

CASE REPORT

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One of the rare causes of recurrent otitis media: Bruton's disease

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Abstract

Bruton's disease is an X-linked immunodeficiency. Recurrent bacterial infections are seen in patients with this disease. A 2-year-old male patient was brought to the otolaryngology clinic due to pain in both ears and tenderness. It was learned from his anamnesis that he had recurrent otitis media and pneumonia attacks previously. Lymphadenopathy was not palpable in head and neck examination. Tonsillar tissue was small in oropharyngeal examination. It was learned that the patient's parents were cousins; there were no other features in his family history. The patient, who had a history of recurrent sinopulmonary infections and whose parents were related, was referred to pediatric immunology clinic with a pre-diagnosis of immunodeficiency. The patient was diagnosed with Bruton's disease. Regular intravenous immunoglobulin treatment every three weeks was started. No new infection was observed in the follow-up.

Keywords: Bruton disease, otitis media, recurrent

Introduction

Bruton's disease is a rare genetic disease caused by a mutation in the Bruton's tyrosine kinase (BTK) gene. Bruton's disease causes no or low level of serum immunoglobulin due to the impairment in B cell development. In patients, bacterial infections begin to appear during the 6-12th months of life when the serum maternal IgG level falls below the protective level and the diagnosis is generally made before 5 years of age [1, 2]. Although the diagnosis can be made early in patients with positive family history, the diagnosis is made after clinical findings appear in most patients. Bruton's disease is a humoral immunodeficiency presenting with recurrent bacterial infections in clinic. The patients suffer from recurrent sinopulmonary infections such as otitis media, sinusitis, bronchitis and pneumonia [3, 4]. According to European Society of Immunodeficiency (ESID) criteria, Bruton's disease diagnosis is made in a male patient when CD19 + B cells < 2% and a confirmed mutation in BTK gene is detected [5]. The patient's

treatment consists of regular immunoglobulin replacement therapy [6]. This case report presents a 2-year-old who was referred to otorhinolaryngology clinic due to recurrent otitis media and pneumonia and who was diagnosed with Bruton's disease.

Case report

2-year-old male patient was brought to our otorhinolaryngology clinic with complaints of pain in both ears and fever. It was learned from his anamnesis that previously he had recurrent otitis media and pneumonia attacks. It was learned that his pneumonia attacks were severe and he had received IV antibiotics treatment in hospital. Ventilation tube was previously applied to both ears of the patient due to recurrent otitis media. Lymphadenopathy was not palpable in head and neck examination. Tonsillar tissue was small in oropharyngeal examination. Ear examination showed hyperaemia in both tympanic membranes and vascularization reaching up to the external auditory canal. The other system examinations were normal. It was learned that the patient was born at term and his developmental steps were normal. It was learned that the first complaints of the patient, who did not have any complaints at birth, started when he was 11 months old. There were no other features in family history of the patient whose parents were cousins. The patient was given oral amoxicillin clavulanic acid and ibuprofen therapy. The patient, who had a history of frequent sinopulmonary

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infections and whose parents were related, was referred to pediatric immunology clinic with a pre-diagnosis of immunodeficiency. In the patient's laboratory tests in pediatric immunology clinic, the results were found as white blood cell (WBC): 17.000/mm³ (4.3-10.3), neutrophil (ANS): 9.2/mm³ (2.1-6.1), lymphocyte (ALS): 4.7/mm³ (1.3-3.5), thrombocyte (PLT): 275.000/mm³ (156.000-373.000), haemoglobin (HGB): 14.2 g/dL (13.6-17.2) and C-reactive protein (CRP): 5.6 gr/dL (0-0.35). His liver and kidney functions and serum electrolyte levels were normal. Serum IgG was measured as 0.4 gr/L (7-16), IgM was measured as 0.16 gr/L (0.4-2.3), IgA was measured as 0.2 gr/L (0.7-4) and IgE was measured as <1 IU/ml (0-29). In flow cytometric analysis, CD3 was found as 79.3%, CD4 was found as 34.8%, CD8 was found as 32.8%, NK was found as 15.75%, CD19 was found as <1% and CD20 was found as <1%. In the genetic analysis, mutation was found in BTK gene (stop mutation, C37C in exon 2). The patient was diagnosed with Bruton's disease at pediatric immunology clinic and intravenous immunoglobulin therapy was started. Otitis media attacks of the patient, who was followed by pediatric immunology and otorhinolaryngology clinic, did not recur.

Discussion

Bruton's agammaglobulinemia was first described by Colonel Ogden in 1952. It is a rare, genetically inherited humoral immunodeficiency diagnosed in childhood [1]. Bruton's is caused by a mutation in the Bruton's tyrosine kinase (BTK) gene located on the long arm of the X chromosome. Therefore, it is seen in boys. BTK gene has an important role in the transformation of Pre-B cells into mature B cells. Its main role is promoting the transition to preB2 stage from preB1. As a result of the mutation in BTK gene, the development of B cell is impaired and mature B lymphocyte levels decrease significantly in the patients' peripheral blood circulation. B cells cannot form the antibody-secreting plasma cells and as a result, all immunoglobulin levels are at significantly low levels with virtually no humoral response. In this disease, lymph nodes and tonsil tissue are small [7, 8]. Our case was male, his serum immunoglobulin levels and peripheral blood B cell markers were very low. Lymphadenopathy was not detected in the head and neck in examination and tonsillar tissue was small.

The criteria developed by European Society of Immunodeficiency (ESID) are used in the diagnosis of Bruton's disease. According to these criteria, Bruton's disease is diagnosed when a mutation is found in the BTK gene and when CD19 + B cells are < 2% in a male patient [5]. In our patient, CD19 + B cells were found as < 1%. In addition, mutation was found in the BTK gene as a result of the genetic analysis of our patient.

In Bruton's disease, clinical findings are seen between the sixth and twelfth months of life when the effects of maternal antibodies are lost. Most of the patients have infections such as recurrent otitis, sinusitis, pneumonia and gastroenteritis [3, 9]. Enteroviral infections can cause chronic meningoencephalitis that can result in subtle neuroregression and later progress to full blown neurologic

impairment and coma [10]. In our patient, clinical findings had started at the age of 11 months. Our patient had recurrent otitis media and pneumonia.

Regularly administered immunoglobulin forms the basis of treatment in Bruton's disease patients. The most common types of treatment are intravenous immunoglobulin (IVIG) or subcutaneous immunoglobulin (SCIG). The aim of immunoglobulin is to keep the patient away from infections [11]. Regular IVIG therapy every three weeks was initiated by the pediatric immunology clinic to our patient. No new infection developed after IVIG in the follow-up of our patient.

As a conclusion, Bruton's disease should be considered among differential diagnosis in patients who are male, who have recurrent otitis media and whose parents are related. These patients should be referred to pediatric immunology clinics to confirm the diagnosis. Early diagnosis and regular immunoglobulin therapy are important for such patients.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

All authors declare no financial support.

Informed Consent

Written consent was obtained from the patient and his parents.

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