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Case report

Group G streptococcal myositis in a patient with myeloproliferative neoplasm

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ABSTRACT

While many cases of streptococcal infection are due to Lancefield groups A and B, there has been a rise in reported cases of infections due to group G streptococcus. We present a case of an individual with a hematologic malignancy who developed myositis secondary to group G streptococcus, with no clearly identifiable source of infection. The patient was managed with antibiotic therapy rather than surgical intervention due to high surgical risk related to severe thrombocytopenia. Targeted antibiotics initiated early in the course of disease may prevent the need for surgical intervention. Early diagnosis and treatment are critical to avoid the high morbidity and mortality of life-threatening infections caused by group G streptococcus.

Introduction

Epidemiologically, most streptococcal infections fall under Lancefield groups A and B, however few cases have been reported from groups C and G, with a variety of clinical manifestations [1,2]. Lancefield groups C and G (GCS and GGS) colonize normal skin and oral flora as well as the genitourinary and gastrointestinal tracts, and infections caused by GCS and GGS are typically opportunistic [3,4]. GCS and GGS are β-hemolytic streptococci, classified as *Streptococcus dysgalactiae* subspecies *equismilis* (SDSE), and possess pyogenic abilities, making them virulent [5]. Although SDSE is distinct from *S. pyogenes*, a substantial overlap of clinical syndromes and virulence factors exists [5,6].

Myositis, defined as degeneration and inflammation of muscle tissue without abscess formation, is distinctly different from necrotizing fasciitis, which involves subcutaneous tissue and skin, to the level of the fascia [7,8]. Streptococcal myositis is a rare infection which carries a high mortality rate if intervention is delayed [7]. The majority of streptococcal myositis cases described in the literature are a result of group A strep (GAS) infections, with an identified or presumable source [3,7,9]. We report a case of myositis caused by group G streptococcal (GGS) infection, with no clearly identifiable source in an immunocompromised individual with a hematologic malignancy.

Case presentation

A 57 year old male with an 8 month history of biopsy confirmed myeloproliferative neoplasm presented with 4 days of fever and generalized body aches. He complained of nausea and fatigue along with bilateral calf pain. He reported no sore throat or oral ulcers, or any trauma to his legs. Risk factors for infection included recent dental extraction, and exposure to grandchildren who had developed upper respiratory tract infections after travel to Mexico. He had received only supportive platelet transfusions while awaiting future bone marrow transplantation.

On examination, temperature was 104.1 °F, pulse 158 beats per minute and blood pressure was 96/64 mmHg. Cardiac examination revealed tachycardia without a murmur, and tenderness to palpation of both calves without edema or lesions; Homans' sign was negative. The remainder of the physical examination was unremarkable, including oral, pulmonary, skin and lymphatic systems.

Laboratory data revealed a white cell count of 20.0 K/uL with 38% bands, a platelet count of 23 K/uL, and a creatine kinase (CK) of 453(iU)/L. Deep vein thrombosis was excluded via venous Doppler examination of both legs. Blood and urine cultures were drawn and the patient was started on empiric vancomycin, imipenem-cilastatin and gentamicin for presumed sepsis.

On day 2 of admission, the patient complained of worsening calf tenderness. Physical examination revealed development of bullae on the lower extremities with swelling and decreased range of motion. Emergent lower extremity CT scans showed indistinct

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margins of calf musculature with no soft tissue gas. Due to concern for compartment syndrome, compartment pressures were monitored serially and peaked as high as 29 mmHg. CK peaked at 11,607 (iU)/L, consistent with rhabdomyolysis. Blood cultures grew Gram positive cocci in chains and further resulted with group G streptococcus. Due to thrombocytopenia, IV antibiotics were continued without surgical intervention. Antibiotics were narrowed to ampicillin with clindamycin.

Subsequently the patient's condition improved with antibiotic therapy, and additional imaging and blood culture results confirmed resolving group G streptococcal myositis, rhabdomyolysis and early compartment syndrome. Further workup, including trans-thoracic echocardiogram and throat culture, was negative.

Discussion

Most reported cases of streptococcal myositis are linked to Lancefield groups A and B, with a rising incidence of reported cases due to group G streptococcus. These infections can be severe and life-threatening, especially when they occur in patients with underlying immunocompromising conditions, such as malignancy or HIV [1].

GGS shares virulence factors with GAS, leading to a similar spectrum of disease [3]. Adhesins help enable bacterial invasion into the bloodstream via colonization of the basement membrane and have been demonstrated in GCS and GGS [5]. M proteins are encoded by the *emm* gene, and are a major virulence factor of β-hemolytic streptococci, likely playing a role in infectivity by allowing resistance to phagocytes and adherence to epithelial cells [5,10]. The ability of GGS to enter the bloodstream coupled with the ability of the M protein to interfere with the coagulation and complement cascades [5] may then lead to inflammatory changes in the skin and soft tissues, resulting in myositis and early compartment syndrome.

Pyrogenic exotoxins such as *speS*, previously identified in GGS, may act as superantigens cross-linking T cell receptors and MHCII, thereby upregulating pro-inflammatory cytokines leading to septic shock [5,7]. Horizontal gene transfer among the different groups of streptococci appears to enhance bacterial virulence and survival, and has been widely demonstrated in GGS species [1,9,11]. We believe that the virulence of GGS combined with the patient's susceptibility for infection in the setting of malignancy likely increased his propensity for severe illness.

Myeloproliferative neoplasm (MPN) is a chronic myeloid disorder; however this patient's bone marrow and cytology were not diagnostic of one of the classic MPN's, such as chronic myeloid leukemia, polycythemia vera or essential thrombocytosis. His bone marrow analysis was negative for BCR-ABL and JAK2 mutations. Subsequent biopsy was suggestive but not diagnostic of early primary myelofibrosis.

Patients with primary hematologic malignancies and resulting immunocompromised states are at increased risk for infection. Hematologic cancers predispose patients to infection via bone marrow involvement and T-cell dysfunction [12]. Although cases have been described in patients linking hematologic cancers and bacteremia [13], to our knowledge this is the first case report of a patient with myeloproliferative neoplasm, streptococcal bacteremia, and myositis.

Primary treatment of this patient consisted of antibiotic management and expectant monitoring of compartment pressures and imaging, which differs from optimal therapy as described in the literature. Fasciotomy was not performed given severe thrombocytopenia and high surgical risk. In most cases of myositis, early surgical debridement is the cornerstone of treatment as antibiotics alone are often not effective [2,14]. Antibiotic therapy should be initiated early with the use of penicillins and clindamycin. Clindamycin, a lincosamide antibiotic and bacterial protein synthesis inhibitor, has been shown to inhibit streptococcal virulence factors including the M protein at the ribosomal level [3,9,14].

Intravenous immunoglobulins have been shown to help in neutralizing antibodies in streptococcal infections, however this approach was not used for our patient [7,14,15]. Presently, there is insufficient data to provide strong support for this treatment approach; in our patient's case, given that he showed clinical improvement with targeted antibiotic therapy, immunoglobulins were not used.

Conclusions

In summary, we present the case of a 57 year old male with altered immunologic defenses. Although no clear source of streptococcal infection could be identified in this patient, we hypothesize that his underlying myeloproliferative neoplasm increased his risk for developing myositis once infected.

Myositis caused by streptococcal infection can be rapidly fatal with a high morbidity and mortality and one must remain vigilant to diagnose this condition to prevent an adverse outcome. Early detection is paramount to survival, and therefore, it is critically important to have a high clinical suspicion for streptococcal myositis. Imaging that does not indicate soft tissue gas or abscess becomes less suggestive of necrotizing fasciitis or pyomyositis, and myositis should therefore be suspected. Prompt treatment with antibiotics and surgical debridement, if appropriate, remain the key to therapy. The early use of targeted antibiotics led to improvement and eventual resolution of our patient's clinical condition, which obviated the need for surgical intervention.

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