ORIGINALARBEITEN

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Congenital Dyserythropoietic Anemia with Ultrastructural Features of Type I and II

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Summary

The autopsy and electron microscopic findings in a pair of brothers with congenital dyserythropoietic anemia (CDA) are presented. In both patients autopsy revealed severe secondary hemochromatosis, including cirrhosis of the liver and fatal heart involvement. According to current ultrastructural criteria, a mixture of CDA type I (interchromatin bridges, wide euchromatin-cytoplasmic connections) and of type II (marginal cisternae, nuclear protrusions, multinuclearity, karyorrhexis) was found in erythroblasts of one patient. In the second patient electron microscopy of bone marrow stored in formalin for several years allowed the diagnosis of CDA with marginal cisternae in retrospect. These findings illustrate the usefulness of electron microscopy for the diagnosis of CDA in unsolved cases of chronic ineffective erythropoiesis, even from formalin fixed material. For subtyping CDA into type I and II, however, other than morphological parameters should be used for definition. In the clinical management splenectomy and a drastic phlebotomy programme have been found favourable.

Zusammenfassung


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Congenital dyserythropoietic anemia (CDA) is characterized by abnormal erythroblasts and erythrocytes and is associated with ineffective erythropoiesis, chronic hemolytic anemia and iron overload. On the basis of morphological and serological criteria three types are currently recognized [3,6,7]. Type I and II are commonly distinguished serologically by the anti-i and the acidified serum test both of which are positive in type II only [3,4]. Morphological features, once considered type-specific, increasingly lose their significance for subtyping because of the occurrence of mixed types [12,13]. Type III appears as a morphologically distinct group marked by gigantoblasts with up to 12 nuclei [15,19]. Between 40 and 50 cases of type II have been reported [4,6,8,9,10,17,18]. In comparison, type I and III are much rarer [3,11,19]. However, since CDA may be asymptomatic [3,14,15], probably more cases are still awaiting diagnosis for which electron microscopy would be of invaluable assistance.

It is the purpose of this communication to illustrate this aspect by describing two autopsy cases of CDA with morphological features of both type I and II occurring in a pair of brothers. Although both were clinically followed up over a period of up to 33 years, the diagnosis was made one year prior to death in one brother and retrospectively in the other, 12 years after autopsy.

Case reports

Patient 1 (elder brother): Since his fourth year of life this patient suffered from severe hemolytic anemia which was diagnosed as an atypical form of thalassemia although no abnormal hemoglobins were found throughout the whole course of the disease. Hemoglobin values were about 6.5 g/100 ml in the beginning, below 3.0 g/100 ml in the last two years of life and 1.9 g/100 ml at the time of death corresponding to a hematocrit of 6%. Acid hemolysis and anti-i tests were not performed. A steroid therapy given during the last two years prior to death had no effect on the hematological symptomatology. Splenectomy was not carried out in this patient. Death occurred at the age of 32 years after a protracted period of cardiac arrhythmia.

Patient 2 (younger brother): The first hospitalization occurred at the age of 10 years because of marked anemia (Hb: 10 g/100 ml). The diagnosis of a familial form of atypical thalassemia was made although in this patient, again, abnormal hemoglobins were not identified. In the following years anemia persisted despite repeated hospitalizations and prolonged therapy with vitamin B 12 and folic acid. At the age of 38 years, a treatment with desferrioxamin was started in an attempt to lower the high serum iron level but was discontinued after 3 years as no beneficial effect was noted. 4 years prior to death, at the age of 40 years, splenectomy was carried out. This resulted in a drastic increase of Hb-values up to 14 g/100 ml. An additional phlebotomy programme was started which was well tolerated and which lowered serum iron level from a maximum of 2.5 down to 1.5 mg/L. The clinical diagnosis of CDA was made 1 year prior to death mainly on the basis of bone marrow smears. Since no anti-i antiserum was available at that time, only anti-I was tested which gave a negative result. Acid hemolysis with autologous and one control serum was negative. Although serological data are inconclusive, a CDA type I was tentatively assumed. Death occurred at the age of 43 years in cardiogenic shock preceded by severe cardiac arrhythmia and atrial fibrillation for 18 months.

Autopsy findings

In both cases the most prominent feature was a heavy siderosis of most organs. Cause of death was cardiac failure in patient 1 and subacute myocardial infarction without detectable occlusion of the coronary arteries in patient 2.