Brain & Development 37 (2015) 362–365

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Case report

Myoclonic axial jerks for diagnosing atypical evolution of ataxia telangiectasia

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Received 20 January 2014; received in revised form 29 May 2014; accepted 2 June 2014

Abstract

Background: Ataxia telangiectasia (A-T) is a common inherited cause of early childhood-onset ataxia, distinguished by progressive cerebellum malfunction, capillary vessel extension, and immunodeficiency. The diagnosis of A-T is sometimes difficult to establish in patients with atypical clinical evolution.

Case report: We experienced a pediatric 12-years-old female patient, who was finally diagnosed with classic A-T, demonstrating progressive dystonic-myoclonic axial jerks with ataxia as a predominant clinical feature. Oculocutaneous telangiectasias and immune status were unremarkable. Her myoclonic jerks were spontaneous or stimulus-sensitive, and partially ameliorated by levodopa treatment, but the ataxia was slowly progressive. A laboratory examination showed moderate atrophy of the vermis and cerebellum on brain magnetic resonance imaging, elevated serum alpha fetoprotein (AFP) levels, and total absence of A-T mutated (ATM) protein activity. We subsequently confirmed compound heterozygous truncating mutations of the *ATM* gene in this patient.

Conclusion: Our findings highlight the importance of recognizing dystonic-myoclonic jerks as one of the extrapyramidal signs of classic A-T. Measurement of AFP levels should be considered in patients with unexplained myoclonic jerk movements with ataxia in whom definitive diagnoses are not identified. Physicians should be aware that there are cases where typical findings of A-T may not be fulfilled.

Keywords: Ataxia telangiectasia; Myoclonic jerk; AFP; Extrapyramidal sign; *ATM* gene

1. Introduction

Ataxia telangiectasia (A-T) is an autosomal recessive disorder characterized by progressive cerebellar ataxia, oculocutaneous telangiectasia, chromosomal instability, immunodeficiency, radiosensitivity, and susceptibility to cancer [1]. The responsible A-T mutated (*ATM*) gene on chromosome 11q22-23 encodes the ATM protein,

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http://dx.doi.org/10.1016/j.braindev.2014.06.001

playing an important role in the cellular response to DNA damage [2].

Although A-T is a common inherited cause of early childhood-onset ataxia in most countries, making an early and definitive diagnosis of A-T can sometimes be challenging for clinicians. Some of the hallmarks of classic A-T, such as ataxia, oculocutaneous telangiectasia, and immunodeficiency, can appear only later in life or even remain absent in variant A-T [3]. Oculocutaneous telangiectasia usually appears between the ages of 2 and 4 years, but it may be occur as late as 14 years [1,4].

We present here a pediatric patient with classic A-T, who had progressive dystonic-myoclonic axial jerks with ataxia as a predominant clinical feature. There were no signs of oculocutaneous telangiectasias or of immunodeficiency. The clinical manifestation of extrapyramidal features, which are reminiscent of a series of spinal cerebellar ataxias or miscellaneous diseases of the basal ganglia, has clinical diagnostic value for the atypical evolution of classic A-T.

2. Case report

The patient, a 12-years-old girl, was delivered by vacuum extraction with mild asphyxia and jaundice. She developed normally until the age of 5 years when she developed sluggish movements, difficulty in hand writing, and mild dysarthria. An initial examination at 7 years old demonstrated mild spastic paraplegia with increased reflexes and tone in the lower limbs, ataxic and mild equinus gait, and developmental delay with skills equivalent to those normally observed at 4 years of age. Brain magnetic resonance imaging (MRI) showed moderate atrophy of the vermis and cerebellum (Fig. 1a and b). There were no prominent telangiectasias or oculomotor apraxia. There was no history of recurrent sinopulmonary infections. Her uncle has spastic paraplegia with relationship to the patient's phenotype unknown. Her parents and brothers are healthy. A tentative diagnosis of hereditary spastic paraplegia with mental retardation was made. During the follow-up period, she slowly developed progressive myoclonic jerks at 8 years. These movements were accompanied by spontaneous axial dystonic posture, which sometimes resulted in chronic myalgic pain. This extrapyramidal symptom was partially ameliorated by levodopa treatment with 100 mg/day (5 mg/kg/day), enabled her to perform daily activity smoother. However, her ataxia was progressive and led to an inability to ambulate without assistance from 10 years of age. Written informed consent and permission of following genetic testing and photo/video recording were obtained from the patient's parents. We obtained informed assent from the patient.

At an evaluation at 11 years old, her weight was 26 kg (−1.4 SD) and her height was 136 cm (−1.1 SD). She had no nystagmus, but had jerky pursuits and undershoot saccades. She had slurred speech with lingual dysarthria. She demonstrated spontaneous or stimulus-sensitive

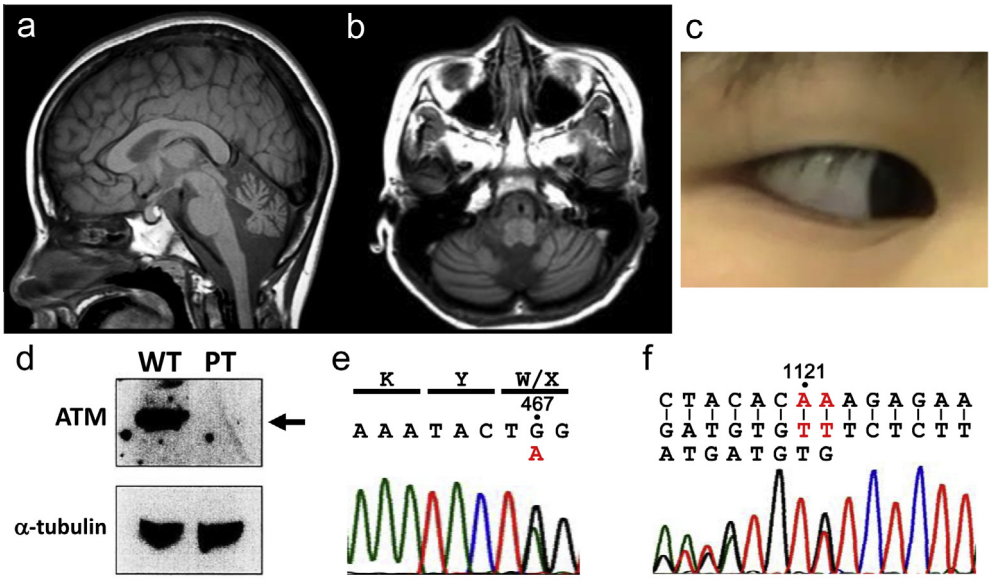

Fig. 1. Characteristics of the patient. (a, b) Magnetic resonance imaging (MRI) of the patient. Sagittal section (a) and axial section (b) of T1-weighted MRI brain images are shown. The patient showed moderate atrophy of the vermis and cerebellar hemispheres. (c) External sclera of the right eye. Her oculocutaneous telangiectasias were unremarkable. (d) Western blotting analysis of ATM protein. ATM was not detected in cell lysates. Alpha-tubulin served as a loading control. WT: wild type, PT: patient, ATM: ATM protein. (e) Electropherogram of ATM exon 5 obtained by sequencing. The red letter indicates the point mutation leading to a heterozygous nonsense mutation, named c.G467A (p.W156X). (f) Electropherogram of ATM exon 9 obtained by reverse sequencing. Red letters indicate the deleted base pairs leading to a heterozygous frameshift mutation, named c.1121_1122delAA (p.E376IfsX2). Forward sequencing results were indecipherable. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)