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ATAXIA TELANGIECTASIA

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INTRODUCTION

The original description of this syndrome was by Madame Louis-Bar in 1941[1] who felt that this might be one of the phacomatoses. Some years later, in 1957, Boder and Sedgwick[2] clarified the clinical manifestations and coined the term "ataxia telangiectasia" for this same disease entity. Smith and Cogan[3] were the first ophthalmologists to give a comprehensive review of the ocular findings.

Etiology and pathogenesis of this condition has not yet been established though it is known to be associated with an abnormal thymus, immunological deficiencies, and often a malignancy.[4] There are no reports on attempted treatment.

The main features of ataxia telangiectasia are:

1) Progressive cerebellar ataxia beginning at about two years of age
2) Cutaneous telangiectasia
3) Frequent sinopulmonary infections
4) Familial distribution

The ocular features are:

1) Bulbar conjunctival telangiectasia
2) Poor convergence
3) Nystagmus, most marked in gaze away from primary position
4) Normal fundi

CASE REPORTS

Case I. (P.C.) — This 19-year-old white boy was the product of a full-term, normal pregnancy and uneventful delivery. He had a daily episode of slight twitching progressing to a generalized seizure in the period from two days to two weeks of age.

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He was then put on calcium and was free of seizures until he had a severe one at 16 months. Further seizures recurred around two years, the last being a febrile convulsion at five years. At two years there were involuntary hand movements. At five years he staggered when running and had occasional difficulty holding up his head. At ten he required support of a wall to walk. By age 12, he was confined to a wheelchair. His eyes were observed not to focus properly, and he drooled a great deal. He had frequent sinopulmonary infections. At 15 conjunctival telangiectasia was noted. Speech was slow, dysarthric and nasal in quality. Cerebellar ataxia was evident as well as choreo-athetoid movements of the hands and face. Ophthalmological examination at age 19 was as follows:

Corrected visual acuity: RE = 20/70, LE = 20/50-3.

The bulbar conjunctiva showed prominent telangiectatic and varicose blood vessels, especially over the area exposed between the lids. The bulbar conjunctiva covered by the upper lids was remarkably free of vascular dilatation. The pupils were round, equal, and reacted sluggishly to light and accommodation. There was inability to move the eyes more than a few degrees in any direction other than inferiorly. Attempts to follow, or to voluntarily look in any direction other than straight ahead, resulted in rotation of his head and a quick nystagmus with fast component in the direction of attempted fixation. In the primary position there was some intermittent nystagmus. There was inability to converge. It was possible to obtain almost full range of ocular excursion by having him fixate on an object and to then turn his head rapidly away from the object of fixation. No patterned response occurred when he was tested on an optokinetic drum. The anterior segments of his eyes were normal on slit lamp examination except for the dilated bulbar conjunctival vessels. Ocular tension was 12 mm (Schiotz) OU. The fundi were normal. The fields were full peripherally when tested with a 3/330 white. No central scotoma could be found with 1/330 white and 2/330 red test object with either eye.

The patient showed varying degrees of conjunctival injection at times of re-examination. His mother felt that sunlight especially caused increased injection of his conjunctiva, and that eye muscle motion was better in the morning and much worse after activity or when he was tired.

Another disease having thymic abnormalities, immunologic deficiency and neuromuscular signs is myasthenia gravis. Since no reports of attempted treatment of ataxia telangiectasia were available, it was decided to attempt empirical treatment with edrophonium chloride (Tensilon®). One ml of Tensilon® (containing 10 mg edrophonium chloride) was injected I.V., and the patient carefully observed for the next hour. No improvement of the eye findings or ataxia occurred. He was brought back another day and given atropine, 0.5 mg I.M. and prostigmine, 1.5 mg I.M. The patient reported dizziness ten minutes later. An hour later he began having facial twitching and tingling sensations in his face and body, possibly related to hyperven-

