Primary Acquired idiopathic sideroblastic anemias
A report of 4 cases and review of literature

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فقر دم الأرومة الحديدية

الخلاصة:

فقر دم الأرومة الحديدية من الحالات النادرة جدا والتي يقل فيه إنتاج كريات الدم الحمراء بسبب وجود خلل في عملية أيض الحديد .و يصنف إلى نوعيين هما: وراثي و مكتسب .
النوع المكتسب قد ينتج من تناول العقاقير أو يكون مصاحبا لبعض الأورام الخبيثة أو قد يكون غير معروف السبب (أولي).في هذه الدراسة سجلت أربعة حالات لفقر دم ألا ورمة الحديدية الأولى المكتسب. وقد كان ثلاث مرضى من الإناث. أعمارهم تراوحت بين 18-56 سنة.كان في اثنان من المرضى الكريات الحمراء دقيقة و ناقصة الصبغة وفي المريضان الآخران كانت الكريات الحمراء ثنائية الشكل.
الفحص النسيجي لنخاع العظم أظهر وجود خلايا ألا ورمة الحديدية في جميع المرضى وكان وسيلة التشخيص فيهم. أظهر نخاع العظم تغيرات حثلية مميزة في مريض واحد فقط.و قد كان هذا المريض معتمدا على عمليات نقل الدم المتكررة مما زاد من احتمال تعرضه للاصابه بمرض الابيضاض النقيي الحاد.

SUMMARY:

Sideroblastic anemias are rare conditions, in which the red cells production will be impaired, due to defect in iron metabolism. They are classified as hereditary or acquired form. The acquired form may be associated with drugs, malignant diseases, connective tissue or the cause can not be identified (idiopathic).

The aim of this paper is to report four cases of primary acquired form of sideroblastic anemia that were seen in Basrah.

Four patients with primary acquired sideroblastic anemias (PASA) were reported, 3 of them were females, their ages ranged from 18-56 years. All of them presented with severe anemia. They were of hypochromic microcytic type in 2 pts, & dimorphic type in other 2 pts. Bone marrow examinations revealed pathological ring sideroblasts in all pts, and only one pt had marked dysplastic changes on bone marrow examination. This pts became transfusion dependent and she would possibly carry a risk of developing of acute myeloid leukemia.

Key word

siderblastic anemia,sideroblast,myelodysplasia,microcytic,hypochromic

Introduction:

Sideroblastic anemias (SA) are rare conditions, in which red cells production will be impaired, due to defect in iron metabolism. [1] They are heterogeneous group of disorder of divers etiology. [2] The sideroblastic anemias display remarkable clinical and hematological heterogeneity [3] but share in common mitochondrial iron loading as evidence of unhinging between intracellular iron metabolism and heme biosynthesis. Molecular defects responsible for this have been identified and appear to display matching heterogeneity. Mutations in the erythroid-specific Aminolevulinic acid synthase 2 (ALAS2) gene cause microcytic anemia, where as mitochondrial DNA deletions are responsible for macrocytic anemia. Speculation about their causes includes disturbed intracellular iron homeostasis involving iron-responsive factors involved in the translational control of ALAS2 and in certain nuclear and mitochondrial genes important for erythroid mitochondrial metabolism. [4-6] because these respiratory chain dysfunction may occur, thereby impairing reduction of ferric iron (Fe3+) to ferrous iron (Fe2+). The reduced form of iron is essential to the last step of mitochondrial heme biosynthesis. [7] Mutation detection enables the early diagnosis. [7] There is no specific treatment for pts with SA but allogeneic bone marrow transplantation may be indicated especially in childhood-onset refractory SA. [8]

The aim of this study was to report these rare four rare cases of primary acquired idiopathic type of sideroblastic anemias. Al these cases were seen in Basrah (southern Iraq).

Patients and methods:

Four patients with PASA were studied from the period of July 1995 to April 2000. Three pts were females. Their ages range from 18 to 56 years with an average of 40±18.67 years. Complete history was taken. Full physical exam was performed(See table I). Investigations which were requested for each patient include: Hemoglobin (Hb), pack cell volume (PCV), White blood cell counts (WBC), Platelet counts, Reticulocyte counts, reticulocyte index, blood film for red blood cell (RBC) & WBC morphology, liver Enzymes, and serum bilirubine (total, direct, &indirect). Bone marrow examinations, (the slides were stained by leishman and Prussian blue stains). Hb electrophoresis, Coomb's tests, Glucose –6-phosphate dehydrogenase (G6PD), chest X-ray and abdominal ultrasound.

Serum iron, iron binding capacity, serum ferritin, serum transferrin, serum B12, and red cell folate were not done because of lacking facilities. Secondary causes of SA like drug (cycloserin, isoniazide, chloromphenicol, tetracycline), lead poisoning, alcohol [1-2,10-12], connective tissue disorder or malignant conditions like leukemia, lymphoma, myeloma, and carcinoma.[2, 11,13] were excluded. The blood film and the bone marrow were examined by expert hematologist.

