

SELF ASSESSMENT ANSWERS

Unsteady gait

Q1: What is the ocular finding depicted in figure 1?

The ocular finding includes conjunctival telangiectasia. Telangiectases are small dilated blood vessels. In the context of progressive ataxia, you should search for this oculocutaneous marker more carefully in the conjunctivae, earlobes, bridge of the nose, eyelids, cheeks, neck, and antecubital and popliteal fossae.

Q2: What is the clinical diagnosis?

The patient exhibited, during gaze shifts, the characteristic pattern of head-eye coordination called ocular motor apraxia (see video). The presence of this sign, along with progressive cerebellar ataxia, recurrent sinopulmonary infections and conjunctival telangiectasia is virtually diagnostic of ataxia-telangiectasia (A-T).¹

Q3: What investigations would you consider?

The diagnosis relies mainly upon the clinical features and family history. Neuroimaging scan often shows non-specific cerebellar atrophy. Serum α fetoprotein (AFP) is usually increased, and the concentration in the present patient was 252 ng/ml (normal: up to 10 ng/ml). Other supporting tests include raised serum concentrations of carcinoembryonic antigen, karyotyping of peripheral blood for identification of 7; 14 chromosomal translocation, in vitro radiosensitivity assay, immunoblotting for ataxia-telangiectasia mutated (ATM) protein, and assessment of ATM kinase activity. The latter tests may be useful in atypical cases, especially in ataxia telangiectasia sine telangiectasia. Ancillary investigations include estimation of serum concentration of immunoglobulins, evaluation of sinopulmonary infections, screening for malignancy and endocrinopathies.

Electroneuromyography for the evaluation of peripheral neuropathy was normal in this patient. Peripheral neuropathy is usually manifested in the later stage of disease.

Q4: How would you follow up this patient?

Genetic counselling of patient and family members is important. At present, no definitive treatment is available to arrest the progression of neurological symptoms. Physical, occupational, and speech therapies are useful to improve performance in the activities of daily living. Periodic medical visits should be emphasised and during such visits, the early signs of malignancy, infection, and endocrinopathies need to be monitored and treated. He should be encouraged to keep the skin covered and to wear a hat and sunscreen when outdoors, to avoid excess sun exposure. Repeated radiological examinations and radiotherapy, use of radiomimetic and neurotoxic agents, and chemotherapeutic drugs, with a high risk of developing a second malignancy, should be avoided.

Discussion

A-T is a rare, autosomal recessive disorder with multisystem manifestations (table 1).

The gene mutated in A-T (ATM) has been mapped to chromosome 11q22–23 and more than 100 mutations have been reported.² Defective response to deoxyribonucleic acid damage, attributable to ATM deficiency, explains the pleiotropic clinical features.³

The diagnosis of A-T may be challenging in cases lacking the typical features. Telangiectasia may not appear before 3 years of age and ocular lesion could be confused with conjunctivitis. There are few clinical syndromes manifesting with ocular motor apraxia (box).

Immunoblotting for ATM protein is the most definitive test for establishing the

diagnosis. However, the test is not widely and routinely available. An α fetoprotein estimation may help support the diagnosis, as it is raised in more than 90% of cases.¹ The extraneural manifestations, especially sinopulmonary infections and malignancy, are accessible to conventional treatment with slight modification, taking into account radiosensitivity, cancer predisposition, and immunodeficiency. The importance of making early diagnosis cannot be overlooked.¹ Early diagnosis ensures limiting exposure to ionising radiation, diagnostic radiographs, and radiomimetic agents. Timely opportunity for genetic counselling of parents at risk of having another affected child would be lost otherwise. Early cancer detection and treatment of patients and heterozygous family members could be pursued without delay. Intravenous immunoglobulin replacement is a beneficial therapeutic option for cases of recurrent and frequent infections.⁴

Final diagnosis

Ataxia-telangiectasia.

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Table 1 Clinical manifestations of ataxia-telangiectasia

Neurological	Gait and truncal ataxia, dysarthria, ocular motor apraxia, choreoathetosis, dystonia, intention tremor, segmental myoclonus, peripheral neuropathy
Dermatological	Oculocutaneous telangiectasia, chronic seborrheic blepharitis, hypertrichosis, infrequent grey hairs, progeric features, cutaneous granulomas
Immunodeficiency	Recurrent sinopulmonary infections, bronchiectasis, bronchialitis obliterans, cutaneous infections, embryonic-like thymus, low serum Ig A, Ig E and Ig G2 concentrations, T cell deficiencies, poor antibody response to pneumococcal polysaccharide vaccines
Cancer predisposition	Lymphoma, leukaemia, ovarian cancer, breast cancer, gastric cancer, melanoma, basal cell carcinoma, leiomyomas, and sarcomas
Radiosensitivity	Chromosomal breakage and apoptosis after exposure of cell cultures to ionising radiation
Cytogenetic	7; 14 chromosomal translocation, chromosomal instability, defective radiation induced checkpoints at different phases of cell cycle, abnormal signal transduction pathways.
Endocrinological	Insulin resistant diabetes mellitus, growth retardation, gonadal dysgenesis, premature menopause

Differential diagnosis of clinical syndromes with ocular motor apraxia

- Ataxia telangiectasia
- Congenital ocular motor apraxia
- Ataxia with oculomotor apraxia type 1
- Ataxia with oculomotor apraxia type 2
- Aicardi's syndrome
- Cockayne's syndrome
- Joubert's syndrome
- Pelizaeus-Merzbacher disease
- Succinic semi-aldehyde dehydrogenase deficiency
- Wieacker's syndrome
- Bilateral parietal damage