Immunological Investigations in Two Brothers with Ataxia Telangiectasia Louis-Bar


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Abstract. Two of three brothers with the classical signs of ataxia telangiectasia were investigated for their immunological disorders at the ages of 13 and 16 years, respectively. The elder brother also suffers from autoimmune hemolytic anemia, a complication which has not yet been described in the course of ataxia telangiectasia.

Immunological investigations made in both brothers showed a reduction in the number and function of T lymphocytes. The number of B lymphocytes was normal, among which there were cells staining for IgA, although serum IgA was absent. It seems possible that this phenomenon is caused by a disturbance in the process of maturation of lymphoid cells with a lack of differentiation into IgA-synthesizing plasma cells.

Key words: Ataxia telangiectasia — Autoimmune hemolytic anemia — Immune deficiency disease.


The autosomal recessive disease, ataxia telangiectasia (AT), first described by Louis-Bar [19] and further investigated by Boder and Sedgwick [5], is characterized clinically by ataxia, intention tremor, dysarthria, and oculomotor disturbances; in addition, there are oculocutaneous telangiectases, sialorrhoea, and a tendency to frequent infections [17]. After a nearly normal development in infancy these symptoms usually become manifest in early childhood. The course is commonly slowly progressive. Severe infections are the most frequent cause of death, although malignant neoplasias occur with more than the usual frequency [5]. The oldest patient known has lived to 41 years of age [15].

The increased susceptibility to infections and tumors is the clinical expression of a constantly demonstrable immunodeficiency [18, 22, 28, 33], which, with thymus dysplasia [25], can affect cellular [24] as well as humoral [10, 25] immunity. The humoral immune deficiency is most marked in the IgA and IgE levels of the serum [1, 11, 34, 39, 42].
Two of three brothers with AT have been studied in the following immunological investigations. One of the brothers also suffers from immune hemolytic anemia; this complication of the disease is known from other immunodeficiency disorders [31, 32, 36], and has, to our knowledge, not yet been described in association with AT.

**Case Reports**

*Family History.* The parents of the patients are both healthy and, in addition, are related to each other in the third generation. All three children developed symptoms of AT and one child (B. F.) died after multiple infections at the age of 7 from purulent pneumonia.

*History of B. J.* After an uncomplicated pregnancy and delivery the infant developed normally; the first symptoms of a subsequent slowly progressive ataxia were noted at the age of 14 months; by the age of 8 years the patient was unable to walk. Purulent respiratory infections, pneumonia, and otitis occurred frequently in this patient. By the age of 2 years conjunctival telangiectases appeared and shortly thereafter skin telangectases were also noted.

*Clinical Findings in B. J.* The patient is underweight and small for his age. There is a horizontal restriction of eye movements and slight nystagmus to both sides, no convergence reaction, and optokinetic nystagmus cannot be provoked. The facies appear unexpressive with some tic-like movements of the facial muscles, decreased mobility of the tongue and slurred speech.

There is general muscular hypotony of the extremities with hyperextensibility of the small and medium joints, muscular hypotrophy and the muscular strength of the distal arm and leg muscles is slightly reduced. There is intention tremor and marked dysdiadochokinesis with dysmetric and atactic finger to nose and heel movement on both sides. Rebound phenomenon is positive. Chorea-athetotic disturbances of finger and hand motion, and some muscle weakness of the body are present. Marked ataxia makes walking impossible. The reflexes of the 15-year-old boy cannot be evoked and pyramidal tract symptoms on both sides are negative. Sensation is normal.

The pneumoencephalogram demonstrates either isolated enlargement of the fourth ventricle or cerebellar atrophy.

*Laboratory Findings for B. J.* For 3 years there has been a marked icterus due to a hemolytic anemia. In several determinations the erythrocytes were between 2.87 and 3.22 million/mm³, hemoglobin between 9.9 and 11.4 g%, leucocytes between 7200 and 13900/mm³ (regarding the lymphocytes in the differential count see Table 2), reticulocytes between 93 and 307/mm³ and bilirubin—nearly exclusively indirect—between 8.2 and 15.4 mg%. Serum Fe was normal and functional tests for liver and kidney were normal as well.

Alpha-1-fetoprotein was markedly increased with 972 ng/ml (normal upper limit: 20 ng/ml).

*Special Haematological Investigations in B. J.* In the bone marrow, aspirated from the sternum, the proportion of erythropoietic cells was markedly increased making up 55% of the total. Juvenile forms comprised 9% of the total. There were normal findings in hemoglobinlectrophoresis, in erythrocyte enzymes, and in evaluation of methemoglobin; Heinz bodies could not be demonstrated. The erythrocyte survival time (Cr³¹, norm: T/2 = 29—31 days) was exceptionally short with a T/2 = 3.5 days. The ratio of spleen to liver was greater than 3. The sequestration potential for heat-denatured erythrocytes was 12.2 min.