

Case Report

An unusual cause of recurrent pneumonia in adults

Varun Dhir, Vinay Sagar, Ashutosh Aggarwal¹, Amit Rawat², Manphool Singhal³

Departments of Internal Medicine, ¹Pulmonary Medicine, ²Pediatric Allergy and Immunology, and ³Radiodiagnosis, Post Graduate Institute of Medical Education and Research, Chandigarh, India

ABSTRACT

Selective IgM deficiency is a rare primary immunodeficiency defined as isolated low levels of IgM. It presents with recurrent infections and has been described as first presenting in adulthood with recurrent respiratory tract infections. Unlike its better known counterpart of IgA deficiency, this particular immunodeficiency is often overlooked. We present a case of selective IgM deficiency who presented with recurrent respiratory infections.

KEY WORDS: Dysgammaglobulinemia, recurrent pneumonia, selective IgM deficiency

Address for correspondence: Dr. Varun Dhir, Department of Internal Medicine, Post Graduate Institute of Medical Education and Research, Chandigarh - 160 012, India. E-mail: varundhir@gmail.com

INTRODUCTION

Selective IgM deficiency (sIgMID) is a rare primary immunodeficiency disorder that can present in adults with recurrent respiratory tract infections. We present a case of sIgMID who presented us with prolonged history of recurrent sinopulmonary infections.

CASE REPORT

A 58-year old Indian male presented in June 2012 with a 4-day history of high grade fever and mucopurulent expectoration. On examination, patient was febrile (101°F) with arterial oxygen saturation of 93% and crepitations in left infra-axillary and infra-scapular region on respiratory examination. Chest radiograph and computed tomography of the thorax revealed consolidation in lingula and left lower lobe and left sided pleural effusion. [Figure 1] Pleural fluid was exudative with sterile cultures for bacteria and mycobacteria. White blood count was elevated (21000/ μ l); however, blood and urine culture were sterile. Patient was empirically started on broad-spectrum intravenous (IV) antibiotics (piperacillin-tazobactam 4.5 g four times a day) with which the patient slowly improved over 10 days.

This patient had a significant history of recurrent sino-pulmonary infection for the past 10 years, requiring multiple hospital admissions. In 2003, he had presented with 1 month of cough with expectoration, fever, loss of appetite and weight. Although, purified protein derivative and sputum stain for acid-fast bacilli was negative, he was started on empirical anti-tubercular therapy on the basis of radiologic findings and treatment continued for 8 months and patient improved symptomatically. In 2004, the patient had frontal and maxillary sinusitis, requiring endoscopic sinus surgery. In 2005, the patient was again admitted with pneumonia, left pleural effusion and posterior cervical lymphadenopathy. Lymph node aspiration revealed reactive hyperplasia. Patient received intra-venous antibiotics for prolonged period of 4 weeks and improved. In 2006, the patient presented with right middle lobe pneumonia along with right chronic suppurative otitis media. Sputum culture grew *Pseudomonas aeruginosa*; he was treated with IV ceftazidime for 4 weeks and improved. Subsequently this patient had episodes of recurrent pneumonia every year, requiring admission and IV antibiotics. In some years, he required multiple admissions for recurrent pneumonia. [Figure 2] Furthermore, he had recurrent sinusitis, requiring repeat endoscopic sinus surgery. During most of the episodes, the patient had neutrophilic leucocytosis with the white blood count ranging from 12,000 to 30,000.

During this 10 years period, he was evaluated extensively, however, no cause was found. Computed tomography did not show any bronchiectasis. Bronchoalveolar lavage and transbronchial lung biopsy done at two different admissions found neutrophilic infiltration with organization. Human

Access this article online

Quick Response Code:



Website:

www.lungindia.com

DOI:

