(1/8=12.5%), *DNMT3A* (1/8=12.5%), *EZH2* (1/8 =12.5%), etc. The enriched *WT1* mutations in *CPSF6-RARG/RARG-CPSF6* AML suggest its involvement in leukaemogenesis.

As summarised in Table 1, all patients were treated with ATRA, and four patients were also treated with arsenic. Among them, six patients were re-evaluated by peripheral blood or bone marrow morphology/flow cytometry during or at the end of induction therapy. Importantly, no signs of differentiation of blast cells were achieved, indicating that CPSF6-RARA-positive AML is unresponsive to ATRA. The four patients receiving intravenous ATO or oral arsenic Realgar-indigo naturalis formula (RIF) had no response, suggesting arsenic resistance. It is worth noting that four patients succumbed to severe haemorrhage events during induction or re-induction, reminiscent of APL in the pre-ATRA era. Close monitoring and aggressive supportive care should be provided to avoid fatal bleeding events. Re-induction with AML-like approaches achieved complete remission (CR) in Patient 2, adopting '7+3' regimen with daunorubicin plus cytarabine (DA). Homoharringtonine plus cytarabine (HA) chemotherapy achieved CR in Patients 5 and 6 who failed previous anthracycline plus cytarabine chemotherapy. Patient 2 achieved long-term leukaemia-free survival for more than 6 years after consolidation with two courses of high dose cytarabine and two courses of DA, while Patients 5 and 6 relapsed and died at 11 months and 32 months, respectively. No-one underwent allogeneic haemopoietic stem cell transplantation (allo-HSCT). The low 2-year and 5-year overall survival rates suggest that allo-HSCT should be performed in first CR for *CPSF6-RARG*-positive AML patients.

In summary, we report a new case of *CPSF6-RARG*-positive AML resembling APL and a novel *CPSF6-RARG* variant that fuses CPSF6 exon 5 to RARG exon 4. Reviewing the literature, *CPSF6-RARG*-positive AML resembles APL, but is unresponsive to ATRA and ATO. Switching to AML-like approaches with aggressive supportive care is recommended. Accurate identification of this rare subtype of AML is essential to guide therapeutic decisions. Further laboratory and clinical investigations are in urgent need.

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Haemoglobin analysis of a newborn with haemoglobin Q-H disease

To the Editor,
We report a rare case of haemoglobin (Hb) Q-H disease in a Chinese newborn, with detailed description of the haemoglobin analysis results. To our best knowledge, this is the first report in the literature which describes cation exchange high performance liquid chromatography (HPLC) and capillary electrophoresis results of a newborn with Hb Q-H disease.

The patient was a newborn male, born of non-consanguineous marriage. His father and mother were both

of Chinese origins. Both parents were asymptomatic. The mother was found to be heterozygous Hb Q-Thailand during haemoglobin pattern study on antenatal screening, which was subsequently confirmed by Sanger sequencing of the *HBA1* gene [NM_000558.5(HBA1):c.223G>C (p.Asp75His)]. Multiplex gap-polymerase chain reaction (gap-PCR) of α-globin genes showed heterozygous $-\alpha^{4.2}$ deletion. Deletions for $--^{SEA}$ and $-\alpha^{3.7}$ were not detected. The father was an α-thalassaemia trait. Molecular analysis of the α-globin genes using multiplex gap-PCR showed heterozygous $--^{SEA}$ deletion. Gene deletions of the $-\alpha^{3.7}$ and $-\alpha^{4.2}$ type were negative. Haematological parameters and haemoglobin analysis results by cation exchange HPLC are shown in Table 1.

The patient was born full term (38 weeks of gestation) with a birth weight of 3.31 kg. He presented with hypochromic microcytic anaemia shortly after birth. His red cell indices after birth are shown in Table 1. Peripheral blood smear showed prominent anisopoikilocytosis with hypochromic microcytic red cells, some target cells, elliptocytes and tear-drop cells. There was moderate polychromasia. Reticulocytes accounted for 7.6% of the erythrocytes.

Haemoglobin analysis was carried out by HPLC on the Variant-II Hemoglobin Testing System (Bio-Rad Laboratories, USA) according to the procedures provided by the manufacturer. Examination of the chromatogram showed absence of Hb A, Hb F and Hb A_2, with presence of Hb Bart's and two variant peaks. The variant peaks had retention times of 3.64 min and 4.56 min (Fig. 1A), and they were most likely to represent $\alpha^{Q}{}_2\gamma_2$ and $\alpha^{Q}{}_2\beta_2$ variants, respectively.

