HAEMOGLOBIN KALAVASOS – A NOVEL ALPHA CHAIN MUTATION

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Introduction

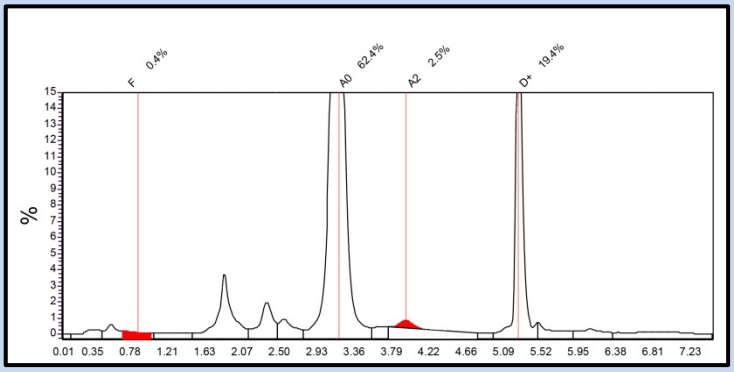
HbA1c is a measure of the amount of glucose bound to haemoglobin (Hb) in red blood cells. The higher the glucose concentrations over the previous 2-3 months, the higher the HbA1c result. The HbA1c test is used to monitor the glucose levels of patients who have been diagnosed with diabetes. Haemoglobinopathies are a group of inherited genetic defects that result in abnormal structure of one of the globin chains of the haemoglobin molecule. In people who have haemoglobinopathies some HbA1c tests give falsely high or low readings that can lead to the over- or under-treatment of diabetes. Therefore it is extremely important to measure HbA1c on an accurate instrument that detects all potential haemoglobinopathies.

Aim

We present a case of a novel mutation (Haemoglobin Kalavasos) in the alpha-2 globin gene which was discovered following routine HbA1c testing on a 65 year old female of Cypriot origin.

Methods

Analysis was originally performed by ion-exchange High Performance Liquid Chromatography (HPLC) on the Tosoh Automated Glycohemoglobin Analyzer HLC-723G7 (Tosoh G7). The sample was re-run in the thalassaemia mode on the same instrument. A fresh sample was also analysed on the Sebia Capilary Zone Electrophoresis (CZE). For further investigation this sample was also analysed on the Tosoh G8 and GX instruments. DNA was performed on the sample and the patient was reviewed by a specialist haematologist.



Sanger sequencing (alpha globin gene)		Sanger sequencing (beta globin gene)	
Alpha 1	**Alpha 2**	**Exon 1&2**	**Exon 3**
Normal	Cd 91 CTT-CAT Heterozygous	Normal	Normal

Results

The Tosoh G7 showed an additional peak constituting 23% of the total area on the chromatogram following the A0 peak. The sample was re-run in the thalassaemia mode on the same instrument and this demonstrated a peak of 20% at 5.2 minutes. Capilary Zone Electrophoresis analysis by Sebia showed no abnormalities. For further investigation the sample was also tested on the Tosoh G8 and GX instruments and both instruments confirmed the abnormality. The HbA1c concentrations as well as the other investigations such as fructosamine excluded dysglycaemia or haematological pathology. A novel mutation in the 2 globin gene at codon 91, namely 275T>A was found. This type of novel mutation was named after the birth place of the patient: Kalavasos.

Conclusion

There was a clear distinction between the different methodologies and their ability to detect haemoglobinopathies. Initial measurement on the Sebia CZE would not have detected this haemoglobinopathy at all. This novel mutation is named haemoglobin Kalavasos and this is the first description of this novel mutation.