ATAXIA-TELANGIECTASIA: SURVEY OF 50 PATIENTS IN IRAN

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ABSTRACT

Ataxia-telangiectasia (AT) is an autosomal recessive disease characterized by telangiectasia, progressive ataxia, sinopulmonary infection, hypersensitivity to ionizing radiation, and a combined immunodeficiency, usually consisting of selective IgA and IgG_2 deficiencies, cutaneous anergy, and often depressed but not absent *in vitro* lymphocyte responsiveness. Reviewing the medical records of 50 patients with AT during 1975 through 1998 admitted to our center, we have noted the following results: the mean age of the patients was 8.3 (range 3 to 14) years, parents of 33 patients were consanguinous, and the sex ratio was 6:5, occuring more in boys than in girls. All 50 patients showed cerebellar ataxia and telangiectasia, 67% were mentally retarded, and 75% have had sinobronchitis and pulmonary infections. 36 patients were tested for α_1-fetoprotein, all of whom showed a positive test. Liver enzymes and plasma glucose levels were not significantly abnormal. 24 patients had IgA deficiency, and 8 patients had IgG_2 deficiency and 15 patients showed low IgE levels. All patients were tested for T-cells which were abnormal in 17 patients and 20 patients were tested for B-cells, which were abnormal in 18 patients. One patient had growth hormone deficiency. 17 patients had malignancies.

Keywords: *Ataxia-telangiectasia, Immunodeficiency.*

INTRODUCTION

Ataxia-telangiectasia is an autosomal recessive multisystemic disorder characterized by progressive cerebellar ataxia, telangiectasia, sinopulmonary infections, hypersensitivity to ionizing radiation,[2] and a combined immunodeficiency, usually consisting of IgA and IgG_2 deficiencies, cutaneous anergy, and often depressed lymphocyte responsiveness.

This disorder has been described by Syllaba and Henner In 1926[17] for the first time who termed the syndrome Vogt's disease.

Another case was reported by Louis-Bar in 1941.[15] Boder and Sedgwick assigned the term "ataxia-telangiectasia" to this syndrome.

Absence of serum IgA was first described by Thieffrey et al.[18] Deficiency of IgE was demonstrated by Ammann (1969), and IgG_2 deficiency has been noted in the majority of patients. In addition to the loss of Purkinge cells in the cerebellum, degenerative lesions have been found in other areas of the central nervous system, along with demyelination of posterior white column. Kastain et al. (1992) showed defective $P53^{5,21}$ in these patients which may play a

role in the increased incidence of malignancy in patients with ataxia-telangiectasia. Savitsky and colleagues[9-12] have identified a 12 kilobase gene on chromosome 11q 22-23 termed ATM* (ataxia-telangiectasia mutated) by positional cloning that was found mutated in AT patients from all complementation groups, indicating that it is the sole gene responsible for AT. This discovery may permit identification of AT heterozygotes (carrier) who are at increased risk of cancer. The ATM gene and susceptibility to breast cancer has been described by Vorechovsy et al.[6,7]

MATERIAL AND METHODS

Medical records of 50 patients with AT who were admitted to Children's Hospital Medical Center, affiliated to Tehran University of Medical Sciences were retrospectively studied.

Clinical, epidemiological, laboratory and immunological results were analyzed. We have also included the results of 17 cases of AT that we had presented in the 16th International Congress of Dermatology in Japan in 1982[22] and the Iranian Journal of Pediatrics.[24-26] We used single radial immunodiffusion method for measurement of serum Ig and complement components, ELISA for IgE and α_1-fetoprotein (Behring), Mayer's technique for CH50, and flowcytometry (Facstar) for T-cell and B-cell markers.

Table I. Clinical findings in 50 patients with AT.

Clinical feature	Number of patients	Percent
Cerebellar ataxia	50	100%
Telangiectasia	50	100%
Mental retardation	22	44%
Recurrent infection	23	46%
Sinobronchitis	25	50%
Pneumonia	27	54%

Table II. Epidemiological findings in 50 patients with AT.

Age of onset	Number of patients	Percent
1-5y	7	14%
6-10y	25	50%
11-20y	13	26%
20-30y	2	4%
Male	26	52%
Female	24	48%
Consanguinity	33	66%
Siblings AT	18	36%
Malignancy	17	34%

Table III. Immunological findings in 50 patients with AT

Test	Number of patients	Percent
IgG	16 Low	32%
	34 Normal	68%
IgA	24 Low	48%
	26 Normal	52%
IgM	2 Low	4%
	48 Normal	96%
IgG^2	8 Low	16%
	14 Normal	28%
IgE	15 Low	30%
CD3 (T-cell)	17Low	34%
	33 Normal	68%
CD4	13 Low	26%
	37 Normal	74%
CD8	5 Low	10%
	45 Normal	90%
CD19, CD20	8 Low	16%
	123 Normal	24%

RESULTS

The following epidemiological, clinical, laboratory and immunological results were obtained which are summarized in Tables I to IV.

Table IV. Immunological findings (continued).

Test	Numbers of patients	Percent
Candida skin test	2 Positive	4%
	7 Negative	14%
DT	17 Negative	34%
	7 Positive	14%
Alpha-fetoprotein	35 High	70%
	3 Normal	6%
Transaminases	5 High	10%
	45 Normal	90%
GTT	8 Normal	16%
17-Ketosteroid	7 Normal	14%
	1 Low	2%

DISCUSSION

AT is a multi-systemic disorder characterized by progressive cerebellar ataxia and oculocutaneous telangiectasia with immune disorders and lympho-reticular malignancies. This disorder is inherited as a single gene disease, with defects in neurological, vascular and immune systems.

Table I shows that all patients had cerebellar ataxia and telangiectasia, but only 23 of them (46%) had recurrent infections such as sinobronchitis and pneumonia, and 22 of them developed mental retardation (44%). Table II shows epidemiological findings including age of onset from as early as one year old to as late as 20 years old.

The most important finding in our study was consanguinity of the parents. 36% of patients had at least a sibling with AT. 34% of patients had malignancy, such as acute lymphoblastic leukemia and lymphoma.

Recently the most outstanding finding has been reported by Savitsky and colleagues (1995) who identified a 12 kilobase gene on chromosome 11q 22-23 termed ATM by positional cloning that was found to be mutated in AT patients.[19]

The incidence of AT in Iran is high, possibly due to familial marriages. Unfortunately there is no cure for this disorder and supportive treatment may prolong survival.

With recent identification of the ATM gene, we are eagerly looking forward to a new modality in the treatment of these patients.

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