On capillary electrophoresis by the Capillarys 2 Flex Piercing system (Sebia, France), the two variants migrated to Z(S) ($\alpha^{Q}{}_2\gamma_2$) and Z(F) ($\alpha^{Q}{}_2\beta_2$), respectively (Fig. 1B,C). The percentages of Hb Bart's, $\alpha^{Q}{}_2\gamma_2$ and $\alpha^{Q}{}_2\beta_2$ were 30.4%, 37.7% and 31.3%, respectively. Alkaline cellulose acetate gel electrophoresis revealed two variants which migrated to the Hb S/D/G position ($\alpha^{Q}{}_2\gamma_2$) and a position slightly anodal to Hb S/D/G position ($\alpha^{Q}{}_2\beta_2$), respectively (Fig. 2A); while on acid agarose gel electrophoresis, the two variants migrated to a position between Hb A and Hb F ($\alpha^{Q}{}_2\gamma_2$) and a position slightly anodal to Hb S ($\alpha^{Q}{}_2\beta_2$), respectively (Fig. 2B). Sanger sequencing of the *HBA1* gene identified a missense mutation NM_000558.5: c.223G > C (p.Asp75His) leading to Hb Q-Thailand. Gene deletions of the $--^{SEA}$ and $-\alpha^{4.2}$ were detected by multiplex gap-PCR. $--^{THAI}$, $--^{MED}$, $--^{FIL}$, $-\alpha^{3.7}$ and $-(\alpha)^{20.5}$ type deletions were negative. The results were compatible with compound heterozygous $--^{SEA}$ deletion and Hb Q-Thailand.

A follow-up assessment at the age of 7 months showed mild pallor, no clinical jaundice, satisfactory growth and no hepatosplenomegaly. The patient was on oral folate supplementation and did not require transfusion.

Hb Q-Thailand is an α-globin chain variant caused by a point mutation (GAC → CAC; Asp → His) in codon 74 of

Table 1 Red cell indices and haemaglobin study results of the proband and his parents

Parameters	Proband	Mother	Father
Sex	Male	Female	Male
Age	1 day	31 years	30 years
Hb (g/dL)	10.6	12.7	14.1
MCV (fL)	72.8	77.1	67.1
MCH (pg)	22.5	25.6	22.0
RBC ($\times10^{12}$/L)	4.72	4.97	6.42
RDW (%)	20.5	13.7	15.3
HbA present?	No	Yes	Yes
HbA_2 (%)	<1.0	2.9[a]	2.8
HbF (%)	<1.0	<1.0	<1.0
Hb Barts (%)	30.4	Not detected	Not detected
Hb Q-Thailand (%)	$\alpha^{Q}{}_2\gamma_2$: 37.7 $\alpha^{Q}{}_2\beta_2$: 31.3	28.4	Not detected
Genotype	$--^{SEA}/-\alpha^{4.2\text{-}Q}$	$\alpha\alpha/-\alpha^{4.2\text{-}Q}$	$\alpha\alpha/--^{SEA}$

Hb, haemoglobin; MCH, mean corpuscular haemoglobin; MCV, mean corpuscular volume; RBC, red blood cells; RDW, red cell distribution width.
[a] The level of HbA_2 reported included the Hb Q_2 ($\alpha^{Q}{}_2\delta_2$).

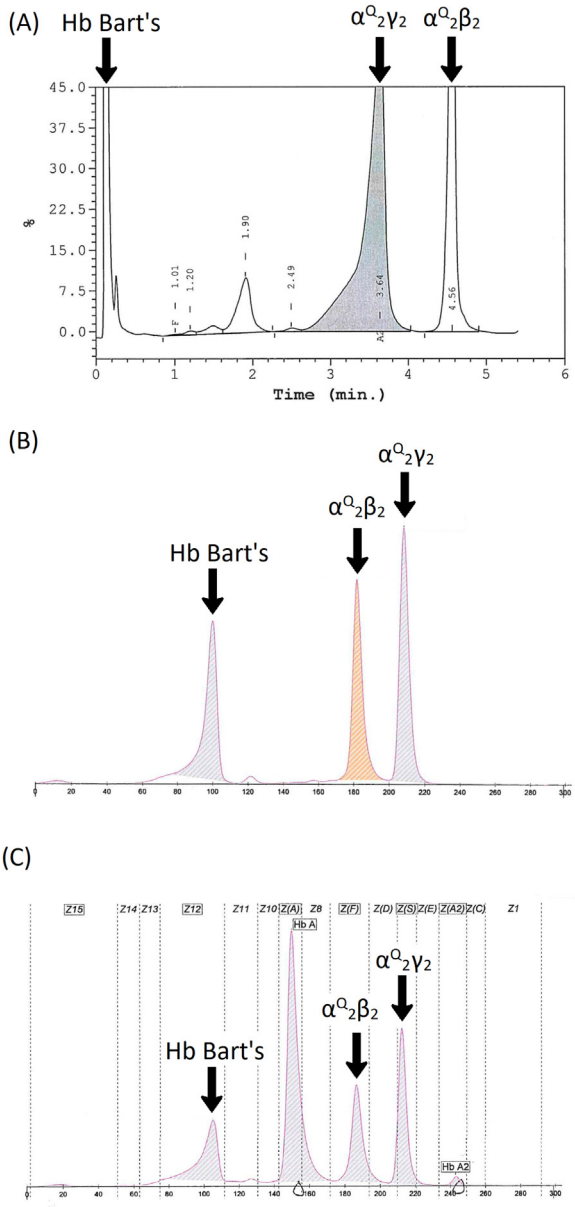

Fig. 1 (A) Cation exchange high performance liquid chromatography analysis of the proband. (B) Capillary electrophoresis result of the proband before 1:1 mixing with normal adult blood. (C) Capillary electrophoresis result of the proband after 1:1 mixing with normal adult blood.

