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**Case Report**

# A case of *Streptococcus cristatus* infective endocarditis mimicking anti-neutrophil cytoplasmic antibody associated vasculitis

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## ABSTRACT

We report a case of a 55-year-old female presenting with infective endocarditis caused by *Streptococcus cristatus* (*S. cristatus*) along with c-anti-neutrophil cytoplasmic antibody (ANCA) positivity. *S. cristatus* is an infrequent cause of infective endocarditis with only 6 reported cases. ANCA positivity is rare in infective endocarditis. In our case ANCA positivity had the potential to mislead towards an autoimmune etiology, but the positive test was eventually understood to be caused by the *S. cristatus* infection. Our case also had unusual presentations like erythema nodosum and thrombotic events. This case also adds scientific literature on the capacity of Streptococcus cristatus to produce serious infections like endocarditis.

**Keywords:** Erythema nodosum, Infective endocarditis, *Streptococcus cristatus*, c-ANCA

## INTRODUCTION

The infection of the heart's inner lining, i.e. endocardium and the valves dividing its four chambers is known as infective endocarditis. The yearly incidence of infective endocarditis (IE), a rare condition, ranges from 3 to 10 per 100,000 people. Despite being comparatively uncommon, it is linked to significant morbidity and mortality; the first-year mortality rate is estimated to be between 25 and 30 percent. Improvement in clinical results requires early diagnosis and treatment. However, because the clinical signs of IE are sometimes non-specific, diagnosis could be challenging.

Staphylococci, Enterococci, and Streptococci are the gram-positive bacteria that cause the majority of instances of infective endocarditis, these three being collectively responsible for 80% to 90% of all cases. Approximately 30% of cases in the industrialised world are caused by Staphylococcus aureus. Other prevalent oropharyngeal colonisers, like the Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella, and Kingella (HACEK) organisms, can occasionally be the causative bacterium in addition to different Streptococci species. Although several additional bacteria have also been found in the past, they only account for only 6% of all cases. Lastly, in the immunocompromised population, fungal endocarditis, which accounts for only 1% of cases, can be a potentially lethal consequence of systemic *Candida* and *Aspergillus* infection.

*Streptococcus cristatus* (*S. cristatus*) is a member of the Mitis group within the Streptococcus genus. It is a commensal bacterium of the human oral cavity, initially described in 1991. It was possible to consistently differentiate this species from other closely related streptococci using new phenetic testing and DNA–DNA hybridisation procedures. It was initially identified as "Gram-positive, catalase-negative cocci that are approximately 1 μm in diameter and grow in chains" and given the name *Streptococcus cristatus*. The pathogenicity of *S. cristatus* is still unknown even after thirty years.[1]

Different types of autoantibodies like those against anti proteinase-3 (PR3) or myeloperoxidase (MPO) can be produced in response to bacterial and viral illnesses. When antineutrophil cytoplasmic antibodies (ANCAs) against proteinase-3 (c-ANCA) or myeloperoxidase (p-ANCA)

are detected in a case, these results may lead the clinician to a diagnosis of an autoimmune condition rather than an infectious disease in the absence of classic IE symptoms. When it comes to ANCA-associated vasculitis (AAV), these antibodies are crucial diagnostic indicators. It is critical to distinguish IE from AAV in order to direct the proper course of treatment. Immunosuppressive treatment is the gold standard for vasculitis, while its use may be detrimental to patients with IE.

## CASE REPORT

A 55-year-old female with history of type 2 diabetes mellitus and systemic hypertension, now presented with 6-month history of intermittent fever and painful skin lesions in distal lower limbs. She also had complaints of excessive fatigability and weight loss. For past 2 weeks, she had increasing frequency of fever with chills. Patient also had abdominal pain since 2 days especially after food intake. Previously, she was diagnosed with left dorsalis pedis artery thrombosis 3 months back and was started on aspirin.