10.4103/0970-2113.135787

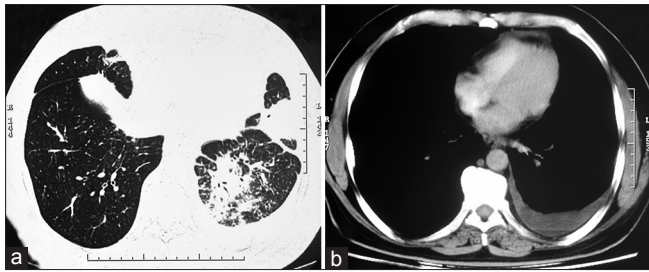


Figure 1: (a) Contrast enhanced computed tomography chest axial image in lung window setting show areas of consolidations in inferior segment of lingular lobe and lateral and posterior basal segments of left lower lobe (b) Axial image in mediastinal window demonstrate left pleural effusion

immunodeficiency virus enzyme-linked immunosorbent assay was repeatedly negative. Nitro-blue tetrazolium test had been repeated twice and showed normal phagocytic function. Autoimmune markers (antinuclear antibody test, antineutrophil cytoplasmic antibodies) were negative. On immunologic work-up, it was found that he had an elevated IgE level (4800 IU/ml) and persistently low IgM level. The IgM level varied from less than 24 mg/dl to 50 mg/dl. However, phenotyping of his lymphocytes revealed normal CD4, CD3 and CD8 counts. [Table 1] Anti-diphtheria toxoid antibody was done and found to be low (0.065 IU/ml). Isohemagglutinin titer could not be done as his blood group was AB positive.

He was treated with cotrimoxazole prophylaxis, pneumococcal and influenza vaccination, however, he continued to have recurrent infections. He had recently with fever, cough and mucoid sputum for 1 week and computed tomography of the thorax revealed bilateral lower lobe, lingual and right middle lobe patchy consolidation with bilateral pleural effusion and mediastinal lymphadenopathy. All blood, pleural fluid and sputum cultures were negative for bacteria and fungi. Fever did not respond to IV antibiotics. Pleural fluid smear for acid-fast bacilli was positive and he has been started on anti-tubercular therapy and prophylaxis with intravenous immunoglobulins (IVIg).

DISCUSSION

sIgMID is a rare primary immunodeficiency disorder with an estimated incidence of 0.03% in the community and 0.1-3.8% in hospitalized patients.^[1,2] It is defined as a dysgammaglobulinemia characterized by isolated low levels of IgM (less than 2 standard deviation). The other immunoglobulin levels are normal, however, IgE is often increased.^[1] Initially described in children with meningococemia, it is now also recognized that it can first present in adulthood.^[3] It is relatively less well-known that its counterpart selective IgA deficiency, which is also more common. When compared to the latter, sIgMID has rarely been described to have familial inheritance (unlike sIgA) and there is no report of formation of anti-IgM antibodies (anti IgA occur in 20-40% of sIgA deficiency). Furthermore, transformation

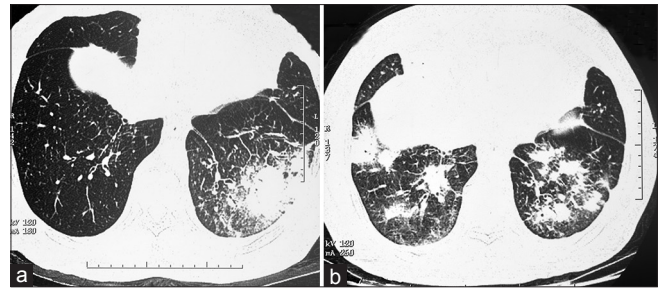


Figure 2: (a) Contrast enhanced computed tomography chest axial images in lung window setting show peripheral patch of consolidation in left lower lobe (b) 1 month later on readmission for recurrent pneumonia, patchy areas of consolidations were seen in lower lobes of both the lungs

Table 1: Immunoglobulin levels and absolute cell counts

Immunological parameter	Normal levels	2006	2009	2010	2012	2013
IgG, mg/dl	800-1800	1030	1015	743	1625	1484
IgA, mg/dl	100-490	213	214	80	207	178
IgM, mg/dl	60-320	50.7	48	57.8	35, <24	36.5
IgE IU/ml	<200	806	179.3		4800	3200
IgG1 mg/dl	377-1189			1160	1154	
IgG2 mg/dl	124-262			192	104	
IgG3 mg/dl	34-118			47	51	
IgG4 mg/dl	7-57			24		
Absolute counts (/µl)						
CD4					621	646
CD8						784
CD19						98

to panhypogammaglobulinemia or Common variable immunodeficiency has not been reported for sIgMID, although subclass IgG deficiencies can occur.^[4]

