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Answers for the CME

1.1 This patient is 53 years and her HPLC/Hb capillary electrophoresis has HbF beyond the fetal age estimating to 91.3%, and absent HbA.

The following differential diagnosis can be considered for prominent band of HbF with absent HbA.

i. Homozygous delta-beta (δβ) thalassaemia
ii. Homozygous hereditary persistence of fetal haemoglobin (HPFH)
iii. Homozygous beta thalassaemia or compound heterozygous beta thalassaemia
iv. Compound heterozygous beta and hereditary persistence of fetal haemoglobin
v. Compound heterozygous beta / delta-beta thalassaemia

1.2 HbF is elevated in all above conditions.
Both homozygous delta-beta thalassaemia and homozygotes of HPFH show absent HbA and HbA2 while HbF is 100% beyond fetal life[1,2]. The two groups of homozygous disorders are distinguished by the phenotype of individuals[3,4]. Homozygotes of HPFH are asymptomatic, whereas δβ-thalassemia homozygotes have thalassemia intermedia-phenotype[3].

Homozygous beta thalassaemia or compound heterozygous beta thalassaemia are not possible with the clinical history as this patients has received blood transfusion only during her pregnancy indicating the non-transfusion dependency. Compound heterozygous beta/HPFH shows HbF of 100%[3]. The exact diagnosis of δβ-thalassemia and hereditary persistence of fetal haemoglobin requires genetic analysis for mutations[5,6]. However, the above clarification narrows down the differential diagnoses.

Compound heterozygous beta/ delta-beta thalassaemia shows HbF and small amount of HbA2 and clinically behaves as thalassemia intermedia[5]. Therefore, compound heterozygous beta / delta beta thalassaemia is more likely.

1.3 In the setting of limited resources for genetic testing, family screening was done for further confirmation.

The results of HPLC of her four children are as follows. The partner was not alive hence results of the children are given below.

	RCC x10^{12}/L	**Hb g/dL**	**MCV fl**	**MCH pg**	**HbA%**	**HbF%**	**HbA2%**	**Diagnosis**
Mother (patient)	4.3	8.3	62.3	19.2	absent	91.3	3.4	Possible compound heterozygous beta/ δβ-thalassemia
Child 1 34 years	5.0	11.6	68.3	23.2	81.5	15.7	2.8	Heterozygous δβ-thalassemia
Child 2 32 years	6.5	2.8	61.2	19.4	95.1	-	4.9	Heterozygous β-thalassemia
Child 3 30 years	6.6	11.9	64.7	21	95.4	-	4.6	Heterozygous β-thalassemia
Child 4 26 years	5.2	10.4	63.1	21	71.9	16.2	2.6	Heterozygous δβ-thalassemia

Family screening findings are in favour of possible beta/delta-beta thalassaemia in this patient.

Delta-beta (δβ) thalassemia is a rare form of haemoglobinopathy caused by a deletion in both the delta and beta genes on chromosome 11[1,3]. The result is diminished production of beta and delta globin chains. The gamma genes on the affected chromosome increase their production of gamma globin. Therefore the excess alpha chains will be combined with gamma chains leading to increased production of HbF[3].

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