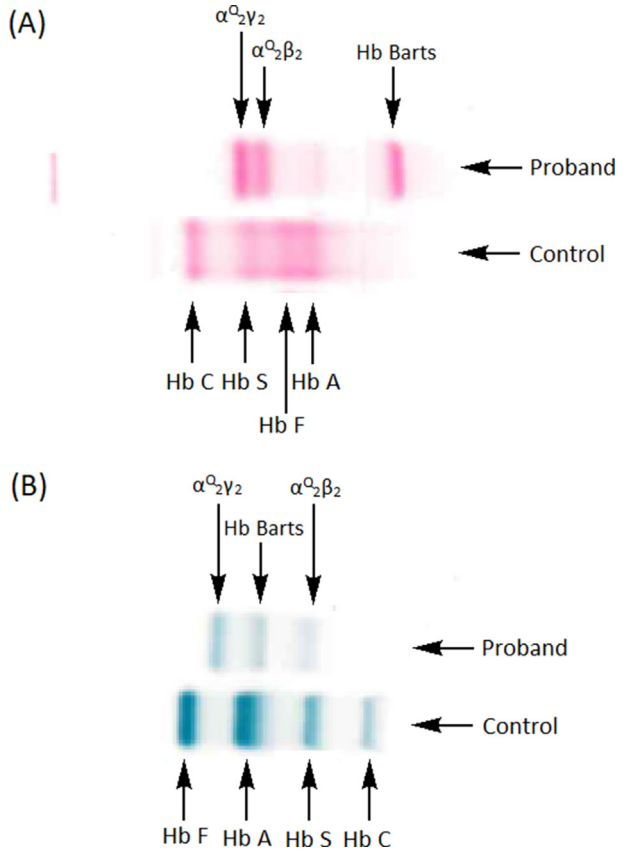

Fig. 2 (A) Alkaline cellulose acetate gel electrophoresis result of the proband. (B) Acid agarose gel electrophoresis result of the proband.

HBA1 gene on chromosome 16, and it is associated with a leftward single α-globin gene deletion ($-\alpha^{4.2}$).[1,2] This haemoglobin variant is most commonly found in Thai, Chinese and Japanese individuals.[3]

Hb Q-H disease is caused by the co-inheritance of Hb Q-Thailand and α^{0}-thalassemia (mainly $--^{SEA}$ deletion). It is a rare disease which is mostly identified in patients of Chinese origins. Hb Q-H disease is associated with the absence of Hb A, presence of Hb Bart's, with Hb Q-Thailand being the predominant fraction of haemoglobin in adults.[4,5] Clinical features of the disease include marked microcytosis, chronic haemolytic anaemia associated with jaundice and hepatosplenomegaly.[6] Although Hb A is absent in patients with Hb Q-H disease, clinical features and blood indices of these patients are similar to that of deletional Hb H disease.[5] This is probably because Hb Q-Thailand has normal oxygen affinity, Bohr effect and cooperativity.[7] This is also supported by the clinical features of the newborn. He did not show hydrops or growth retardation in antenatal follow-up and did not require transfusion up to last follow-up.

To our best knowledge, haemoglobin analyses of newborns with Hb Q-H disease have rarely been reported. The results of cation exchange HPLC and capillary electrophoresis of these patients have not been reported in the literature previously.

Our case demonstrates the haemoglobin analysis results in a newborn with Hb Q-H disease. There was absence of HbF and HbA, and presence of Hb Bart's with two major haemoglobin variants, namely $\alpha^{Q}_2\gamma_2$ and $\alpha^{Q}_2\beta_2$. The percentage of $\alpha^{Q}_2\gamma_2$ variant was slightly higher than that of the $\alpha^{Q}_2\beta_2$ variant. The $\alpha^{Q}_2\gamma_2$ variant had a retention time of about 3.6 min on HPLC by the Variant-II Hemoglobin Testing System. It migrated to Z(S) on capillary electrophoresis by the Capillarys 2 Flex Piercing system. The $\alpha^{Q}_2\gamma_2$ variant migrated to Hb S/D/G position on alkaline cellulose acetate gel electrophoresis and a position between Hb A and Hb F on acid agarose gel electrophoresis. This knowledge is useful for haematologists and laboratory scientists for rapid diagnosis of Hb Q-H disease in newborns, especially if molecular tests are not readily available in the laboratory.

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A rare case of metastatic endometrial stromal sarcoma mimicking primary breast carcinoma: a diagnostic pitfall

To the Editor,

Non-mammary metastases to the breast are rare and account for approximately 2% of all malignant breast neoplasms,[1] with this number dropping below 1% if haematological malignancies are excluded.[2] Metastatic tumours to the breast