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Case Report

Brain edema with clasmatodendrosis complicating ataxia telangiectasia

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Abstract

Ataxia-telangiectasia is a chronic progressive disorder affecting the nervous and immune systems, caused by a genetic defect in the ATM protein. Clasmatodendrosis, a distinct form of astroglial death, has rarely been reported in ataxia-telangiectasia. Neuropathology of our patient disclosed diffuse edema of the cerebral and cerebellar white matter with prominent clasmatodendrosis, implicating ATM in the regulation of astroglial cell death.

Keywords: Ataxia-telangiectasia; Clasmatodendrosis; NF-kappa B; Tumor suppressor protein p53

1. Introduction

Ataxia telangiectasia (AT) is an autosomal recessive disorder caused by a defect in the *Ataxia-telangiectasia mutated (ATM)* gene. ATM is a serine/threonine protein kinase involved in the detection of DNA damage. When DNA is damaged, ATM kinase phosphorylates the tumor suppressor protein p53. In the absence of ATM kinase, p53 cannot prevent the cell from moving into the next phase of the cell cycle, resulting in cell cycle arrest and apoptosis [1].

Neuropathologically, AT is characterized by chronic degenerative changes of the nervous system involving the cerebellum, brainstem, spinal cord and spinal ganglia. We herein report an autopsy case of AT showing clasmatodendrosis, a peculiar type of astroglial death.

2. Case report

The patient was a 25-year-old male. There was no consanguineous marriage in his family, but his younger brother also had the same disease. He developed ataxic gait and speech at 6 years of age. The diagnosis was made, and was later confirmed by the detection of exon

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49–52 deletion in *ATM*. Gait disturbance was progressive, and he became wheelchair dependent at 14 years. Dysarthria and dysphagia also worsened. Despite changes in food regimen, he repeated aspiration pneumonia with its frequency and severity increasing with age. At the age of 25, he sustained bilateral pneumothorax, followed by dyspnea a month later. On admission, he had emaciation, scoliosis and generalized muscle atrophy. The conjunctiva showed telangiectasia. Respiratory sounds were weak over the bilateral chest. Neurological examination revealed intellectual impairment, ataxia, dysarthria, dysphagia, hypotonia and hyporeflexia. He died of respiratory failure and septicemia 10 days after admission.

Autopsy revealed acute and chronic pneumonia with pleural adhesion and atelectasis, atrophy of the lymphoid organs, arrested sperm maturation in the testis, and the absence of malignancies. The brain weighed 1227 g, and showed atrophy of the cerebellum (Fig. 1a). Microscopic examination revealed atrophy of the cerebellar cortex with a moderate loss of Purkinje and granular cells (Fig. 1b), remaining Purkinje cells with abnormal shape and orientation (Fig. 1c and d), eosinophilic filamentous inclusion in the inferior olivary neurons (Fig. 1e), loss of myelinated fibers in the gracile fasciculi and spinocerebellar tracts (Fig. 1f), loss of neurons in the Clarke's column (Fig. 1g), and loss of satellite cells in the spinal ganglia with bizarre nuclei in the remaining neurons (Fig. 1h). Blood vessels were unremarkable with the absence of 'gliovascular nodules'. Notably, there was brain edema, severe in the cerebellum (Fig. 2a) and moderate in the cerebrum (Fig. 2b). The white matter was affected more severely than the gray matter, showing diffuse and prominent clasmatodendrosis. Astrocytes in the cerebellum (Fig. 2c) and the cerebrum (Fig. 2d and e) showed swelling and vacuolization of the cell bodies, and disintegration and beading of the processes. There was neither hypoxic-ischemic changes of neurons nor infiltration of inflammatory cells, except for a small number of macrophages around the blood vessels.

3. Discussion

Clasmatodendrosis is an irreversible, 'necrobiotic' change of astrocytes, showing extensive swelling and

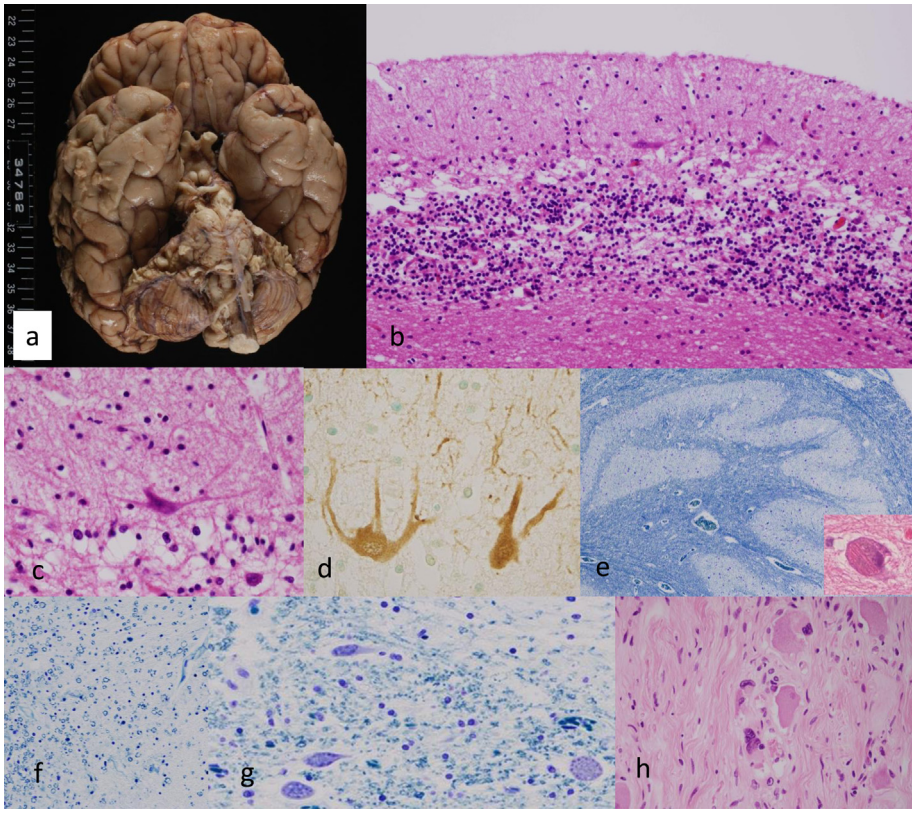

Fig. 1. Pathologic findings related to ataxia telangiectasia (AT) (b, c, e (inset) and h, hematoxilin-eosin staining; d, anti-calbindin D28 k immunostaining; e, f and g, Klüver-Barrea staining). (a). Gross appearance of the basal aspect of the brain, showing marked cerebellar atrophy. (b) Atrophy of the cerebellar cortex with a moderate loss of Purkinje and granular cells. (c, d) Abnormal shape and branching of cerebellar Purkinje cells. (e) Inferior olivary nucleus showing mild astrogliosis and eosinophilic filamentous intracytoplasmic inclusion (inset). (f, g) Cervical spinal cord showing a loss of myelinated fibers in the fasciculus gracilis (f) and neurons in the Clarke's column (g). (h) Spinal ganglia showing a moderate loss of satellite cells and the presence of bizarre nuclei in the remaining cells.