The largest series on sIgMID in adults consists of 36 patients having serum IgM levels in the range of 12-46 mg/dL.^[4] Most of the patients had recurrent infections, especially of the respiratory tract. The most common was relapsing acute or chronic rhinosinusitis (53%) followed by recurrent pneumonia (17%) and recurrent otitis media (11%). Upper respiratory allergies confirmed by skin testing were present in 61%, asthma in 64%, nasal polyps in 19% and vasomotor rhinitis in 14%. In this series on adult patients, no atypical infection or meningitis was described. The predisposition to allergies was also noted by a smaller series on 15 patients, which found a high prevalence of atopic conditions such as asthma and allergic rhinitis.^[5] The index patient also had raised IgE and recurrent rhinosinusitis. The exact mechanism or part these atopic disorders play in the pathogenesis of this disease is unknown. In addition, gastrointestinal diseases such as celiac disease and ulcerative colitis are also reported associations.^[4]

The cause of this disorder is unclear, with no specific genetic or molecular basis defined. Limited numbers of cases have been associated with chromosomal abnormalities, autoimmune diseases, Wiskott-Aldrich syndrome, Bloom

syndrome, Russell-Silver syndrome and celiac disease. The T cell, B cell, NK cell numbers and phagocytic responses are normal (as in our case). Although IgG levels are normal, decreased specific IgG antibody responses to tetanus toxoid and/or pneumococcal polysaccharides have been reported. Postulated mechanisms include B lymphocyte defect in IgM production, inadequate T cell help, excessive T cell suppressive activity and abnormal CD4/CD8 ratios.^[6-9] These patients are more likely to require prolong courses of antibiotics to eradicate established infections. Measures should be taken to prevent the recurrent infections with vaccination against capsulated organisms and viruses even if patients respond partially to vaccinations. Despite these measures, if patient continues to have frequent infections prophylactic antibiotics can be administered. In few cases, clinical response had been seen in patients with IVIG therapy.^[5] Although, there are only trace amounts of IgM in IVIG, the rationale of IVIG in some cases may be related to the failure of even IgG responses to capsular organisms in these patients despite a normal (or elevated) level of IgG.^[5]

REFERENCES

1. Cassidy JT, Nordby GL. Human serum immunoglobulin concentrations: Prevalence of immunoglobulin deficiencies. *J Allergy Clin Immunol* 1975;55:35-48.
2. Hobbs JR. IgM deficiency. *Birth Defects Orig Artic Ser* 1975;11:112-6.
3. Hobbs JR, Milner RD, Watt PJ. Gamma-M deficiency predisposing to meningococcal septicaemia. *Br Med J* 1967;4:583-6.
4. Goldstein MF, Goldstein AL, Dunsky EH, Dvorin DJ, Belecanech GA, Shamir K. Selective IgM immunodeficiency: Retrospective analysis of 36 adult patients with review of the literature. *Ann Allergy Asthma Immunol* 2006;97:717-30.
5. Yel L, Ramanuja S, Gupta S. Clinical and immunological features in IgM deficiency. *Int Arch Allergy Immunol* 2009;150:291-8.
6. Takeuchi T, Nakagawa T, Maeda Y, Hirano S, Sasaki-Hayashi M, Makino S, *et al.* Functional defect of B lymphocytes in a patient with selective IgM deficiency associated with systemic lupus erythematosus. *Autoimmunity* 2001;34:115-22.
7. Yamasaki T. Selective IgM deficiency: Functional assessment of peripheral blood lymphocytes *in vitro*. *Intern Med* 1992;31:866-70.
8. Ohno T, Inaba M, Kuribayashi K, Masuda T, Kanoh T, Uchino H. Selective IgM deficiency in adults: Phenotypically and functionally altered profiles of peripheral blood lymphocytes. *Clin Exp Immunol* 1987;68:630-7.
9. Moffitt JE, Guill MF, Wray BB, Brown DA, Peacocke NW, Ades EW. Effect of interleukin-2 and mitogen on *in vitro* immunoglobulin production by peripheral blood lymphocytes from patients with selective IgM deficiency. *Ann Allergy* 1988;61:424-7.

How to cite this article: Dhir V, Sagar V, Aggarwal A, Rawat A, Singhal M. An unusual cause of recurrent pneumonia in adults. *Lung India* 2014;31:296-8.

Source of Support: Nil, **Conflict of Interest:** None declared.