CASE REPORT

Common variable immunodeficiency presenting in a man with recurrent pneumonia caused by *Staphylococcus lugdunensis*

Nkechi Chiugo Mbaebie, Sylvia Vania Alarcon Velasco, Jason Touhey

Department of Internal Medicine, Berkshire Medical Center, Pittsfield, Massachusetts, USA

Correspondence to
Dr Nkechi Chiugo Mbaebie,
nmbaebie@bhs1.org

Accepted 8 March 2018

SUMMARY

Common variable immunodeficiency (CVID) refers to a group of disorders where differentiation and maturation of B cells into plasma cells are affected, leading to decreased or defective immunoglobulin production and subsequent immunodeficiency. Symptoms may present at any age between 5 and 72 years, although more severe forms often manifest earlier in life. Milder forms may not be detected. We present an intriguing case of a 69-year-old man presenting with recurrent pneumonia caused by a rare organism *Staphylococcus lugdunensis*, eventually determined to be caused by CVID. The patient had a good clinical outcome after receiving immunoglobulin replacement therapy.

BACKGROUND

Common variable immunodeficiency (CVID) refers to a group of disorders where differentiation and maturation of B cells into plasma cells are affected, leading to decreased or defective immunoglobulin production and subsequent immunodeficiency. It is the most 'common' form of severe antibody deficiency affecting both children and adults,¹ although the incidence of CVID is between 1:10 000 and 1:50 000, making it a rare disease.²

'Variable' refers to the various clinical manifestations of this disorder, including recurrent infections, granulomatous interstitial lung disease, autoimmune disorders, gastrointestinal disease, lymphoma and other malignancies.^{3–4} Greater than 90% of patients with CVID develop recurrent bacterial infections affecting the respiratory and gastrointestinal tract.⁵ Symptoms may present at any age between 5 and 72 years, although more severe forms often manifest earlier in life. Milder forms may remain undetected.⁶

The pathogenesis of CVID remains poorly understood, but appears to involve mutations in any of the pathways involving B cell maturation, differentiation into plasma cells or ability to produce immunoglobulins. This accounts for the variability in severity and specific clinical manifestations.

Diagnostic criteria for CVID include significantly reduced total serum concentrations of IgG, low IgA and/or IgM, and poor or absent response to immunisation. It is diagnosed by excluding other aetiologies for these findings.¹

The goal of treatment of this disease is to prevent infections as well as the development of chronic lung disease secondary to recurrent infections.

CASE PRESENTATION

A 69-year-old man presented with fever, chills, and shortness of breath, pleuritic chest pain and productive cough with yellowish and rust-coloured sputum for 4 days.

His medical history was significant for recurrent pneumonia caused by *Streptococcus pneumoniae* and *Staphylococcus lugdunensis*, disseminated atypical mycobacterial infection, and psoriatic arthritis diagnosed 3 months prior to presentation. Medications included apremilast 30 mg perorally twice daily for psoriatic arthritis.

Examination revealed a rectal temperature of 39.1°C (102.4°F), tachypnoea with a respiratory rate of 24 breaths per minute and oxygen saturation of 88% on room air, with auscultation findings of rales on the right mid to lower lung zones.

A review of his medical records revealed an astonishing number of hospitalisations with recurrent infections. A total of 10 hospitalisations were noted in the previous year for pneumonia, and there were previously multiple other hospitalisations for recurrent sinopulmonary infections.

INVESTIGATION

Complete blood count showed marked leucocytosis with a left shift and an elevated venous lactate. Chest X-ray revealed infiltrates on the right mid to lower lung zones seen to be worsening compared with prior chest X-ray (figure 1).

Two sets of blood cultures grew multidrug-resistant, coagulase-negative staphylococcus, identified as multidrug-resistant *S. lugdunensis* (figure 2). Cultures obtained during five previous hospitalisations also isolated *S. lugdunensis*. Sputum culture and bronchoscopy performed with bronchial washings also revealed *S. lugdunensis*.

