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LETTER TO THE EDITOR

Pneumocystis jiroveci pneumonia as an atypical presentation of X-linked agammaglobulinemia

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X-linked agammaglobulinemia (XLA) is usually presented with clinical manifestations of bacterial respiratory and/or gastrointestinal infections below the age of 1 year, when the maternal IgG through placenta disappears from the circulation of the baby. Here, we describe an infant with XLA, who presented with interstitial pneumonia suggestive of *Pneumocystis jiroveci* (formerly *Pneumocystis carinii)* infection.

1 Patient report

A 3-month-old boy was admitted to Mie Hospital because of a long-standing cough, tachypnea and cyanosis. Physical examination showed a weight of 5.8 kg, temperature of 36.3°C, pulse of 170/min, respiration rate of 68/min, oxygen saturation on room air of 60%, respiratory retraction, and abnormal lung auscultation, but there was no lymphadenopathy. Chest radiology showed alveo-interstitial pneumonia (Fig. 1a), and chest computed tomography demonstrated diffuse ground-glass opacities (Fig. 1b). Laboratory tests showed a white blood count of 15,500/μl with 31.9% neutrophils and 54.4% lymphocytes, along with C-reactive protein of 0.02 mg/dl. The patient needed supplement oxygen, but did not require mechanical ventilation. He was first suspected of viral or *Chlamydia* pneumonia, and clarythromycin was administered but there was no improvement. Serum IgM against *Chlamydia trachomatis* and cytomegalovirus were negative. The patient's serum IgG, IgA and IgM levels were 108, 0 and 15 mg/dl, respectively, and the peripheral B cells were absent, suggesting an XLA despite the lack of a family history. With parental consent, the patient was diagnosed as having XLA based on a missense mutation (Arg28His) in the Bruton's tyrosine kinase (*BTK*) gene. The responses to phytohemagglutinin and concanavalin A are 56900 and 30900 cpm (control 141 cpm), respectively. Although T cell number and function were normal, he was suspected to have *Pneumocystis jiroveci* pneumonia. An elevated level of β-D glucan of >300 pg/ml (normal value <20) and KL-6 of 8750 U/ml (normal value, <500), suggested interstitial pneumonia caused by *Pneumocystis jiroveci*; however, polymerase chain reaction of sputum showed a negative result of *Pneumocystis jiroveci*. This may have been due to inadequate collection of sputum. He was treated with administration of sulfamethoxazole-trimethoprim (ST) and intravenous immunoglobulin (IVIG), with clinical improvement. The patient is currently well with IVIG replacement therapy and prophylactic administration of ST (Fig. 2).

2 Discussion

Interstitial pneumonia is caused by many organisms such as cytomegalovirus, adenovirus, fungus, and *Pneumocystis jiroveci*. An infant with interstitial pneumonia may be suspected of having an immunocompromised host with T cell deficiency, although there may have been *Pneumocystis jiroveci* pneumonia even in immunocompetent infants [1, 2]. XLA is a humoral immunodeficiency resulting from a block in early B cell development, and it is

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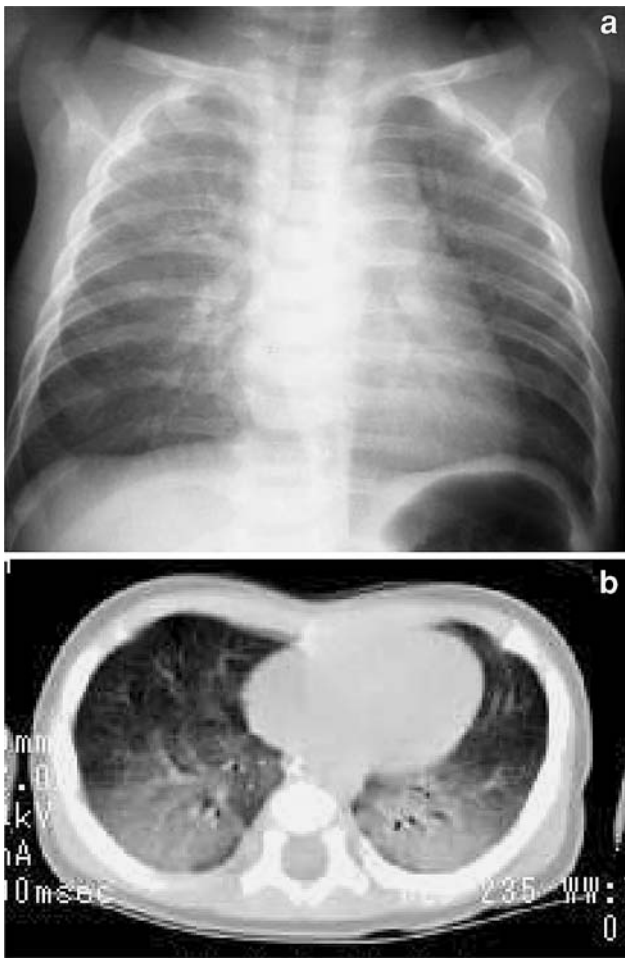

Fig. 1 Radiological findings in the patient. **a** Chest radiograph demonstrated bilateral perihilar opacities. **b** Computed tomography demonstrated diffuse ground-glass opacities in both lungs

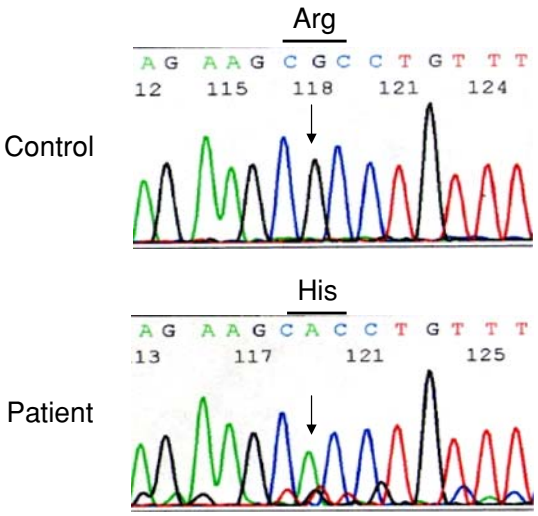

Fig. 2 *BTK* mutational analysis. DNA sequences of the exon 2 of the *BTK* gene in the patient and a control are shown. *Arrows* indicate position 215 in which the patient demonstrates a G to A mutation, indicating an amino acid substitution of Arg28His

clinically characterized by recurrent bacterial infections [3]. Although XLA patients sometimes demonstrate enteroviral infections, they usually show a normal response to viral and fungus infections because of normal T cell functions. However, 3 XLA patients with *Pneumocystis jiroveci* pneumonia have been reported [4–6]. One of these three was an adult receiving immunosuppressive therapy, but 2 patients were infants as in our case. It has recently been reported that Toll-like receptor signaling is impaired in XLA [7, 8] and that may be associated with the development of *Pneumocystis jiroveci* infection in XLA patients. Prophylactic administration of ST as well as IVIG replacement therapy would be recommended for the treatment of XLA patients.

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