Pseudo-Sickle Anemia: Two Case Reports

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Sickle cells in peripheral blood smear are usually seen in sickle cell disease. However in certain very rare conditions, pseudosickle cells may be seen. The present study reports two cases of iron deficiency anemia with presence of pseudo sickle cells in the peripheral blood films which lead to a diagnostic dilemma.

Case Reports

Case 1 A 47 year old Hindu female belonging to Uttar Pradesh presented with persistent pallor and generalised weakness. On general physical examination she was anicteric and no hepatosplenomegaly was observed. Her past history was negative for jaundice and venous thrombosis. She was on oral haematinics off and on for persistently low Hb levels. The hemogram showed Haemoglobin (Hb) 7 gm/dL, mean corpuscular volume (MCV) 63 fl, mean corpuscular haemoglobin (MCH) 18.1 pg, mean corpuscular haemoglobin concentration (MCHC) 28.7 %, red blood cells distribution width CV (RDW-CV) 21.7 % and reticulocyte count $0.0491 \times 10^6/\mu\text{L}$. Peripheral blood film (PBF) showed microcytic hypochromic anaemia with presence of few sickle cells. Sickling test with 2 % sodium metabisulphite revealed increased sickling of RBC's immediately as well as after first hour of incubation at 37 °C (Fig. 1). Patient was provisionally diagnosed as sickle cell anaemia. However, Haemoglobin Electrophoresis and High Performance Liquid Chromatography (Hb-

HPLC) revealed normal chromatogram. The family studies were normal. Hb-HPLC was repeated and confirmed, ruling out diagnosis of sickle cell disease and other rare haemoglobinopathies. Peripheral smears and sickling test were reviewed and were found to yield the same results. Sample was incubated with isotonic saline and showed increased sickling immediately and after first hour. However incubation with hypertonic saline showed crenated cells and no increase in sickling ruling out Hb Setif. Patient serum ferritin was done and found to be low (1.39 ng/ml). Finally, patient was diagnosed as having iron deficiency anaemia with pseudo sickle cells in PBF.

Case 2 A 2.5 years Hindu male child belonging to Delhi presented with pallor and weakness. His hemogram showed Hb 7.7 gm/dL, MCV 43.3 fl, MCH 12.6 pg, MCHC 29.2 %, RDW-CV 24.9 % and reticulocyte count $1.12 \times 10^6/\mu\text{L}$. PBF showed microcytic hypochromic anaemia with presence of few sickle cells. Sickling test was positive. But, a normal chromatogram on Hb-HPLC ruled out the presence of sickle cell anemia and other abnormal haemoglobinopathies. His serum ferritin was low (10.1 ng/mL). Patient was diagnosed with iron deficiency anemia with presence of elongated cells i.e. pseudosickle cells in PBF.

Sickle cells are sickle shaped RBC's with pointed ends and absent central pallor, seen in PBF of sickle cell disease. However, there are rare conditions in which pseudosickling may be seen.

Studies done on animals like Angora goats have shown that distorted red cells resemble sickle cells in vivo [1].

In humans, Sickling test by 2 % sodium metabisulphite is the screening test for sickle cell disease; however presence of HbS is confirmed by Hb-HPLC. But there are conditions which show false positive sickling test by 2 % sodium

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Fig. 1 Positive sickling test by 2 % sodium metabisulfite (100X)

metabisulphite. These include rare haemoglobinopathies like HbC (Harlem), HbC (Georgetown), HbH, HbI, Hb Barts and Hb Setif [2]. It may also be seen in conditions with decreased paO_2 like high altitude, iron deficiency anaemia, certain infections like malaria, Parvovirus, extremes of temperature, acidosis and exposure of RBCs to 4 % sodium metabisulphite [3].

Abnormal haemoglobin—Hb Setif has been shown to cause psuedosickling in vitro when RBCs containing Hb Setif are incubated in normal saline or iodine containing buffer. Hb Setif was first described by Wajcman et al. [4] in an Algerian family, and since then many cases have been reported in Iran [5] and Australia. Hb Setif containing RBCs show pseudosickling in vitro due to intracellular crystallisation of insoluble Hb [$\alpha 94(\text{G1})\text{Asp} \rightarrow \text{Tyr}$]. They are not found in vivo and do not produce a clinical disorder. Pseudosickling in these cases are increased by

increasing osmolality (hypertonic saline) and by increasing temperature to 37 °C as compared to room temperature [6].

Kasmani et al. [7] reported a case of Psuedosickle cell anemia in an adult female with presence of iron deficiency. Her peripheral smear showed presence of elliptocytes and poikilocytes which mimicked sickle cells. This was confirmed electrophoretically.

Sickle cells on peripheral smear with positive sickling test but a normal HPLC are indicative of pseudosickle cells. In such cases, a review of peripheral smear and serum ferritin levels should be done to rule out iron deficiency anemia.

Conflict of interests The authors declare that they have no conflict of interests.

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