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GEN17

COINHERITANCE OF HB ADANA WITH HB CONSTANT SPRING: A CASE REPORT

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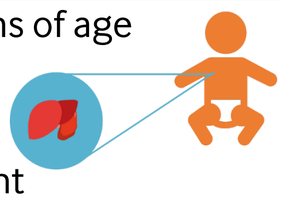
INTRODUCTION

- Compound heterozygosity of non deletional alpha thalassemia often have more severe presentation compared with coinheritance of non deletional alpha thalassemia with deletional alpha thalassemia.
- The prevalence of non-deletional alpha thalassemia co inheritance, specifically the Hb Adana/Hb Constant Spring in Malaysia is around 0.4%[1].
- Haemoglobin Adana (Hb Adana) arises from point mutation of Codon 59 of either alpha 1 or alpha 2 gene, which will lead to substitution of Gly→Asp, and leads to instability of the haemoglobin molecule. (*HBA1*: c.179G>A or *HBA2*: c.179G>A)[2].
- Haemoglobin Constant Spring (Hb CS) on the other hand is an abnormal haemoglobin caused by a mutation at the termination codon of α2-globin gene.
- Hb Adana is most commonly seen in the Malay population whilst Hb CS is seen in the Chinese populations. For both, the carriers are clinically asymptomatic, and the diagnosis of Hb Adana is challenging as the protein is not detectable on routine haemoglobin analysis.
- Non deletional alpha thalassemia, in combination with the deletional mutations mostly have mild-to-moderate anaemia. In contrast, patients who were compound heterozygotes non deletional mutations, generally will have more severe anaemia, and much earlier presentation, usually in childhood [3].
- We present here, an infant with Hb Adana/Hb CS who presented at three months old with severe anaemia.

CASE REPORT

- An eight-month-old female infant presented at three months of age with severe anaemia and hepatosplenomegaly.
- Hb at presentation was 4.5 g/dL and the blood film showed microcytosis with marked anisopoikilocytosis with prominent basophilic stippling.
- Capillary electrophoresis performed revealed lowered Hb A (86.9%), raised Hb F (9.2%) and abnormal peak at Zone C (2.4%).
- Molecular study performed with ARMS PCR revealed co- inheritance of Hb Constant-Spring and Hb Adana, whilst GAP PCR revealed no deletional mutations.



- Both parents are asymptomatic. Capillary electrophoresis of her father showed small peak at Zone C (0.6%) with heterozygous Hb Constant Spring detected on ARMS PCR. As for the mother, the haemoglobin analysis revealed no abnormality, however, non deletional missense mutation of Codon 59 was detected on ARMS PCR. No deletional mutation was detected on GAP PCR for both parents.
- This baby is currently needing monthly blood transfusion, with the aim of stem cell transplant after 1 year of age.

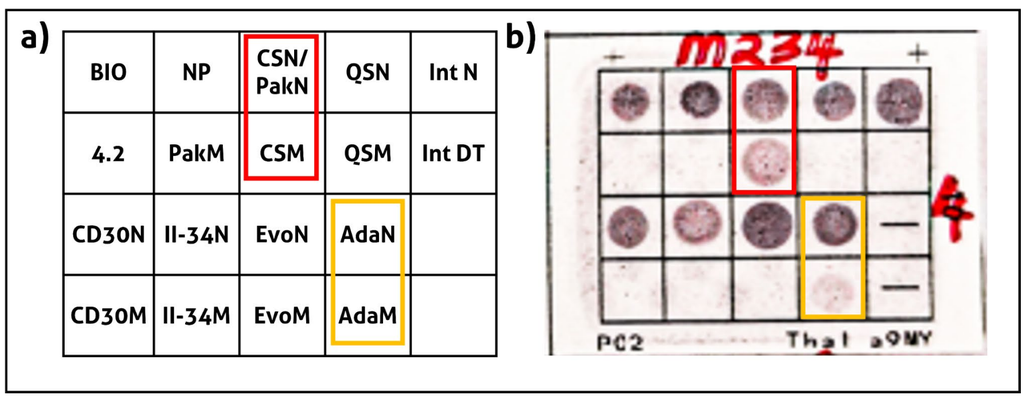


Figure 1: Flow-through Hybridization using Hybribio Thalassemia Geno Array Diagnostic Kit. a) Location of probe designed in the membrane template. Red box indicate Hb Constant-Spring and yellow box indicate Hb Adana. b) Patient has mutated Constant Spring and mutated Adana.

