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Case Report **OPEN ACCESS**

Primary immunodeficiency disease in children: A significant but rare cause of failure to thrive

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ABSTRACT

This case illustrates the rare cause of failure to thrive (FTT) that initially presented with recurrent ear discharge. A five-year-old boy with a history of recurrent ear infections for the past year was treated for acute symptoms during each visit. He later was diagnosed with acute mastoiditis secondary to otitis media by a private otorhinolaryngologist and was referred to a tertiary hospital for admission and parenteral antibiotic commencement. The anthropometric evaluation noted he fell under the group of FTT and had an incidental finding of lower tract respiratory infection that turned out to be tuberculosis infection. Multiple complications occurred during his admission, including candidemia, disseminated tuberculosis, and deep-seated collections. Hence, he was worked up for primary immunodeficiency and was given extensive supportive treatment.

Keywords: primary immunodeficiency, failure to thrive, tuberculosis, recurrent otitis media

INTRODUCTION

Primary immunodeficiency (PID) is a heterogeneous group of inherited diseases characterized by an inborn error in the immunity system. There are more than 400 types of PIDs. It can be further divided into three categories: defects in humoral/antibody production, cellular/immunity defect, or a combination of both.

In Malaysia, PID is still under-reported. The prevalence rate of PID reported in Malaysia was 0.37 per 100,000 population [1]. The common forms of PID in Malaysia, as classified by the International Union of Immunological Societies from 1979 until 2020, were among patients with defects in cellular and humoral immunity, followed by antibody deficiencies, congenital phagocyte function defect, dysregulation of immunity, and the least form reported in Malaysia was autoinflammatory disorder [1, 2].

CASE REPORT

A five-year-old boy presented with recurrent history of greenish, non-foul smelly ear discharge for the past nine months along with fever. He had four episodes of similar symptoms before this, which were resolved with antibiotics and anti-pyrexia. However, he developed sudden onset of earache and was diagnosed with acute mastoiditis secondary to chronic suppurative otitis media by a private otorhinolaryngologist. He was referred to a local tertiary hospital for initiation of parenteral antibiotics.

Upon further questioning, he also had a chronic chesty cough for the past three months and poor weight gain for the past year. The anthropometric assessment noted his weight and height were below 3rd centile for his age. Ear examination revealed a tender right mastoid area with purulent discharge covering the right tympanic membrane. The left ear canal was erythematous, and the tympanic membrane bulged. Multiple shotty right anterior cervical lymph nodes were felt. Lung examination noted reduced breath sounds over the left middle and lower zone of his lungs.

Initial workup revealed his complete blood count noted to have hypochromic microcytic anaemia with thrombocytosis, predominantly neutrophils. His inflammatory markers increased with an erythrocyte sedimental rate level of 90 mm/Hr and C-reactive protein of 190.4 mg/L. His baseline renal and liver functions were normal. However, the chest radiograph noted to have left lower lobe consolidation. sputum sent for acid-fast bacilli smears were negative. Two sputum samples were sent for gene expert and second gene expert sample of his sputum came back with mycobacterium bacilli detected. TB culture eventually support the TB diagnosis. An initial PID workup was sent and revealed a low level of total T cells and a high level of NK cells.

He was started on parenteral amoxycillin-clavulanic acid and anti-tuberculosis. Unfortunately, he was noted to have persistent spikes of temperature during this admission, which was attributed to retropharyngeal abscess and otomastoiditis as evidenced by CT imaging. Hence, he was subjected to surgical aspiration and histology taken from the abscess wall confirmed features of caseating chronic granulomatous inflammation. His temperature, however failed to be settled.

Table 1. 10 warning signs of PID

Warning signs of PID
Eight or more new ear infections within a year
Two or more serious sinus infections within a year
Two or more months duration of antibiotic but minimal effect
Two or more episodes of pulmonary infection within one year
Failure to thrive
Recurrent abscess or deep skin infections
Persistent candidiasis (skin or oral) after the first year of life
Need for a parenteral antibiotic to treat infection
Two or more deep-seated infections
Family history of PID

His blood cultures eventually returned as candida parapsillosis infection and parenteral fluconazole was commenced for initiated two weeks. Despite extensive treatment, he also developed left shoulder joint septic arthritis that requires arthrotomy and washout from the orthopaedic team.

Despite all the hurdles, this patient recuperated well after the second procedure. His serial chest imaging showed improvement, and his weight also increased in trend. He was given follow-up under primary care to continue monitoring his weight and anti-tuberculosis upon discharge.

DISCUSSION

PID in the paediatric age group is still a rare disease. The low incidence of PID reported in Malaysia may be reflected in the under-reported case or poor awareness among healthcare workers as well [3]. **Table 1** shows a wide range of clinical signs and symptoms in PID based on Jeffrey Modell Foundations [4, 5].

Based on the case, the patient had manifested several warning signs that may point towards PID includes FTT, persistent candidiasis, requirement of antibiotics with minimal effect, deep-seated infection, recurrent ear infection, and pulmonary infections. As the first encounter, primary care doctors should have high-index suspicion with patients who presented with recurrent infection and FTT. All cases of suspected PID should underwent an initial work-up includes complete blood count, albumin level, urinalysis, serum immunoglobulin levels, and basic chest radiograph to aid in patient's diagnosis [4, 6].

Discussion with immunologist or the treating paediatrician is necessary to determine the extent of workup needed to evaluate the type of PID. Based on the initial investigations including full blood count and immunoglobulin level, one can determine whether PID is caused by defect in humoral immunity, cellular-mediated, or combined disorder. Further test includes flow cytometry and genetic testing should be performed to confirm the type of PID after careful history and tailored with the initial investigations results [7]. A person with PID would have a high risk of morbidity and mortality. They are more prone to have recurrent pulmonary infections, infective diarrhoea, granulomatous disease, enteropathy, and development of autoimmunity later in life. Thus, early detection by primary care doctors may help to prevent the complications of PID [8].

Treatment of PID is a complex process and need to be tailored individually. It can be divided into supportive and definitive therapy. Early initiation of supportive treatment includes antibiotics or antifungal, balanced nutrition, vaccination, and immunoglobulin replacement therapy are crucial to prevent further deterioration [9, 10]. Definitive therapy includes such as haematopoietic stem cells transplantation and bone marrow transplant are the treatment option that life rescuer for patient with severe types of PID for example severe combined immunodeficiency (SCID) [9]. Further hope on gene therapy is still debatable and under research.

From this case, we can learn that primary care doctors should help in early detection of any possible PID cases. Initial baseline investigations, supportive treatment such as antibiotic initiation and early referral by primary care team is crucial. Further supportive treatment can be done with the involvement of primary care and respective specialist team. Other than that, long-term follow up under nearest clinic should be maintain not only to the patient, but to other family members as well. This includes encourage other family member to receive additional immunisations such as influenza or pneumococcal vaccine.

CONCLUSION

As a conclusion, primary care physician play an important role to detect child with suspected PID. Thorough history taking and physical examination may provide clues on the disease hence early referral for supportive treatment and further investigations to prevent further morbidity and mortality.

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