ATAXIA-TELANGIECTASIA

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Ataxia-telangiectasia is a syndrome characterized by gradually progressive cerebellar type ataxia and defects of ocular movements, and by conjunctival telangiectasia in the early years of life. Ford[1] refers to Mme. Louis-Bar's initial report of this disease in 1941 and states that others (Wells and Shy in 1956,[2] and Boder and Sedgwick[3]) have reported about sixty cases since that time. We encountered no reports of this syndrome in Turkish medical literature.

Case Reports

Patients D.Y. (an eight year old girl), Z.Y. (a five year old girl), and A.Y. (a three year old boy), three of the four living children of the same parents, were admitted to Hacettepe Children's Hospital in October 1963. Their chief complaints were ataxic gait, uncoordinated ocular movements, and frequent upper respiratory tract infections. The case history revealed that the parents were related. The patients had a normal one and a half year old sibling, and another sibling had died at 5 years of age after a course similar to the patients'.

Physical examination: All three patients had severe ataxia of cerebellar type. There was bulbar telangiectasis which decreased towards the cornea (Figures 1 and 2). The facial expressions of all three children were mask-like, with excessive nasal secretion and saliva flow. Neurological examination of A.Y. was normal expect for the ataxic condition. Bilateral horizontal nystagmus was visible in both D.Y. and Z.Y., and deep tendon reflexes were diminished.

Laboratory examination: Routine urine and blood tests were normal. Serum electrophoresis gave normal results for all members of the family. Electroencephalograms were normal, with the exception of a slight dysrhythmia in D.Y. No anomalies could be seen in x-rays of the skull. Urinary tests for amino-aciduria in all members of the family, including the parents, were negative.

The patients were discharged from the hospital after five days with instructions to continue the antibiotic therapy for protection of the upper respiratory tract from recurrent infection. Regular physical therapy was instituted in order to prevent the neurological disorder from incapacitating the patients. They were also advised to return to the neurology clinic every two to three months for further check-ups. No changes have been noted in their overall condition in the regular follow-up examinations.

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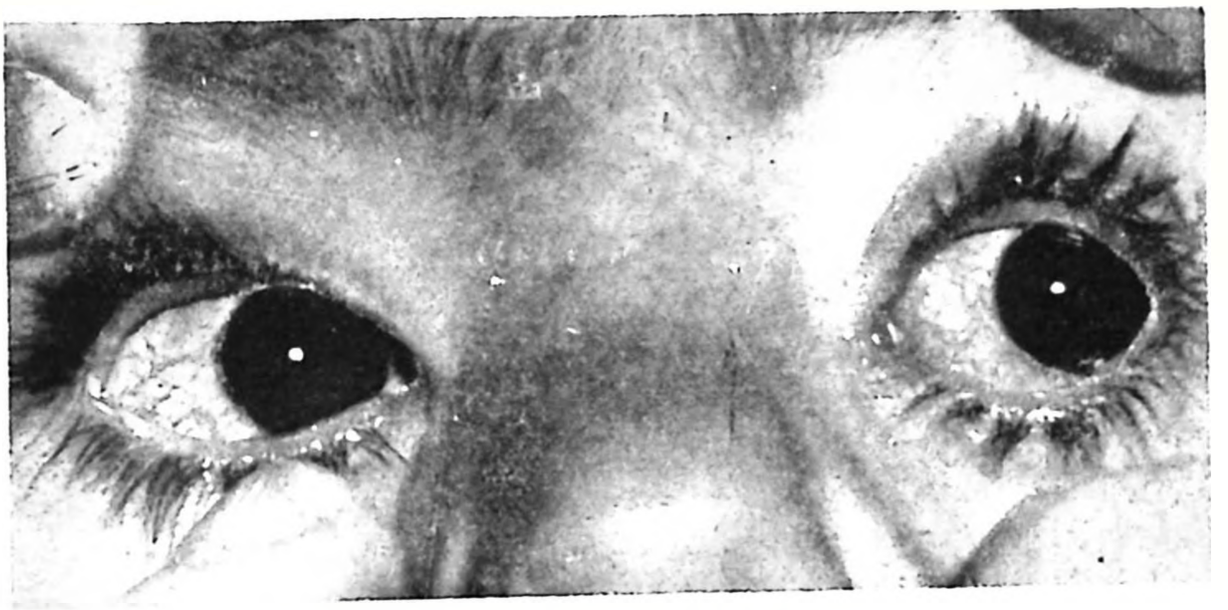

Figure 1. Bulbar telangiectasia.

