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Child With Ataxia Telangiectasia Developing Acute Myeloid Leukemia

An 11-year-old boy, who was diagnosed as having ataxia telangiectasia (AT) at 5 years of age, was referred to our hospital because of a right submandibular progressive enlarged mass for 2 months. He also suffered from being unstable to stand and recently had twisting of the trunk and tremor in all areas of his body. On physical examination, the patient looked pale and had multiple cervical lymphadenopathies and telangiectasia of the bulbar conjunctiva. His gums easily bled, and he had mild gingival hypertrophy. No hepatosplenomegaly or mucocutaneous petechiae were noted. Neurologic examination revealed nystagmus, squint, dysarthric speech, diminished reflexes, dysmetria, and ataxic gait. Laboratory investigations showed leukocytosis, anemia, and thrombocytopenia (WBC count = 28,500/μL; platelets = 59,000/μL; hemoglobin = 5.2 g/L; hematocrit = 27.5%). Biochemistry tests revealed ALT of 27 U/L, AST of 29 U/L, blood urea nitrogen of 9 mg/dL, creatinine of 0.5 mg/dL, and lactate dehydrogenase of 352 U/L. The α-fetoprotein level was high (242 ng/mL). There were decreased levels of immunoglobulin (Ig) A (6.67 mg/dL) and IgE ($<$ 0.1 mg/dL). Electrophysiologic study showed mild to moderate motor-predominant spinal motor pathology with sensory involvement. Brain magnetic resonance images revealed isolated cerebellar atrophy with small size of vermis (Fig 1). The ventricles were all normal. Analysis of the *ATM* gene revealed compound heterozygous mutation (2413 C to T, arg805ter; 1402-3 del AA, lys468fs). Bone marrow examination showed hypercellularity with an excess of blastic cells (80% to 85%) with primitive nuclear morphology, little cytoplasm, easily discernible nucleoli, and distinct nuclear membrane and markedly depleted hematopoietic cells (Fig 2). These blasts were positive in peroxidase stain (Fig 3) but negative in periodic acid-Schiff stain. Flow cytometric analysis of the bone marrow aspirate revealed the following: CD13, 42.51%; CD33, 77.33%; CD34, 43.64%; HLA-DR, 34.71%; and negative for B- and T-cell markers. The karyotype of the bone marrow cells was 45,XY, -7, $+10$,t(12;14)(p11.2;q32), -14, -22. Acute myeloid leukemia (AML) was diagnosed. After AML was diagnosed, the patient received chemotherapy according to the Taiwan Pediatric Oncology Group AML-97A protocol.[1] Induction treatment consisted of cytarabine (100 mg/m^2, continuous infusion, days 1 to 7) and idarubicin (9 mg/m^2, intravenous push, days 1 to 3). Intrathecal methotrexate (15 mg) was administered on day 1. However, the patient did not achieve remission after two courses of induction therapy and consequently died as a result of severe pneumonia.

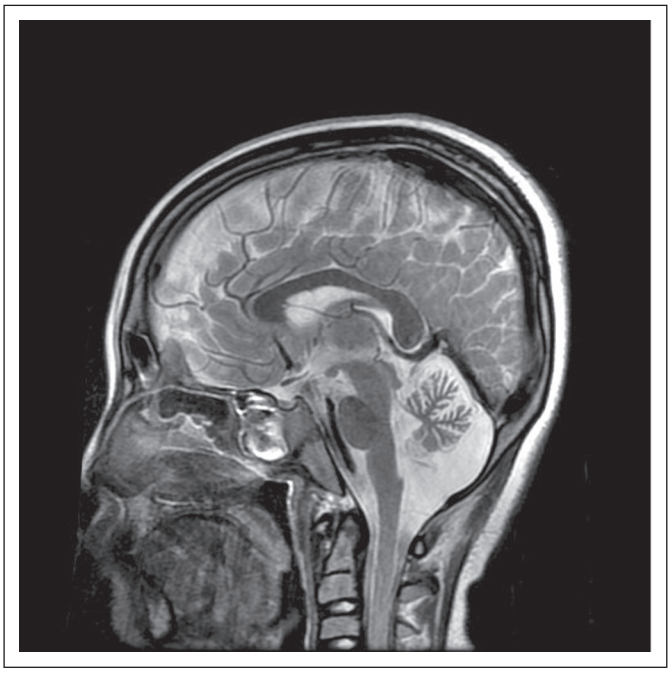

Fig 1.