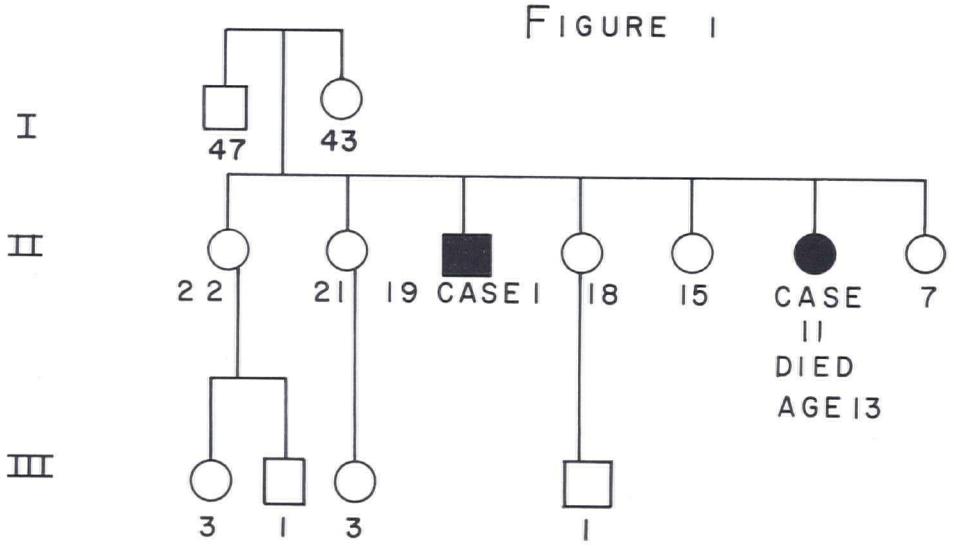
tilation, which subsided over the next hour. Again, there was no improvement of his ocular motility or ataxia.

Case II. (D.C.) — This was a sister to Case I, six years younger, who died less than a year ago. She had similar neonatal seizures, ataxia and cerebellar dysfunction but no sinopulmonary infections. A note in her medical records described conjunctival telangiectasia at age eight years. The extraocular muscles were described as moving normally. Ten days before she expired she experienced profound nausea, vomiting and headaches with increased ataxia to the right side. A mild right supranuclear facial weakness developed with deviation of the tongue to the right. Bilateral papilledema was noted subsequently and she developed pneumonia, followed by sudden respiratory arrest. She was maintained on a Bennett respirator until she expired. Pathological examination revealed an infiltrating medulloblastoma in the right cerebral hemisphere.

GENEOLOGY

Figure 1 shows the pedigree of the immediate family of these children. Everyone on the pedigree chart has been examined and no sign of the disorder was found except in the two cases described.

FIGURE 1



NOMENCLATURE OF THE HUMAN IMMUNOGLOBULINS

Present Usage	Proposed Usage[6]
γ, 7Sγ, 6 6Sγ, γ_2, γss	IgG
B_2A, γ_1A	IgA
γ_1M, B_2M, 19Sγ, γ-macroglobulin	IgM

Figure 2

Immunologic Studies

Both patients demonstrated normal hemoglobin, total and differential white cell count, chest xray, urinalysis and initial skull radiographs.[5] The bone marrow displayed normal cellularity. Serum protein immunoelectrophoresis and quantitative estimation of the serum immunoglobulins demonstrated a lack of IgA (see Figure 2) immunoglobulins, but normal levels of IgG and IgM. All other siblings showed normal IgG and IgM, but some had decreased though not totally lacking IgA. No circulating antibody to a variety of allergens was detected by skin testing. Delayed hypersensitivity skin reactions to coccidiodin, blastomycin, histoplasmin, old tuberculin and trichophyton antigens were not positive. Both patients showed delayed rejections of skin homographs. The patients' circulatory antibody responses to injections of various vaccines were measured. The antibody titers to polio, influenza and adenovirus antigens were extremely poor in both patients. Case I also demonstrated diminished response to diphtheria and tetanus vaccines, in contrast to normal values shown by his sister. Fluorescent antibody studies on the formalin fixed brain tissue of Case II obtained at autopsy failed to reveal the presence of IgG gamma globulins fixed to cerebellum.

Comment

Ataxia telangiectasia is a syndrome characterized by cerebellar ataxia, repeated sinopulmonary infections and ocular telangiectasia. Abnormal thymic function can readily account for the immunological defects seen.[4,7,8,9,10] The low or absent IgA immunoglobulins which are seen in most, but not all, patients with this disorder usually serves to distinguish these cases from the other heredofamilial ataxias. The ophthalmological manifestations can serve as an early distinguishing feature in those cases not associated with decreased IgA immunoglobulins.

Summary

Two sibling cases of ataxia telangiectasia are presented. The similarity of some aspects of this disease to myasthenia gravis suggested that possibly the same treatment might be beneficial. However, test doses of Tensilon® and of prostigmine both failed to effect any improvement.

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