The patient reported that he has had numerous respiratory infections since adolescence and an immunodeficiency was therefore suspected. Immunoglobulin levels revealed low IgG, IgA and IgM on multiple occasions (table 1). HIV-1 and HIV-2 were also found to be negative.

DIFFERENTIAL DIAGNOSIS

Primary versus secondary hypogammaglobulinaemia were considered. There was no evidence of malignant or premalignant conditions, including

To cite: Mbaebie NC, Alarcon Velasco SV, Touhey J. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-224184

Figure 1 Interval development of patchy airspace infiltrates in the right middle lobe and right lower lobe concerning for worsening pneumonia. There was no pleural effusion and mild cardiomegaly is unchanged. No acute osseous abnormalities are appreciated.

chronic lymphocytic leukaemia, lymphoma, multiple myeloma or Waldenstrom's macroglobulinaemia. There was no evidence of bone marrow suppression. Good syndrome was ruled out as abdominal and chest CT excluded any thymoma or thymic carcinoma.

With the constellation of symptoms, history of recurrent sinopulmonary infections since adolescence and immunological laboratory finding, and lack of other immune deficiencies, a diagnosis of CVID was made.

TREATMENT

S. lugdunensis, which grew in the blood, sputum and bronchial washing, was found to be multidrug-resistant. Based on sensitivities, the patient was started on vancomycin. Intravenous immunoglobulin (IVIG) infusion at an initial dose of 300 mg/kg was given and was well tolerated. With clinical improvement the patient was discharged home on hospital day 7.

OUTCOME AND FOLLOW-UP

IVIG was repeated after 3 weeks in the outpatient infusion centre, with a plan to repeat every 3–4 weeks for 3 months, and then transition to subcutaneous route, guided by nadir levels of IgG. Repeat immunoglobulin levels have continued to decline.

Susceptibilities	
M.I.C	
Org 1: Staphylococcus Sp Coag Neg	
	Org 1
Ampicillin	R
Cephalothin	R
Ciprofloxacin	R
Gentamicin	R
Nitrofurantoin	S
Oxacillin	R
Penicillin	R
Tetracycline	S
Trimethoprim/Sulfamethoxazole	R
Vancomycin	S

Figure 2 Laboratory report showing multidrug-resistant culture and sensitivity of *Staphylococcus lugdunensis*. MIC, Minimum Inhibitory Concentration.

Table 1 Immunoglobulins obtained 1 month apart

Immunoglobulin	Initial test (mg/dL)	Repeated test (mg/dL)	Normal reference range (mg/dL)
IgG	405	258	768–1728
IgA	298	284	99–396
IgM	19	17	38–266

DISCUSSION

CVID is characterised by hypogammaglobulinaemia and varying degrees of defective T-cell and macrophage function. Hypogammaglobulinaemia can be primary or secondary.⁷ The most common aetiology for secondary hypogammaglobulinaemia is medication-induced, with immunosuppressants, glucocorticoids, rituximab therapy and antiepileptics being the most common medications leading to hypogammaglobulinaemia.⁸

A careful review of present and past medications of this patient did not reveal use of the aforementioned medications. However he had been started on apremilast for his newly diagnosed psoriatic arthritis about 3 months prior to presentation. A review of the adverse reactions for this medication did not reveal hypogammaglobulinaemia as a known adverse event; however, future studies may explore such a possibility. Additionally, his recurrent infections spanned many years dating back to adolescence; thus, the apremilast was unlikely to be causative of his hypogammaglobulinaemia.

Common organisms noted to cause recurrent bacterial infections in patients with CVID are encapsulated bacteria such as *Streptococcus pneumoniae*, *Haemophilus influenzae* and atypical bacteria from the *Mycoplasma* species. This patient was found to have a respiratory colonisation of *S. lugdunensis*, which was also found in the blood, sputum and bronchial washings. The role that this organism plays in milder forms of CVID is yet to be determined.

