Olgu Sunumu (Case Report)

Tekrarlayan Pseudomonas Tonsilitinin Nadir Ama Önemli Bir Nedeni: Yaygın Değişken İmmün Yetmezlik

A Rare But Important Cause of Recurrent Pseudomonas Tonsillitis: Common Variable Immunodeficiency

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Özet

Üst solunum yolu enfeksiyonları (ÜSYE) birinci basamak hekimlerin ve iç hastalıkları uzmanlarının en sık karşılaştığı klinik durumlardan biridir. En sık etiyolojik sebep virüslerdir ve klinik tablo genellikle kendi kendini sınırlayıcıdır. Bununla birlikte, viral ÜSYE belirtileri, grup A Streptococcus (GAS) gibi önemli farenjit etkenlerinin belirtileri ile büyük oranda benzerdir. Atipik prezentasyonlarda ve bakteriyel enfeksiyonlardan şüphelenildiğinde boğaz kültürü alınarak yapılan mikroskopik inceleme sıklıkla başvurulan bir laboratuvar tetkikidir. Boğaz kültürü sonucunda tespit edilen atipik mikroorganizmalar laboratuvar hatası ve/veya bulaş olarak değerlendirilmekte altta yatabilecek olan immün yetmezlik durumları akla gelmemektedir. İmmün yetmezlik tablolarının çocukluk çağı hastalıkları olarak algılanması ve bu konuda farkındalığın azlığı sebebiyle hastaların tanılarında gecikme olmaktadır. Biz bu vakada tekrarlayan tonsillofarenjit şikayetleri ile tarafımıza başvuran, boğaz kültürü sonuçlarında önce gram (-) mikroorganizma sonraki boğazkültüründe ise pseudomonas aerigunosa üreyen hastanın ileri tetkikleri sonucunda akciğerinde bronşiektazi sekeli saptanan, panhipogammaglobulinemi tespi tedilen, periferik lenfosit alt grup analizinde hafıza B hücre sayısında düşüklük görülen bir hastayı sunmayı amaçladık. Hastaya yaygın değişken immün yetmezlik tanısı konulmuş olup sonrasında 400 mg/kg intravenöz immünglobulin replasmanı ile şikeyetleri tamamen kaybolmuştur.

Sonuç olarak, immün yetmezlik hastalarıyla en çok karşılaşması muhtemel 1. Basamak hekimlerinin ve iç hastalıkları uzmanlarının özellikle uyarıcı işaretler varlığında hastaları immün yetmezlik açısından değerlendirmesi veya immünoloji bölümüne yönlendirilmesi hem erken tedavi açısından hem de komplikasyonların yönetimi açısından oldukça önemlidir.

Anahtar Kelimeler: Üst solunum yolu enfeksiyonu, Yaygın değişken immün yetmezlik, Hipogammaglobulinemi

Abstract

Upper respiratory tract infections (URTI) are one of the most common clinical situations encountered by primary care physicians and internal medicine specialists. Viruses are the most common etiologic cause and the clinical picture is usually self-limiting. However, the symptoms of viral URI are substantially similar to those of major pharyngitis agents such as group A Streptococcus (GAS). When atypical presentations and atypical bacterial infections are suspected, microscopic examination of the throat culture is a frequently used laboratory test. Atypical microorganisms detected as a result of throat culture are evaluated as laboratory error and / or contamination and a possible underlying immunodeficiency conditions are overlooked. The diagnosis of the patients is delayed due to the perception of immune deficiency as childhood diseases and the lack of awareness in this regard. In this case, we aimed to present a patient with recurrent tonsillopharyngitis complaints whose first throat culture results was positive for a gram (-) microorganism and second throat culture was positive for pseudomonas aeruginosa. As a result of further investigations of the patient's lung, bronchiectasis sequelae and diminished count of switched memory B cells were detected. The patient was diagnosed with common variable immunodeficiency, and her complaints disappeared completely with 400 mg / kg intravenous immunoglobulin replacement. In conclusion, it is very important to evaluate the patients especially in the presence of stimulant signs in terms of immunodeficiency, or to refer them to the Immunology department, to manage the complications.

