Neurosciences Quiz

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Chronic childhood ataxia: ataxia-telangiectasia

Case Presentation

A 9-year-old girl started having some problems walking at the age of 36 months, with clumsiness, irregular steps, lateral veering, and wide-based awkward motions. For the past few years she had developed slow, sinuous, involuntary movements with her right hand. The perinatal developmental history was normal. Family history was remarkable for consanguinity; 3 siblings (2 girls and one boy) with similar illness, and 3 healthy boys. One of the affected girls died at age of 14 years due to recurrent lung infection.

Her medical history was remarkable for frequent lung and ear infection, and several episodes of unexplained fever. She is now oxygen dependent. She was bright, alert and cooperative. The resident noted some dilated venules on her bulbar conjunctiva (**Figure 1**). Her right upper extremity showed some choreoathetoid movements. She had dysarthria, optic apraxia, and unsteady wide-based gait. Deep tendon reflexes were diminished, and plantar responses were equivocal.

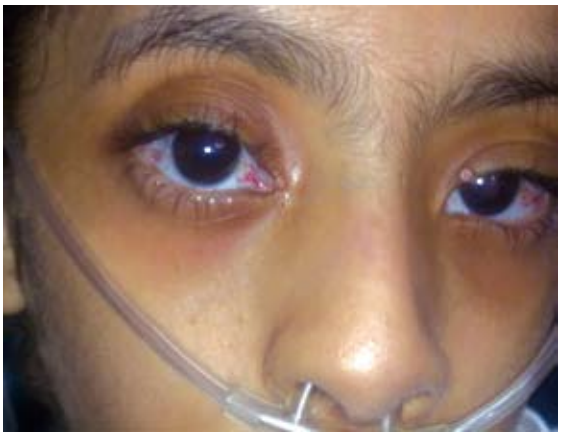

Figure 1 - Telangiectasias on the bulbar conjunctiva bilaterally.

Questions

1. Where do you localize the lesion?
2. What are the differential diagnoses, and the most likely diagnosis?
3. What is the mode of inheritance?
4. Describe the most important ocular abnormality in this disorder?
5. What are the extraneurological signs?
6. Why they are prone to have recurrent infection?
7. How can you reach the diagnosis?
8. What is the longterm sequelae of this disease?

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Answers & Discussion

1. The localizations typically point to 2 structures: cerebellum and basal ganglia.
2. In the evaluation of ataxia it must first be determined if the process is static or progressive, and acute or chronic. This case illustrates progressive ataxia. Tumors of the posterior fossa are important causes of progressive ataxia, and should always be ruled out particularly because they are more common than supratentorial tumors between the ages of 1-8 years. They usually manifest with signs of cerebellar involvement, such as unsteady gait, incoordination, and nystagmus, and signs of increased intracranial pressure due to obstruction of the fourth ventricle. Vomiting and headache are commonly an initial complaint. Papilledema, sixth, and other cranial nerve palsies can also occur. These signs are not illustrated in our case. Supratentorial brain tumors can also cause chronic ataxia and manifest with gait abnormalities and cerebellar signs.[1] Progressive or intermittent cerebellar ataxia can also be a prominent sign of hereditary metabolic disorders where it can occur in isolation or be accompanied by other signs and symptoms that indicate a more widespread involvement of the central or peripheral nervous system. In addition to ataxia, neurological findings may include spasticity, hyperreflexia, optic nerve atrophy, extrapyramidal signs, seizures, myoclonus, dementia, psychomotor retardation, peripheral neuropathy, and so on. Among the progressive hereditary degenerative encephalopathies, ataxia-telangiectasia best explains the findings described in this case. Ataxia-telangiectasia is characterized by progressive ataxia, dysarthria, choreoathetosis, typical cutaneous telangiectasias, and recurrent infections.[2] Other hereditary disorders with ataxia that manifest in early childhood include, for example, GM2 gangliosidosis characterized by ataxia, but also dysarthria, optic atrophy, and progressive cognitive decline. Ataxia is also a manifestation of the late childhood form of neuronal ceroid lipofuscinosis, but typical features are myoclonic or other types of seizures that can be the presenting symptom. In addition, clinical findings include retinal degeneration, developmental regression, progressive dementia, and so on. Metachromatic leukodystrophy can manifest with a gait disturbance in the late infantile form, but other important features are tremor, spasticity, progressive intellectual decline, optic atrophy, and so on.[1,2] Another progressive disorder causing ataxia is Friedreich's ataxia, characterized by significant cerebellar dysfunction, but other features such as spasticity, areflexia, and sensory disturbances help pinpoint the correct diagnosis. Wilson's disease, abetalipoproteinemia, Refsum's syndrome, mitochondrial disorders, and early-onset cerebellar ataxia with retained tendon reflexes and also hereditary disorders manifesting with ataxia in childhood, however, the clinical findings help in formulating the diagnosis. Other causes of chronic or progressive ataxia are congenital malformations, such as Arnold-Chiari malformation, that manifest with ataxia but prominent symptoms are usually occipital with neck pain, head tilt, cranial nerve abnormalities, hyperreflexia, and so on.[2] In summary, based on the information in the case presentation, ataxia-telangiectasia is the preferred diagnosis.[3]
3. Ataxia-telangiectasia is a hereditary neurocutaneous disorder transmitted by autosomal recessive inheritance and characterized by a multitude of manifestations involving different systems. The gene mutations are localized on chromosome 11q22.23.[3]
4. Ocular abnormalities are an important sign, particularly oculomotor apraxia, which manifests with an inability to initiate lateral movements, voluntarily or on command, despite integrity of the anatomical pathway subserving motor function.[3]
5. Extraneurological signs represent an important part of the disease. Telangiectasias are venous plexuses that are first noted when the child is 3-5 years of age, particularly on the bulbar conjunctiva (**Figure 1**), ear lobes, nose, flexor surfaces of the extremities, upper chest, and so on. They tend to prefer the areas exposed to the sun or to friction.[4]
6. These patients have abnormalities of both cell-mediated and antibody immunity increasing the risk of recurrent infections, in particular recurrent sinopulmonary and middle ear infections.[5]
7. The clinical combination of progressive ataxia, oculomotor apraxia, cutaneous telangiectasia, and recurrent infections strongly suggest the diagnosis. The levels of serum alpha-fetoprotein and carcinoembryonic antigen are usually elevated. Immunological deficiencies can also be demonstrated.[4]
8. The prognosis is poor and the causes of death are recurrent complicated infections and neoplasms, particularly Hodgkin's and non-Hodgkin's lymphomas and acute T cell leukemias.[5]

References

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