S. lugdunensis is a coagulase-negative staphylococcus. It has been associated with a wide variety of infections, including cardiovascular infections (severe native and prosthetic valve endocarditis, myocarditis, and infected myxoma), osteomyelitis, prosthetic/native joint infections, skin and soft tissue infections (furuncles, cellulitis and abscesses), central nervous system infections, peritonitis, and urinary tract infections. It is not a common pathogen in the respiratory tract.⁹ It is also known to be highly sensitive to methicillin; however, the strain identified in this patient was multidrug-resistant, sensitive only to vancomycin. The reason for this resistance may be related to the numerous antibiotic exposures in the quest to treat his recurrent pneumonia. The role of *S. lugdunensis* in causation of respiratory infections in patients with CVID is an interesting research question and should be explored in future studies.

CVID can present at any age between 5 and 72 years of age, but it is mostly diagnosed after puberty. Milder forms of the disease are often undetected or diagnosed later in life, as in our patient, who was diagnosed at the age of 69. Physicians should consider the diagnosis of CVID in a patient with recurrent infections, particularly of the respiratory tract and especially if an unusual organism is identified, as in this case. Identification of low immunoglobulin levels in the absence of other causes of immune deficiency should prompt one to treat with immune globulin to help manage active infection and prevent recurrent infection and its consequences.

Patient's perspective

"It has been a mystery why I continued to have repeated respiratory infections which started in my adolescent age but was not severe, but continued to worsen as I got older. The last few years have been very traumatic with repeated hospitalization on account of Pneumonia. I am relieved that we have finally found the cause of this dilemma as I have tried everything I have been advised in the past without much success. This new therapy has continued to keep me out of the hospital so far and I am most appreciative of this."

Learning points

- This case highlights the importance of increasing awareness among physicians that milder forms of common variable immunodeficiency (CVID) may be diagnosed even in adulthood.
- Immunodeficiency conditions should be considered in any patient presenting with recurrent infections, regardless of age, especially when the offending organism is uncommon.
- Other non-encapsulated bacteria-causing organisms could be seen in patients with CVID.

Contributors NCM organised the literature review for this study, wrote the initial draft of this paper, was part of the team that treated the patient, identified this case as unusual and worthy of a case report, and finalised the discussion. SVAV participated in the literature review, helped with formatting of images and paper, and helped with the initial draft of the discussion. JT did an extensive editing of this

paper, and rewrote most of the background, case presentation and discussion, and made sure there were no plagiarised sentences. He was part of the team that cared for the patient.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Conley ME, Notarangelo LD, Etzioni A. Diagnostic criteria for primary immunodeficiencies. Representing PAGID (Pan-American Group for immunodeficiency) and ESID (European Society for Immunodeficiencies). *Clin Immunol* 1999;93:190.
- 2 Yalcin AD, Aydemir N, Turgut H, *et al*. Common variable immunodeficiency syndrome with right aortic arch: a case report. *BMC Infect Dis* 2004;4.
- 3 Hammarstrom L, Vorechovsky I, Webster D, *et al*. SIgAD) and common variable immunodeficiency (CVID). *Clin Exp Immunol* 2000;120:225.
- 4 Schutz C, Niehues T, Ehl S, *et al*. Immunodeficiency and immune dysregulation: A new phenotype of combined immunodeficiency with autoinflammation, autoimmunity and lymphoma. *Autoimmun Rev* 2010;9:477–82.
- 5 Samasca G, Chereches-Panta P, Fufezan O, *et al*. Coeliac disease and variable immunodeficiency- case report. *Revista Romana de Medicina de Laborator* 2011;19. Nr. 2/4.
- 6 Kalicki B, Kapusta K, Snidy A, *et al*. Common variable Immunodeficiency- case report. Central European. *J Immunol* 2013;36.
- 7 Rich R, Fleisher A, Shearer T, *et al*. Clinical Immunology- principles and practice. *Mosby-Year, St. Louis* 2001.
- 8 Cunningham-Rundles C, Bodian C. Common variable immunodeficiency: clinical and immunological features of 248 patients. *Clin Immunol* 1999;92:34–48.
- 9 Becker K, Heilmann C, Peters G. Coagulase-negative staphylococci. *Clin Microbiol Rev* 2014;27:870–926.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>. BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow