Case report:

A Rare Case of Ataxia Telangiectasia in Malaysia

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Abstract
Ataxia telangiectasia is a primary immunodeficiency disease that affects multiple organs systems. Affected patients typically manifest ataxia, immune function abnormalities, sinopulmonary infections, and telangiectasia. Ataxia telangiectasia is listed as a rare disease by the Office of Rare Diseases [ORD] of the National Institutes of Health [NIH]. Because ataxia telangiectasia is so rare, doctors may not be familiar with the symptoms, or methods of making a diagnosis. Not all children develop in the same manner or at the same rate; it may be some years before ataxia telangiectasia is properly diagnosed. We report a rare case of ataxia telangiectasia in Malaysia who was diagnosed only at the age of 10 years.

Keywords: ataxia; telangiectasia; immunodeficiency

Introduction
Ataxia telangiectasia is a rare primary immunodeficiency disease that affects multiple organs systems. Affected individuals have absent or dysfunctional ATM protein, resulting in impaired double-stranded DNA and increased oxidative stress¹. Affected patients typically manifest ataxia, immune function abnormalities, sinopulmonary infections, and telangiectasia². We report a rare case of ataxia telangiectasia in Malaysia who was diagnosed only at the age of 10 years.

Case report
The boy was delivered preterm at 32 weeks of gestation with birth weight of 1.96 kg to non-consanguineous parents. He was admitted for 1 week for neonatal jaundice and required phototherapy. Immunization completed for his age. There was no history of immunodeficiency or chronic diseases in the family.

At two years of age, the boy presented to Hospital Universiti Sains Malaysia (HUSM), Malaysia, with motor developmental delay. He was still unable to walk at that time. On examination, there was no dysmorphic features or spasticity. CNS examination showed hyperflexion and increase tone of both limbs. Other systems were unremarkable. On investigation, CT brain was normal. Diagnosis made at that time was dyskinetic cerebral palsy. The patient was then referred for rehabilitation and occupational therapy. However, he defaulted followed up after that.

The patient was referred back to HUSM 6 years later (8 years of age) for letter to special school. His teacher claimed that the patient needed to go to the special school as he was a “slow leaner”. The patient was still dyskinetic but was able to read and write. On further evaluation, patient had unsteady gait. There was no intention tremor or past-pointing. The management was referring the patient to the special school as she was having learning difficulty.

After 2 years of followed up at the paediatric clinic, a doctor realized that the patient not only having learning difficulty but also recurrent chest infection for the past 2 years. He was treated at general practitioner as bronchial asthma. At this time, he still had unsteady gait. There was presence of telangiectasia at the conjuntivae, nystagmus, multiple healed infected skin lesion and generalized lung crepitations. In addition Romberg sign was negative and cerebellar sign was positive. The evidence of cerebellar dysfunction was clearly shown in her hand writing. The hand writing quality deteriorated when comparing at the age of 8 and 14 year-old (figure 1).

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Alpha fetoprotein was raised (147.4 ng/ml). Serum immunoglobulin levels showed normal IgG but increased IgA & IgM (table 1). Full blood picture showed presence of neutrophilia. There was no lymphopenia. Based on history, physical findings and laboratory investigation, the final diagnosis of ataxia telangiectasia was made.

Patient defaulted followed up again until he was 12 years old (2 years later). There was no new complaint except the abnormal gait become worse. The patient needed assistance during walking. He was still having frequent chest infection with wheezing and haemoptysis. Growth was below 3rd centile.

Examination showed ataxic gait, positive cerebellar sign and crepitation with occasional rhonchi at both lungs. Chest x ray reported by radiologist showed left bronchitis with pneumatic changes. CT scan showed cylindrical bronchiectasis with chronic emphysematous changes. Patient was planned for IgG subclass, lymphocyte function and genetic study. However patient defaulted followed up again.

**Table 1: Serum Immunoglobulin levels of the patient**

<table>
<thead>
<tr>
<th>Immunoglobulin</th>
<th>Result [g/L]</th>
<th>Reference range [g/L]</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>8.8</td>
<td>6.5-17.0</td>
</tr>
<tr>
<td>IgA</td>
<td>5.63</td>
<td>0.45-3.50</td>
</tr>
<tr>
<td>IgM</td>
<td>2.09</td>
<td>0.50-1.80</td>
</tr>
</tbody>
</table>

**Ethical approval:** This case report was taken ethical approval before submission for publication

**Discussion**

Ataxia Telangiectasia (A-T) is listed as a rare disease by the Office of Rare Diseases [ORD] of the National Institutes of Health (NIH). The prevalence estimated to be less than 1 in 100 000.3 In Malaysia, there was no published report regarding A-T. Because A-T is so rare, doctors may not be familiar with the symptoms, or methods of making a diagnosis. Not all children develop in the same manner or at the same rate; it may be some years before A-T is properly diagnosed. This patient was diagnosed only at the age of 10 years. In this case, inability of patient to comply with the follow up treatment further delays the diagnosis.

In the early stages of the disease, patients with A-T display a cerebellar motor phenotype, including dysmetria of the extremities and ataxic gait.4 Ataxia is typically observed during the first year of age. However, the normal development of motor skills between ages 2-5 years tends to mask the progression of ataxia, so that parents may report an improvement in gait. At this point, many children are misdiagnosed as having ataxic cerebral palsy. As in our case, the patient was diagnosed as dyskinetic cerebral palsy at the age of 2 years.

After 5 years of age the neurologic symptoms continued to deteriorate. During school years patients may have increasing difficulty with reading because of impaired eye movement coordination. At the same time other problems with fine motor functions may arise. Retardation of somatic growth is observed in a large proportion of the patients. The heights and weights of patients are typically at the 10th percentile by adolescence. The growth was below the 3rd percentile in this patient at the age of 12 years. The stunting of growth is not well understood. Chronic pulmonary disease may be a contributing factor in this case.

Laboratory markers are important for both diagnosis and prognosis. The most constant marker is increase levels of serum alpha-fetoprotein (AFP). Serum AFP increases with age in A-T patients. The mechanism of serum AFP elevation is not well understood. A parallel mechanism of the neurodegenerative process and the liver AFP production may exist. Patients with A-T have disturbed naive B-cell and T-cell homeostasis, most likely because of reduced B-cell and T-cell production linked to disturbed V(D)J recombination, and consequently have a limited B-cell and T-cell receptor repertoire.

Treatment of A-T is symptomatic and supportive. Prevention of recurrent infections by IVIG (intravenous immunoglobulins) is useful. Early treatment of infection is crucial to avoid complications. Changes in motor performance in patients treated with steroid lead to an increase in the activation in relevant cortical areas. This finding suggests that steroid treatment could improve motor performance facilitating cortical compensatory mechanisms in ataxia telangiectasia patients.

**Conflict of interest:** None
References


