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Hemoglobin Andrew-Minneapolis: Hemolytic Erythrocytosis and Severe Iron Overload in Toxic Liver Cirrhosis

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We report this case involving a 50-yr-old man of Central European descent who presented at our outpatient department with psoriasis. The known preexisting conditions in this case included alcohol-related toxic liver cirrhosis and untreated type 2 diabetes. The patient had an HbA1c level of 6.2%, which was determined during a routine diabetic monitoring visit. We also assessed HbA1c levels via HPLC (Variant; Bio-Rad, Hercules, CA, USA) and noted an anomaly in the HbA fraction. Subsequent chromatographic, electrophoretic, and genetic examinations confirmed Hb Andrew-Minneapolis, a rare genetic Hb anomaly. always been present in this patient, yet the possible causes of its occurrence had not been investigated. On analysis of the patient's Hb on HPLC, we found an obvious peak of 39.1%. Distinct bands were also noted in the acidic and alkaline hemoglobin electrophoresis (Hydrasys; Sebia, Norcross, GA, USA) results. Capillary zone electrophoresis (Capillarys; Sebia, Norcross, GA, USA) showed an obvious peak of 24.9%. Hemogram analyses (XE-5000; Sysmex, Kobe, Japan) on EDTA-anticoagulated blood (Hb=18.3 g/dL, reference range: 13.5-17.2 g/dL) revealed hyperchromia, macrocytosis (mean corpuscular Hb=37 pg/cell, refernce range: 27-33.5 pg/cell; mean corpuscular volume=103 fL, reference range: 80-99 fL) and reticulocytosis (2.8%, reference range: 0.5-2.0%).

Arterial blood gas analysis (Rapidlab 1265; Siemens, Munich, Germany) revealed that the partial pressure of oxygen was 68.5 mmHg, slightly lower than the reference range of 70-100 mmHg. The p50 value also decreased, measuring 19 mmHg (reference value: >27 mmHg). Serum sample analysis (Dimension Vista 1500; Siemens, Munich, Germany) indicated that hemolysis (free Hb=386 mg/L, reference value: ≤50 mg/L) was occurring, and the patient had a reduced haptoglobin level of 0.17 g/L (reference range: 0.3-2 g/L). Additionally, the ferritin level distinctly increased to 1,206 ng/mL (reference range: 13-252 ng/mL) and was accompanied by 100% transferrin saturation (reference level: ≤45%). The soluble transferrin receptor level also increased to 1.92 mg/L (reference value: 0.83-1.76 mg/L). Hemochromatosis was excluded via PCR (Lightcycler; Roche, Basel, Switzerland). Gamma-glutamyltransferase (γ-GT), ALT, and AST levels were all slightly elevated. Scleral icterus was visible and the total bilirubin level was 8.3 mg/dL (reference range: 0.2-1.0 mg/dL). Vitamin B12 and folic acid deficiencies were ruled out. Gene sequencing (Applied Biosystems, Carlsbad, CA, USA) revealed the presence of a beta-globin mutation that results in Hb Andrew-Minneapolis [beta 144 (HCI)Lys→Asn]. The polymorphism Hb F-Sardinia [A gamma (E19)Ile→Thr] was also detected.

Hb Andrew-Minneapolis is a rare anomaly that results in the formation of a Hb molecule with high oxygen affinity. This results in a left shift of the Hb-oxygen dissociation curve and consecutive erythrocytosis [1]. Only limited reports of falsely high HbA1c levels exist [2, 3]. We suspect that our patient had falsely

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low HbA1c levels because fasting glucose values were repeatedly >200 mg/dL, and daily blood glucose levels were always pathologically high. The patient presented with hyperchromic macrocytic erythrocytosis with marked hemolysis, indicating an instability of this Hb variant. This anomaly has not been described previously. Likewise, no reports exist substantiating possible iron overload in this variant. Existing liver cirrhosis must obviously be taken into account, as secondary iron overload can occur in alcohol-related toxic liver cirrhosis [4]. However, tranferrin saturation of this high of a level has not been previously described. Misjudgements of the patient's type 2 diabetes were due to falsely low results of HbA1c levels. Interestingly, only falsely high HbA1c levels have been reported [2, 3].

Hemoglobinopathy with increased oxygen affinity is a rare, yet important, condition in the differential diagnosis of erythrocytosis. To the best of our knowledge, a relationship between Hb anomalies and increased oxygen affinity has not yet been reported in scientific literature. Hb Andrew-Minneapolis, in combination with liver cirrhosis, may be responsible for the undefined iron overload presented here. Whether Hb F-Sardinia (single nucleotide polymorphism) [5], in combination with Hb Andrew-Minneapolis, is involved in the manifestation of iron overload remains unclear because this is the first case reported.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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