Keywords: Upper respiratory tract infection, Common variable immune deficiency, Hypogammaglobulinemia

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INTRODUCTION

Upper respiratory tract infections (URTI) are one of the most common clinical conditions encountered by primary care physicians and internal medicine physicians (1). Viruses are the most common etiologic cause and clinical findings are typically self-limiting (2, 3). However, the symptoms of viral URTI are substantially similar to those of specific pharyngitis pathogens such as group A Streptococcus (GAS). With atypical presentations and suspected bacterial infections, microscopic examination of a throat swab culture is a frequently used laboratory test. Atypical microorganisms detected as a result of a throat swab culture are considered laboratory errors and / or contamination and the presence of possible underlying immunodeficiency conditions are not considered. In this case, we aimed to present an adult patient who presented to a physician with symptoms of recurrent tonsillitis and was diagnosed with Common Variable Immunodeficiency following further examinations.

CASE PRESENTATION

A 28-year-old female patient presented to Clinical Immunology and Allergy outpatient clinic with symptoms of frequent illness and frequent throat infections over the last year. The patient who presented to the physician with frequent throat infections over the last year had received numerous symptomatic treatments and had provided throat cultures twice at different centres due to throat infections, and gram-negative bacterial growth was observed in the first throat culture and antibiotic treatment was given. Complaints of a sore throat and fever recurred shortly after antibiotic treatment in the patient taking antibiotics at the appropriate doses and times. Therefore, the patient consulted a physician and Pseudomonas aeruginosa was found in a throat culture taken from the patient. Upon no significant improvement in symptoms after treatment with a different class of antibiotics for 15 days, the patient visited our clinic.

The family history of the patient revealed no consanguinity of the parents; no family members had been monitored for primary immunodeficiency or died at an early age due to infection; and the patient's father had received chemotherapy for Non-Hodgkin's lymphoma and is currently in remission. A physical examination revealed oropharyngeal hyperemia. Crackles were heard in the lower zones of the right lung. Also the spleen could be felt 2 cm beneath the ribs. Complete blood count values, CRP and sedimentation rates were found to be within normal range in the tests requested due to the patient's family history of lymphomalignancies, complaints of recurrent upper respiratory tract infections, splenomegaly and abnormal lung sounds. The patient had panhypogammaglobulinemia with IgG: 2.78 g/L (7-16 g/L), IgM: 0.32 g/L (0.4-3.5 g/L) and IgA: 0.261 g/L (0.7-2.4) g/L). A chest X-ray was consistent with bronchial enlargement in the middle lobe of the right lung. A high-resolution CT scan revealed bronchiectasis and changes in fibrotic sequelae consistent with the same site (**Figure 1**).

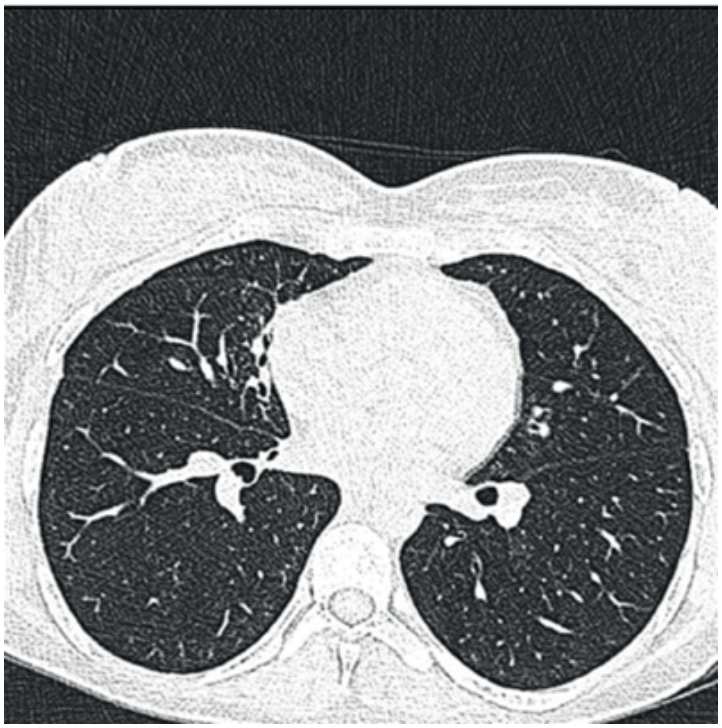

Figure 1. A high-resolution CT scan revealed bronchiectasis and changes in fibrotic sequelae consistent with the same site

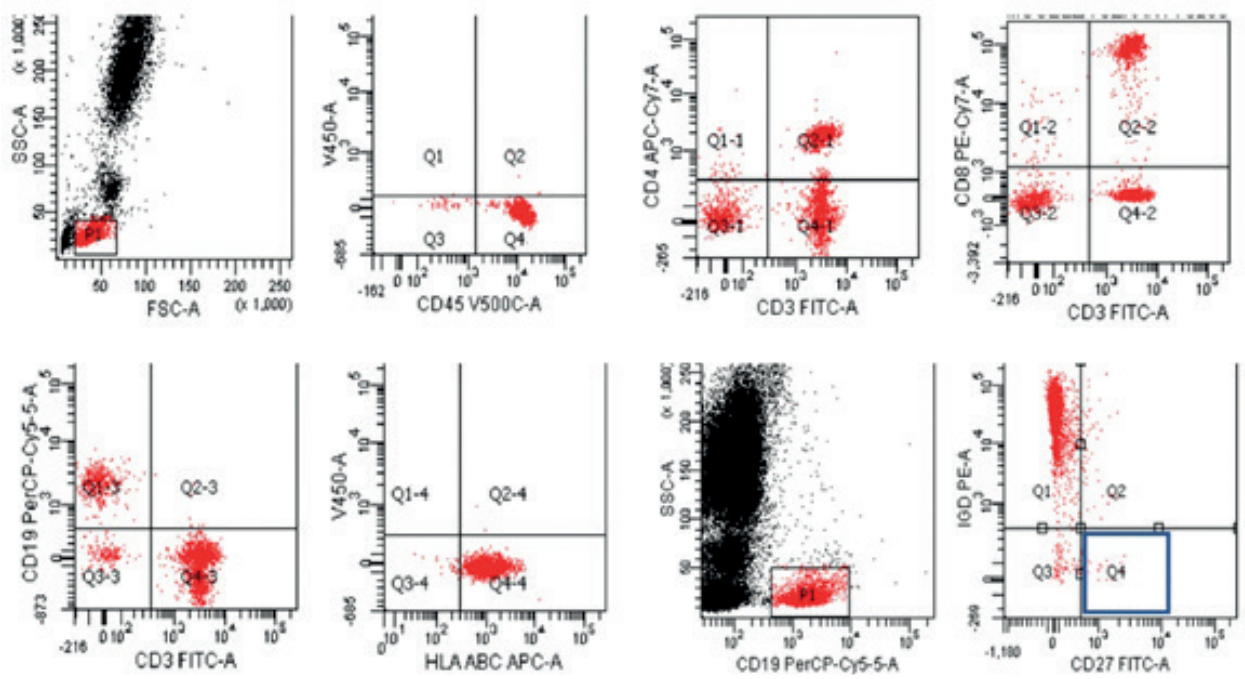

Figure 2. Peripheral lymphocyte subgroups

In the peripheral lymphocyte subgroups studied due to hypogammaglobulinemia, there was a decrease in the cytotoxic T lymphocyte (CD8+) cell ratio of the helper T lymphocyte (CD4+) cell ratio. The percentage of memory B cells (CD19+CD27+IgD-) was very low (0%) (**Figure 2**).

The tetanus antibody response, which shows the patient's response to protein antigens, was normal. However, the pneumococcal antibody response to polysaccharide antigens was not evaluated. Blood group antigens Anti-A and Anti-B were positive at 1:8 titer and were within normal limits. Patients immunoglobulin levels were repeated and panhypogammaglobulinemia persisted in the patient. After excluding other possible causes of secondary hypogammaglobulinemia, the patient was diagnosed with Common Variable Immunodeficiency (CVID) according to ICON (International Consensus Document) criteria (4). Treatment was initiated with intravenous immunoglobulin replacement therapy (30 g/3 weeks) at doses of 400 mg/kg/3 weeks and antibiotic prophylaxis (azithromycin 500 mg PO weekly) for bronchiectasis.

The clinical and laboratory characteristics of the patient are summarized in **Table 1**.

Table 1. The clinical and laboratory characteristics of the patient

	Normal Ranges	Date 19.06.2018	Date 05.07.2018
Hemoglobin (g/dl)	12.1-17.2	13.8	13.6
Neutrophils (/mm³)	1500-7.300	4680	7300
Lymphocytes (/mm³)	800-5500	2670	2200
Platelet (1000xcell/mm³)	150-400	255	292
IgG (g/L)	7-17	**2.78**	**3.31**
IgM (g/L)	0.4-2.3	**0.322**	**0.395**
IgA (g/L)	0.7-4	**0.261**	**0.233**
IgE (IU/ml)	0-100	19	
IgG1 (g/L)	4.05-10.11		**1.69**
IgG2 (g/L)	1.69-7.86		**1.12**
IgG3 (g/L)	0.11-0.85		0.443
IgG4 (g/L)	0.03-2.01		0.0543
Tetanous antibody (IU/ml)	≥0.5	**0.40**	
Anti-HBS antibody	0-10 mIU/ml	**Negative**	
CD3(+) T cells (%)	**Male:** 48-82.6 % **Female:**56.8-84.1%	77	
CD4 (+)T cells (%)	**Male:** 23-52.6 % **Female:**26.9-55.5 %	31	
CD8 (+)T cells (%)	12.8-40.2 %	41	
CD19 (+) B cells (%)	6.3-20.8 %	18	
CD 16-56(+) T cells (%)	**Male:** 5-31.3% **Female:**3.5-24.9%	**3**	
IgD(+) IgM(+) CD27(-) B cells (%) Naive B cells			**95**
IgD(-) IgM(-) CD27(+) B cells (%) Switched Memory B cells	≥ 2%		**0**
Isohemagglutinin	≥1/4	Anti-A:1/8, Anti-B:1/8	
Anti NuclearAntibody (ANA)		Negative	
Anti-HIV Antibody		Negative	

DISCUSSION

Although primary immunodeficiency patients most frequently present to physicians with recurrent respiratory tracts infections, delayed diagnosis is common as primary immunodeficiencies are relatively rare diseases, are perceived to be more common in pediatric patients, are heterogeneous, and there is a lack of awareness about this issue. Even at the best centres, the duration of diagnosis is 6-8 years (5). 10 Warning Signs recommended by the Jeffrey Modell Foundation is very useful in the early diagnosis and treatment of immunodeficiency patients. These warning signs are 2 or more ear infections in one year; 2 or more sinus infections in one year in the absence of allergies; 1 pneumonia per year for more than one year; diarrhea with weight loss; recurrent viral infections (herpes, condyloma, warts); recurrent need for intravenous antibiotics to clear infections; persistent fungal infections; recurrent, deep abscesses of the skin or internal organs; infections with non-pathogenic (harmless) bacteria; and family history of immunodeficiency. Primary immunodeficiency should be suspected in adults with one or more of these warning signs. The most common cause of symptomatic primary immunodeficiency in adults is common variable immunodeficiency. Respiratory tract infections such as recurrent bronchitis, otitis and pneumonia in particular are the most common causes of presentation. In addition, there is an increased risk of autoimmune diseases, lymphomalignancies, chronic lung diseases and gastrointestinal tract diseases. In a study of 473 CVID patients, Resnick et al. identified the reason of