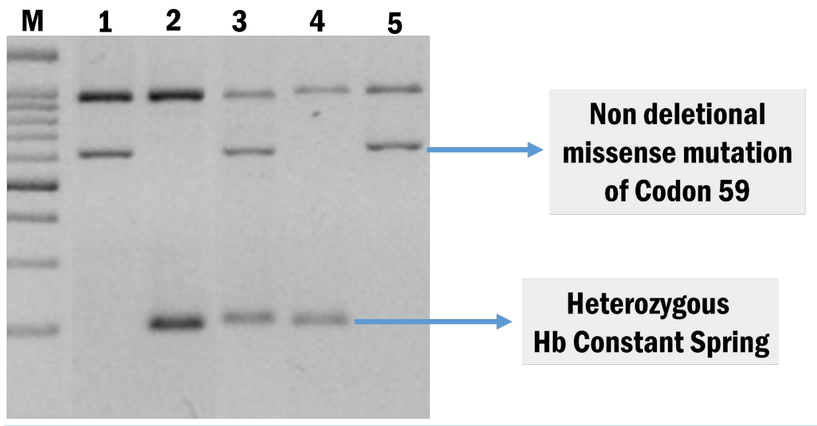


Figure 2: Agarose gel electrophoresis showing the **ARMS-PCR** for heterozygous Hb Constant Spring, non deletional missense mutation of Codon 59 and co- inheritance of Hb Constant-Spring and Hb Adana. M=Marker (DNA Ladder); 1= CD59; 2=CS; 3=Patient (CD59 and CS); 4=Father (CS); 5=Mother (CD59)

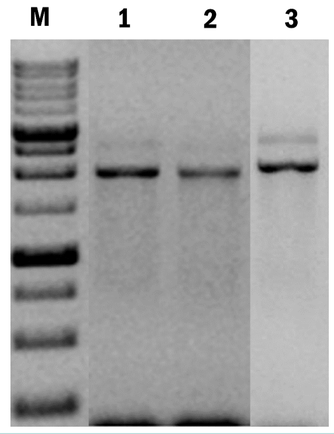


Figure 3: Agarose gel electrophoresis showing no deletional mutation was detected on GAP PCR for both parents and patient. M=Marker (DNA Ladder); 1=Father;2=Mother;3=Patient

DISCUSSION

- This case illustrates the severity of coinheritance of non deletional alpha thalassemia in an infant. Because the phenotype of patients with coinheritance of Hb Adana with other alpha thalassemia are varied, it can be difficult to predict clinically the prognosis in terms of blood transfusion requirements and growth.
- The phenotype largely depends on whether *HBA 1* or *HBA 2* gene is affected. Codon 59-point mutation affecting *HBA 2* gene has generally more severe phenotype. Although Hb Adana that was originally described in Turkey affected the *HBA 1* gene, Hb Adana in Malaysia and Indonesia by far affected the *HBA 2* gene[4].

DISCUSSION

- Since Malaysia and Indonesia share common cultures and are in the same region, it is not surprising that the same location of the mutation is observed. This is contributed by the diversity of α thalassemia mutations, with the process of natural selection and genetic drift.

CONCLUSION

- Coinheritance of non deletional alpha thalassemia should be considered in a multi-ethnic population like Malaysia.
- There is a need for early recognition of these patients to ensure appropriate monitoring, treatment and family planning can be inculcated.

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