A *Streptococcus Intermedius* Brain Abscess Causing Obstructive Hydrocephalus and Meningoventriculitis in an Adult Patient With Chronic Granulomatous Disease

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Abstract

An inherited abnormality of phagocytosis, chronic granulomatous disease (CGD), represents an immunodeficiency characterized by recurrent infection and granuloma formation due to a genetic defect in NADPH oxidase. The 36-year-old male patient with CGD described in this case featured a brain abscess due to *Streptococcus intermedius* infection, complicated by meningoventriculitis and obstructive hydrocephalus. His condition was managed with broad-spectrum antibiotics, interferon gamma-1b, and bilateral external ventricular drains. This report addresses a particular paucity in the literature involving *Streptococcus intermedius* central nervous system infection in the adult CGD population.

Résumé

Anomalie héréditaire de la phagocytose, la granulomatose septique chronique est une forme d'immunodéficience caractérisée par des infections récurrentes et la formation de granulomes, due au déficit d'une enzyme, la NADPH oxydase. L'homme de 36 ans dont il est question ici est atteint de cette maladie et présente un abcès cérébral découlant d'une infection à *Streptococcus intermedius*, compliqué d'une ventriculite et d'une hydrocéphalie obstructive. Le traitement consiste en l'administration d'antibiotiques à large spectre et d'interféron gamma-1b et en la mise en place d'un drainage ventriculaire externe. L'article éclaire un sujet rarement abordé dans la littérature, celui de l'infection cérébrale à *Streptococcus intermedius* chez l'adulte atteint de granulomatose septique chronique.

Introduction

Chronic granulomatous disease (CGD) is an uncommon inherited immunodeficiency that is typically characterized by a lifelong recurrence of severe bacterial and fungal infections. This disorder, inherited as either an autosomal recessive or X-linked trait, is due to a genetic defect in the phagocytic NADPH oxidase complex. Consequently, these phagocytes display inadequate clearance of ingested microorganisms due to an impaired “respiratory burst.” This oxygen consumption surge is intended to generate superoxide and downstream oxygen derivatives, including hydrogen peroxide, a process of antimicrobial oxidation inherent to normal phagocytosis. This impairment in innate immunologic defense owes to the life-threatening infections and granuloma formations in CGD.^{1,2}

The prominent sites of infective and granulomatous involvement in CGD are the lungs, skin, lymph nodes, gastrointestinal tract, and liver. The recurrent infections in CGD are most commonly due to the pathogenic microorganisms *Streptococcus anginosus* group, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Candida species*.^{3,4}

There is scarce documentation of central nervous system (CNS) infection in CGD patients, particularly in adults. Although most cases of CGD-associated CNS infection are attributable to fungi, there is a relative absence of reports of streptococcal CNS infection in the CGD population. One such streptococcal species of the *Streptococcus anginosus* group (previously recognized as the *Streptococcus milleri* group), *Streptococcus intermedius*, is no exception.^{5,6}

The following report describes the case of a 36-year-old male CGD patient with a *Streptococcus intermedius* brain abscess, the complications of which included ventriculomeningitis and obstructive hydrocephalus. We also explore the literature around CNS infection and brain abscesses, with respect to CGD and *Streptococcus intermedius*.

Case

A 36-year-old man with CGD presented to an emergency centre with a one-day history of progressive headache, neck pain, chills, nausea, and myalgia. He was feeling well prior thereto, having just returned a few days beforehand from a one-week trip to Las Vegas, which featured an uneventful stay apart from heavy alcohol consumption (an otherwise occasional drinker). He reported no sick contacts or animal exposures and was otherwise dealing with chronic sinus congestion.

His X-linked CGD has made for a history of recurrent pneumonia (and previously treated for fungal and mycobacterial infections) and bronchiectasis, in addition to granulomatous

colitis and proctitis, several years ago. His first CGD-related infection involving *Pseudoallescheria boydii* pneumonia and osteomyelitis of the ribs and spine (leading to a thoracic resection and engendering a kyphotic spine) was in fact detailed in a previous case report.⁷ He has, however, been free of CGD-related infection in the few years before presentation, including the absence of a regular cough or constitutional symptoms. His only medications were for infection prophylaxis (trimethoprim/sulfamethoxazole 160 mg/800 mg taken orally, twice daily; itraconazole 200 mg orally, once daily; and interferon gamma-1b 82 mcg subcutaneously, three times per week). The patient admitted to inconsistent medication adherence during the months prior to presentation. His medical history was otherwise remarkable for the following chronic issues: gastroesophageal reflux disease, dyslipidemia, hyperuricemia, sinusitis, folliculitis, and benign nephrosclerosis (with microalbuminuria) secondary to previous amphotericin B use. He was working as a teacher and had no recent sexual contacts. He was neither a smoker nor an intravenous drug user. His family history revealed a brother who had died from CGD-related complications.

His initial physical examination (recorded at another hospital) illustrated an alert and oriented man who did not appear toxic or in distress. His vital signs were as follows: temperature 36.5°C, blood pressure 110/70 mmHg, heart rate 80 beats per minute, respiratory rate 18 breaths per minute, and oxygen saturation of 91% on room air (97% on two litres per minute of oxygen by nasal prongs). He reported pain with neck movement, though there was no neck rigidity. Kernig’s and Brudzinski’s signs were negative. His cranial nerves were normal on examination, as were his motor, sensory, and coordination systems. He featured an unremarkable precordial exam and palpable, regular peripheral pulses. His respiratory exam illustrated a kyphotic thorax with left-sided crackles on auscultation (a long-standing physical finding). His abdomen was soft, non-tender, and negative for organomegaly. He had no active joints.

His serum laboratory investigations were normal, including his complete blood cell count (hemoglobin, white blood cells, and platelets), electrolytes, and tests for liver function, renal function, inflammation, and coagulation. His chest X-ray illustrated right-greater-than-left reticulonodular opacification (resolved days later). His initial cerebrospinal fluid (CSF), drawn from a lumbar puncture (LP), was turbid and revealed (findings confirmed by tests at another hospital) elevated white blood cell count 10.3×10^6 cells/L (95% polymorphonuclear neutrophils), elevated protein 5.3 g/L and low glucose < 0.07 mmol/L. This initial CSF sample featured a normal cryptococcal antigen test, negative polymerase chain reaction (PCR) tests (for meningococcus, pneumococcus, and herpes simplex virus

[HSV]), negative cultures (bacterial, fungal, mycobacterial), and a negative India ink stain test.

Initial broad-spectrum antibiotic coverage for the patient's newly diagnosed meningitis included meropenem 2 g IV Q8H (for *Pseudomonas*, *Burkholderia*, and community-acquired organisms), vancomycin 1 g IV Q12H (for beta-lactam-resistant pneumococcus and *Staphylococcus aureus*), ampicillin 2 g IV Q4H (for *Listeria*), trimethoprim/sulfamethoxazole 320/1600 mg IV Q6H (for *Nocardia*), and voriconazole 260 mg IV Q12H (for *Aspergillus* and *Scedosporium*).

Four days after admission, the patient demonstrated a mild depression in his level of alertness, prompting a computed tomography (CT) scan of his head (which revealed a ring-enhancing lesion in the corpus callosum) and a repeat LP (which revealed an elevated opening pressure of 39 mmHg). On day six, his level of consciousness deteriorated and was followed by respiratory failure and a generalized tonic-clonic seizure, requiring intubation and transfer to the intensive care unit (ICU). A repeat CT scan of his head illustrated bilateral hydrocephalus and uncal herniation. He was given a small volume of mannitol, and the neurosurgery service was consulted. A right external ventricular drain was inserted, but resulted in neither ventricular decompression nor an improvement in the patient's clinical status. A second ventriculostomy was therefore performed on the left lateral ventricle. With bilateral external ventricular drains in place, the patient's neurologic state improved.

Magnetic resonance imaging of the patient's head on day eight revealed successful decompression of the lateral ventricles. It also allowed for better characterization of the initially observed corpus callosum lesion on CT. It highlighted a cystic mass consistent with an abscess (measuring 2.7 cm biconically, 3.0 cm anteroposteriorly, and 1.5 mm rostrocaudally) in the splenium, along the posteroinferior aspect of the corpus callosum, which had ruptured into the trigone of the left lateral ventricle. This abscess was due to a *Streptococcus intermedius* infection, confirmed by a PCR-positive result of the ventricular CSF and of the stereotactically biopsied abscess, via a left parietal burr hole. Interferon gamma-1b was eventually started on day ten to enhance the patient's immunologic defense, until he was later transferred from the ICU to the neurosurgical ward, after which he was continued back on trimethoprim/sulfamethoxazole, itraconazole, and interferon gamma-1b antimicrobial prophylaxis.

Discussion

The patient in this case report typifies the lifelong recurrence of infections with which CGD patients struggle. The life-threatening nature of his most recent infection involving a brain abscess, as described here, was ascribed to two severe

complications: obstructive hydrocephalus (mass effect) and meningoventriculitis (communication with the ventricular system).

The genetic defect in NADPH oxidase in CGD phagocytes (including macrophages, neutrophils, and monocytes) confers an impaired microbicidal oxidative burst due to limited superoxide and hydrogen peroxide generation. Accordingly, CGD patients are thought to be more susceptible to catalase-positive organisms that can degrade both phagocytic and pathogenic hydrogen peroxide. Conversely, CGD patients are generally not prone to infection by catalase-negative organisms (e.g. *Streptococcus*), as they do not degrade their own hydrogen peroxide, which is eventually supplied to CGD phagocytes as bactericidal reagents. The notion of catalase-dependent virulence in CGD is, however, dependent on hydrogen peroxide production. *Streptococcus intermedius*, a catalase-negative organism, may be pathogenic in CGD because it does not produce hydrogen peroxide.^{4,5,8}

Although *Streptococcus intermedius* is a commensal organism, its pathogenicity often involves purulent infections. While it has been more commonly described in the context of liver abscesses,^{9,10} several reports have detailed brain abscesses due to *Streptococcus intermedius* infection in adult^{11–19} and pediatric^{18,20–26} immunocompetent patients. In regards to immune-compromised hosts, there is one published report of HIV27 and only one report of CGD-associated²⁸ *Streptococcus intermedius* brain abscess to our knowledge.

In spite of the scarcity of CGD-associated CNS infection due to *Streptococcus intermedius* in the literature, there are reports of CNS infections due to other organisms in (predominantly pediatric) CGD patients. The overwhelming majority of such reports involve *Aspergillus* CNS infections with and without abscesses.^{29–38} Several cases have described CNS infections complicated by obstructive hydrocephalus in CGD pediatric patients,^{33,39–41,45} but we found only one other report in the literature of obstructive hydrocephalus in an adult CGD patient.¹⁶ Other previously described cases of CNS infection in CGD patients involve tuberculosis,⁴¹ *Salmonella*,^{42,43} *Phaeoacremonium parasiticum*,⁴⁴ *Alternaria infectoria*,⁴⁵ and *Scedosporium prolificans*.⁴⁶

Conclusion

This case adds to the available literature on CGD that is especially scarce in adult reports of *Streptococcus intermedius* CNS infection. This example of CGD-related infection reinforces the priority for early, aggressive intervention in light of the significant risk of rapid deterioration. It also emphasizes the precariousness of non-adherence to prophylactic pharmacotherapy. Furthermore, it underlines the importance of

isolating the pathogen in a situation where an infected immune-compromised host typically exhibits atypical microbiology.

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