Trials of high dose pyridoxine therapy (100mg\day) orally for three to six month were given to all pts and their responses were assessed by repeated estimation of Hb, PCV, reticulocyte count and blood film examination.

Results:

Four pts with PASA were reported in this study. Three were females, and one was male. Their ages ranges from 18 to 56 years with an average of 40 years. (See table I)

All pts had severe anemia with Hemoglobin level less than 7gm\dl, and PCV was less than 25,and they needed frequent blood transfusion. (See table I). They have normal reticulocyte index. The blood film examination for RBC morphology showed microcytic hypochromic anemia in 2pts (50%) and dimorphic blood pictures (microcytic and macrocytic red blood cells) in other two (50%) pts.(see table II)

The basophilic stippling were seen in the four pts on blood film examination. Bone marrow examinations showed pathological ring sideroblast on Prussian blue stain. This was the pathognomic finding in the four pts. On leishmane stain there were mark erythroid hyperplasia in all pts but there was no evidence of dysplastic changes in three pts. Only one pt (case 2) had mark dysplastic changes with binucleated & trinucleated normoblast. There was no evidence of blast cell of myeloid series in 3 pts, and only one pt. had 3% blast cell.

Discussion:

The average age of pts with PASA in this study was 40 years. Two of them (50%) were above age 50 years, only one pt was young (18 years), these were consistent with other studies [1,2,5], and in contrast with congenital form of SA, which usually occurs in very young and even in infants [5,14]

Three pts were females and only one pt was male and this was consistent with most studies. In contrast with congenital form, which mostly occurs in males, since it's inheritance, is a sex-linked recessive [1,4-5,10,11,14]

All pts had severe anemia of hypochromic microcytic or dimorphic blood pictures type with basophilic stippling and this consistent with most studies. [1,2,4]

One pt (Case no2) had severe anemia, which became transfusion dependent form. She needed an average of 2 units of blood per month, this consistent with other studies that 20% of acquired form of SA may become transfusion dependent. [12,14]. This makes her carry risk of transformation to acute myeloid leukemia. Sharwrtze found that 10% of transfusion dependent SA would transform to acute myeloid leukemia, while other studies suggest 20-30 % risk. [12-14]

Bone marrow examinations revealed only erythroid hyperplasia in 3 pts, this was consistent with other studies. One pt revealed marked dysplastic changes on her bone marrow examination, which was not responded to a trial of B12, folic acid and pyridoxine. This pt had 3% blast cell, while the others hadn't. So this pt had other risk factors for transformation to acute myeloid leukemia [12-14].

The other three pts also didn't show any response to a trial of pyridoxine, this consistent with most studies on PASA, [1,5,14] but in contrast with studies on hereditary form which showed a response to pyridoxine in 33% of pts [1-6,10,11,16]

Conclusion:

This study had reported four pts with PASA in Basrah, despite being rare conditions. PASA may be missed diagnosed as iron deficiency anemia. PASA should be considered in the differential diagnosis of any hypochromic microcytic anemia or dimorphic anemia especially if not responded to iron therapy. Bone marrow exam stained by Prussian blue will be a diagnostic test.

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Table I The clinical features of the studied pts

CASE .NO	AGE	SEX	PRESENTATION	PHYSICAL FINDING	HB	PCV	FREQUENCY OF BLOOD TRANSFUSION
1	56	male	Pallor ,palpation and shortness of breath on exertion	pallor, palpable liver 6cm& splenomegally 8cm	5gm	15	Received 4units of blood on admission and then 1unit /3month
2	55	female	Pallor easy fatigability for 6 month	heaptosplenomegally 4cm ,pallor	6 gm	20	Received 4 units on admission &then she needed 1unit/month for 1year then 2units /month for last 2 years
3	18	female	Pallor 3 month	Hepatosplenimegally of 5cm	6 gm	16	Received 3 units on presentation &other unit 4month later
4	31	female	Pallor and easy fatigability	Hepatosplenimegally of 5cm	7 gm	20	Received 3 units on presentation and then 1 unite/6 month

Table II Blood film and bone marrow features and liver function test studied pts.

Case no.	**blood film morphology**	**Bone marrow exam**	**liver function test**
1	Dimorphic blood picture, And basophilic stippling	Erythroid hyperplasia, and pathological ring sideroblast	Normal bilirubine ,SGOT, SGPT, alkaline phosphatase ,&normal ultrasonic texture of liver and spleen
2	Microcytic hypochromic anemia with basophilic stippling and	Erythroid hyperplasia ,mark dyerythropoiesis,3%blast cell and pathological ring sideroblast	Normal bilirubine ,SGOT, SGPT, alkaline phosphatase ,&normal ultrasonic texture of liver and spleen
.3	Dimorphic blood picture and basophilic stippling	Erythroid hyperplasia, and pathological ring sideroblast	Normal bilirubine ,SGOT, SGPT, alkaline phosphatase ,&normal ultrasonic texture of liver and spleen
4	Hypochromic microcytic anemia with and basophilic stippling	Erythroid hyperplasia, and pathological ring sideroblast	Normal bilirubine ,SGOT, SGPT, alkaline phosphatase ,&normal ultrasonic texture of liver and spleen