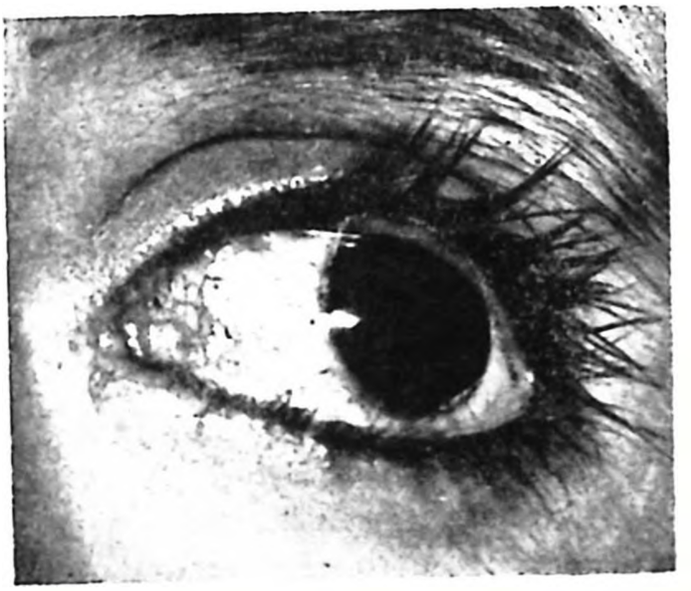

Figure 2. Telangiectasia decreasing toward the cornea.

Discussion

The principal symptoms of this syndrome can be summarized as follows: 1. progressive cerebelar ataxia starting in early childhood; 2. telangiectasia in the bulbar conjunctiva, generally symmetrical, seen in later years; and 3. inclination to upper and lower respiratory tract infections.

The patients discussed here were normal in infancy, developed ataxic gait between their first and second years, and abnormal arm and hand movements later on. Several authors report that although patients with this syndrome seem normal at birth, their motor functions such as gait, sitting, and crawling, are retarded. Ataxia is seen mostly in cerebellar and choreo-athetoid forms. Intentional tremors are present. Speech defects also occur, which, in the later stages, make the speech of these patients incomprehensible. There is also continual saliva flow, and the face is often expressionless. Ataxia increases in time and eventually the patient is bed-ridden. This form of ataxia should be distinguished from Friedreich's ataxia which is caused by spinocerebellar degeneration and generally occurs later in life. Other distinguishing features of Friedreich's ataxia are lack of recurrent infections, the presence of footdrop, and myocarditis.

Telangiectasic veins, after which the disease has been named, are seen symmetrically on both the medial and lateral aspects of the bulbar conjunctiva, and decrease near the limbus of the cornea. Veins in the plica semilunaris and in the distal tarsal conjunctiva may also be slightly affected. However, the proximal bulbar conjunctiva and the cornea are not affected. In acute cases, telangiectasia can be noted on the ears, eyelids, nose, the front part of the neck, the hands, the inner parts of the elbows and the knees. "Cafe au Lait" spots are also often present.

Centerwall and Miller, noticing that telangiectasias appear in the symmetrical parts of the body which are exposed to the sun, and that the lesions develop slowly, speculated on the possible effects of the sun on these patients, and compared this syndrome with other photosensitive conditions such as Hartnub's disease, in which aminoaciduria and skin rashes resembling pellagra occur under direct sunlight. Reversible ataxia is also present in this disease. Although amino-aciduria is found in some patients with ataxia telangiectasia, this is not a general finding, and it was not seen in the three patients reported here. Kaposi's disease (xeroderma pigmentosum) is also a photosensitive skin disease characterized by skin rashes on the parts exposed to direct sunlight, and telangiectasia may also occur. Epilepsy, mental retardation, deafness, and other central nervous system disorders may accompany Kaposi's disease. A third syndrome, described in 1954 and called congenital telangiectasic erythema, is characterized by butterfly-shaped erythematosis, telangiectasic plates, blue lips, "cafe au lait" spots on the body, and dwarfism. There is however no sign of ataxia. In Rendu-Osler-Weber disease (hereditary hemorrhagic telangiectasia) there are vascular lesions like small red spots over the entire body, and especially on the mucous membranes. Our patients had no such mucosal lesions.