At presentation, patient was febrile and appeared pale, sick and emaciated. She had tender nodular erythematous lesions below the knees, in both lower limbs suggestive of erythema nodosum. Her vitals were within normal limits but she had feeble left dorsalis pedis artery pulsations. Systemic examination revealed a grade 2 systolic murmur over mitral area. Abdomen was soft with normal bowel sounds but tenderness was elicited in the umbilical area on palpation.

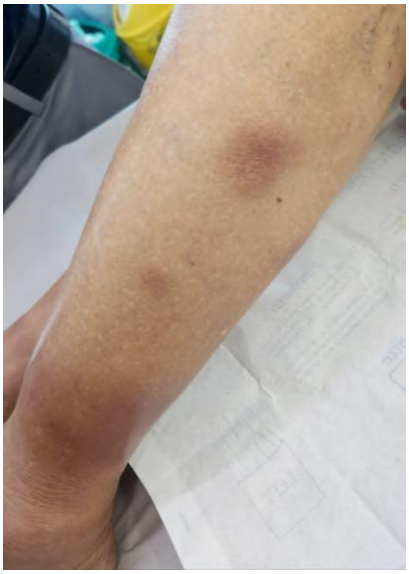

**Figure 1: Erythema nodosum in lower limbs.**

Initial blood investigations showed anemia, hypoalbuminemia and elevated inflammatory markers (CRP and ESR). Three sets of blood cultures were sent. Workup done for tropical fever, tumour markers, hypercoagulable conditions and myeloma screening were negative.

Ophthalmological examination with fundoscopy showed Roth spots (Figure 2). On repeated probing patient revealed a history of rheumatic fever in childhood for which she had taken parenteral penicillin prophylaxis till 19 years of age. As per a recent ECHO taken 3 months back at another centre, she was reported to have no residual valvular lesions.

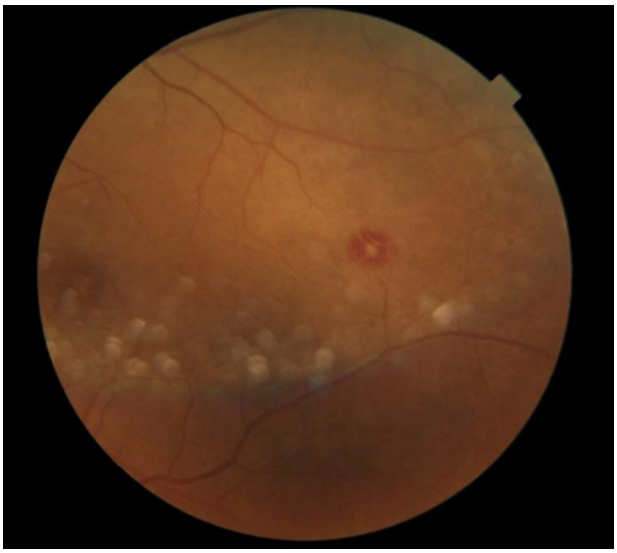

**Figure 2: Fundoscopic image showing Roth spot.**

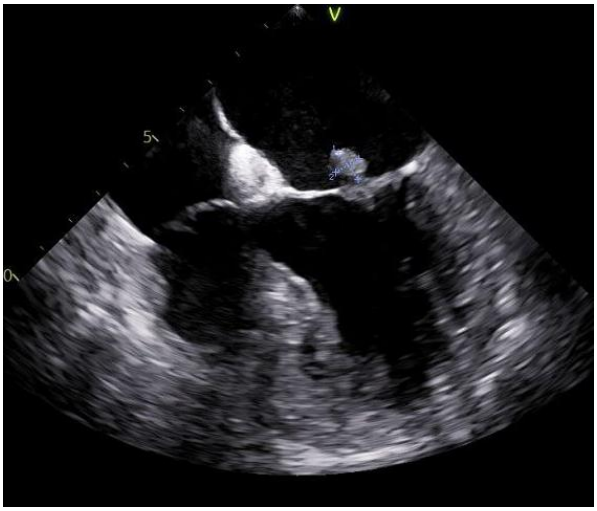

**Figure 3: Echo showing valvular vegetations in mitral valve.**

Urgent echocardiogram was done which showed moderate mitral regurgitation, moderate mitral stenosis, and vegetations on anterior and posterior mitral leaflets with independent mobility (Figure 3). These findings were confirmed by transesophageal echocardiogram and was suggestive of rheumatic heart disease with infective endocarditis. Blood cultures showed growth of *Streptococcus cristatus* in all 3 samples.