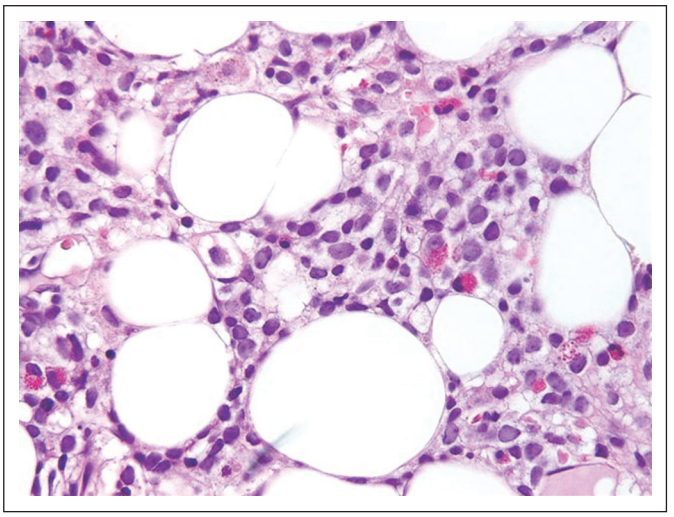

Fig 2.

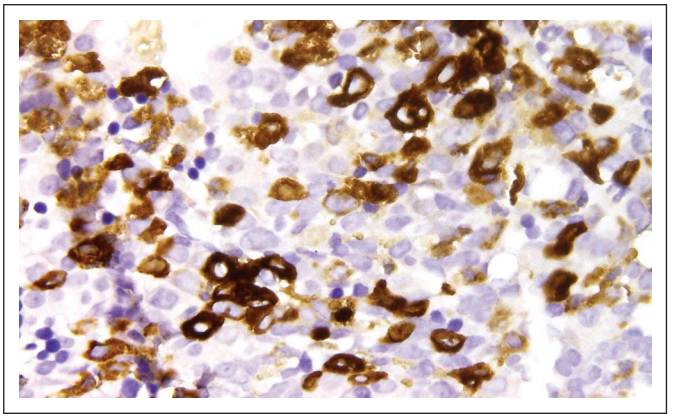

Fig 3.

AT is a recessive disorder caused by mutations in the *ATM* gene at 11q22-q23 and characterized by progressive cerebellar ataxia, oculocutaneous telangiectasia, variable immune deficiencies, cancer susceptibility, and radiation sensitivity.[2] Ataxia is usually the first symptom to occur at the age of 12 to 18 months, whereas telangiectasia occurs a few years later. Approximately 10% of patients with AT develop cancer, of which 75% are non-Hodgkin's lymphomas of various histologic subtypes.[3] The other 20% of cancers include acute and chronic lymphocytic leukemias, adenocarcinoma of the GI tract, basal cell carcinomas, and brain tumors.[4] However, even if the presence of lymphoid disorders has been reported in patients with AT, there is a total absence of myeloid tumors except for one adult patient in the related literature.[5] At least 70% of patients with AT develop immunodeficiency.[6] They often lack IgA and IgE and have a progressive T-cell defect. Recurrent sinopulmonary infections can begin early in life and then lead to recurrent pneumonia, bronchiectasis, and chronic restrictive pulmonary disease.[6] Therefore, severe bronchopulmonary infections are the most frequent cause of death, followed by the combination of pulmonary infection and malignancy, which occurs with more than the usual frequency. Patients with AT are hypersensitive to ionizing radiation, but patients with AT and acute lymphoblastic leukemia showed poor response to therapy.[3] In a report by Toledano and Lange[7] on 22 patients with acute lymphoblastic leukemia in the Immunodeficiency Cancer Registry, none of the patients survived longer than 36 months. More information is required regarding dosage of chemotherapeutic agents so as to prolong remission in these patients. However, there is no standard chemotherapy for patients with AT and AML. Only one adult patient with AT and AML has been reported in the literature, and he died of severe sepsis. Our patient received standard AML induction chemotherapy and died of severe pneumonia. To the best of our knowledge, this is the first case of AT developing into AML in a child. This patient's case emphasizes the importance of recognizing genetic disorders such as AT that have a predisposition to develop into cancer, including AML.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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