Von Hippel-Lindau disease (cephaloretinal angiomatosis) most nearly resembles ataxia telangiectasia. This disease involves progressive sight

defects and ataxia caused by progressive retinal and cerebellar angiomatosis. No retinal lesions were seen in our patients.

In some patients with ataxia telangiectasia, ocular movements may be highly defective. The defects are generally in conjugate movements although they may appear as bilateral horizontal and vertical nystagmus. Accommodation disturbance, though rare, is sometimes encountered. An 18 year old Negro girl, reported by Smith and Cogan[5], had lost 50 per cent of her visual acuity.

A tendency to lower respiratory tract infections is also characteristic of ataxia telangiectasia. Chronic nasal flow beginning in early childhood, sinusitis, otitis media, bronchitis, pneumonia, and later bronchiectasia develop. Various explanations of this tendency have been suggested. Pickup and Pugh[6] are of the opinion that discoordination between swallowing and respiratory movements causes nasopharyngeal secretions to be aspirated. Boder and Sedgwick[7] also reported a case of ataxia telangiectasia in which the patient showed apparent bulbar symptoms before death. On the other hand, in one of Boder's cases, the esophagus was examined by x-ray and no anomaly could be seen in either esophageal peristalsis or in swallowing function.

In many cases of ataxia telangiectasia hypogammaglobulinemia is reported. Gutmann and Lemli[8] reported low levels of gamma globulin in three cases but in Boder and Sedgwick's cases there was no decrease in gamma globulin levels. Electrophoresis showed gamma globulin levels in our patients to be normal. In one case reported by Gutmann and Lemli, postmortem examination of an eight year old girl revealed the absence of the thymus gland and hyperplastic lymph nodes in the mediastinal cavity. Boder reported an increased number of neoplasms associated with these patients and found during postmortem examination. In one of the eleven postmortem examinations reported by Boder and Sedgwick, Hodgkin's disease and bronchiectasia were seen. In another case, reticular cell sarcoma was seen in a patient who also had metastases of the central nervous system. The same authors reported another case (living when the article was written) in which there was a round-cell sarcoma resembling reticular cell sarcoma or lymphosarcoma around the patient's neck. These reports indicate a relationship between neoplasia and ataxia telangiectasia although the exact connection has not yet been clearly described.

Pelc and Vis[9] found proline and hydroxyproline in the urine of their patients, but other authors have not reported it, no did we encounter it in our patients.

Pulmonary infections are sometimes attributed to bronchial hypersecretion, but there is no definite evidence to support this. Vascular anomalies of the lungs, as in Rendu-Osler-Weber syndrome, are also thought to be a cause of this symptom, but postmortem examinations have not revealed any evidence of such anomalies, except in one case in which the pulmonary veins were somewhat enlarged.

A common aspect of the postmortem examinations of the nervous system is the apparent reduction in number of Purkinje, granular, and basket cells of the cerebellar cortex. Slight changes have been noted in the dentate nucleus and in the cerebellar white substance. In some cases, there were also slight changes in the cerebrum.

In six cases reported by Hansen[10] electroencephalograms were normal. Of five pneumoencephalograms, three were normal, one revealed a slightly enlarged fourth ventricle, and another showed diffuse enlargement of the ventricular system.

Heredity is a factor common to all cases of ataxia telangiectasia reported in the literature. The mode of inheritance of this syndrome is thought to be autosomal recessive. Both clinical and pathological findings suggest that ataxia telangiectasia should be grouped with neuroectodermal dysplasia, congenital ectodermosis, or phakomatosis.

Summary

Three cases of ataxia telangiectasia in members of the same family are reported, along with a review of the literature dealing with this syndrome.

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