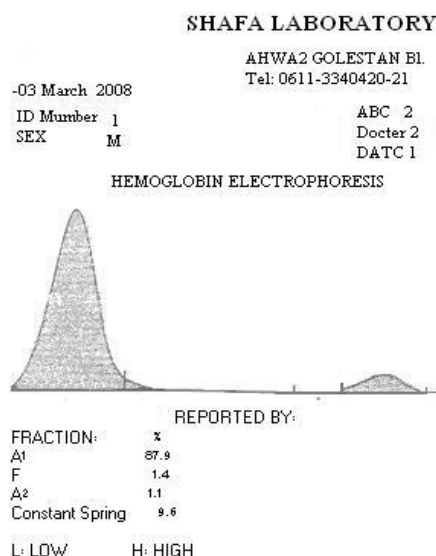
A 9-year-old female was referred in Shafa Hospital with jaundice. She had weakness and dark urine. In physical examination, the patient had pallor, icteric sclera and splenomegally. Laboratory data in first admission were, WBC=11000/ $\mu$ l (P= 75%, L=20), Hb= 8.5 gr/dl, Plt= 337000, MCV= 83.5, MCH= 25, MCHC= 31, retic= 5.2%, BUN= 14, Cr= .5, Na=142, K= 4.6, SGOT= 21, SGPT= 19, ALP= 313, T-Billi= 4.3, D-Billi=.5, Direct-Coombs= positive, and BMA revealed hypercellular marrow and erythroid hyperplasia suggestive hemolytic anemia.

Hb electrophoresis in first admission identified, A= 90%, F= 2.4% and A<sub>2</sub>= 7.5%. Consult with ophthalmologist did not show Keizer flecher ring.

Abdominal sonography showed splenomegally and normal liver, gallbladder and kidneys. The patient were treated with prednisolon 1mg/kg and discharged from hospital with good condition.

After one year, the patient admitted in our hospital with icter and dark urine. In this admission, laboratory's data were normal levels except, T-Billi= 4.4 with D-Billi= .5 and Hb –electrophoresis with A= 90.6%,

F=1.4%, A<sub>2</sub>= 1.4 and Constant Spring= 6.6% (fig 1).



**Fig 1:** Hb electrophoresis of our patient with an abnormal band next to A<sub>2</sub>

PCR- testing for Hb Constant Spring in our patient identified homozygous mutation in codon 142.

### Discussion

In approximately 50% Of individuals with HbH disease in Southeast Asia, small quantities of hemoglobin Constant Spring are found (4).

Hemoglobin Constant Spring (HbCS) is a hemoglobin variant with an elongated a globin chain secondary to a chain termination mutation. The diagnosis of HbCS by electrophoresis is difficult (5). The CS mutation only affects the  $\alpha_2$  gene, which account for absent 2/3 of normal  $\alpha$ -globin chain production. Furthermore, the mRNA of  $\alpha^{CS}$  is very unstable compared with normal  $\alpha$  mRNA and accounts for less than 1% of protein output of normal  $\alpha_2$ -gene. Interestingly, in terms of path biology, the synthesis of even small amounts of elongated  $\alpha^{CS}$  results in more severe anemia than is seen analogous deletional  $\alpha$ -thalassemia (1). Therefore, it has been suggested that  $\alpha^{CS}$ -chain may have deleterious

effects on cellular and membrane properties of Hb CS-containing RBCs and these changes in turn could account for increased hemolysis (1). There is possibility that the unstable  $\alpha^{CS}$  mRNA precipitate and aggregate leading to pathology of red cells and to the basophilic appearance (6).

### Conclusion

We believe that our patient had pathology in Hb CS-containing RBCs and these pathology lead to destruction of her RBCs in reticuloendothelial system and she had a RBC sick syndrome resemble thalassemia intermediate and immune hemolytic anemia in our patient was due to this RBCs sick syndrome. We believe in approach of a patient with hemolytic anemia attention, it is necessary to pay attention to a hereditary RBC disorders.

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