To evaluate the persistent abdominal pain, CECT abdomen was taken which showed splenomegaly with splenic

infarcts, renal scars and occlusion of left terminal branch of superior mesenteric artery. In view of erythema nodosum, autoimmune markers were sent and autoimmune screening showed low complement 3 protein along with positive c-ANCA.

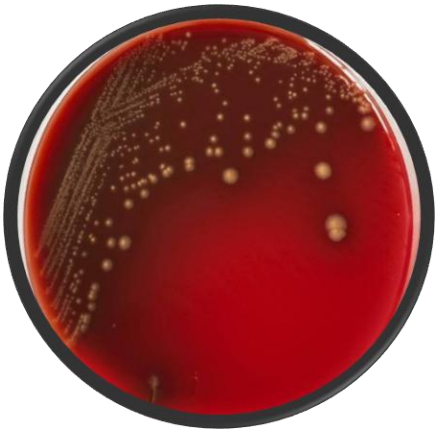

**Figure 4: *S. cristatus* colonies in blood agar.**

Patient was diagnosed to have native valve subacute bacterial endocarditis of mitral valve caused by streptococcus cristatus, c-ANCA positivity was thought to be secondary to the infection. She was treated with parenteral ceftriaxone 2 g IV daily for 6 weeks.

Patient improved with treatment and showed resolution of erythema nodosum lesions, fever spikes and abdominal pain. Repeat echo after 6 weeks, showed clearance of vegetations and reduction in mitral regurgitation. c-ANCA repeated on follow up was negative.

## DISCUSSION

We describe a rare case of native valve subacute bacterial endocarditis caused by *Streptococcus cristatus*, confirmed with 3 blood cultures yielding significant growth of *Streptococcus cristatus* species. Literature showed only 6 previously reported cases of infective endocarditis with this organism.[2] As of our knowledge our case stands as the first case of this kind reported from India. Our patient was treated by monotherapy with parenteral ceftriaxone for 6 weeks. This case adds more scientific evidence about the ability of *S. cristatus* to cause serious infections such as bacteraemia or endocarditis.

As the patient presented with intermittent fever, weight loss and erythema nodosum the possibility of autoimmune disease was considered and autoimmune markers were sent. In our case, the patient had PR3-ANCA positivity and reduced complement levels. Further literature review showed previous reported case of *Streptococcus cristatus* infection with c-ANCA positivity.

Infective endocarditis can sometimes present similar to ANCA-associated vasculitis, with a positive ANCA test.[3] This condition can trigger the production of various autoantibodies, causing either chronic infection or vasculitis symptoms in affected patients.[4] A study comparing ANCA positive and negative infective endocarditis cases found that ANCA positive cases showed a higher incidence of lower limb edema and positive blood cultures. Additionally, the survival rate was lower in those with ANCA positivity.[5]

In infective endocarditis, the emergence of ANCA positivity complicates the decision on the optimal treatment for immune conditions. Adding immunosuppressive drugs to therapy in these patients could heighten the risk of infection-related mortality, making the use of such drugs alongside antibiotic treatment a debated issue.

Our patient presented with an unusual presentation of erythema nodosum and thrombotic events. About 0.6% of cases of infective endocarditis develop erythema nodosum.[6] It is the most prevalent type of panniculitis, defined by tender erythematous nodules that are primarily found in the pretibial region of the lower limbs. Although rare, erythema nodosum can be an early indicator of infective endocarditis. Although the precise cause of erythema nodosum is uncertain, it seems to be caused by an overreaction to a number of antigenic stimuli.

In this patient, the previously reported left dorsalis pedis artery thrombosis, previous renal scarring, splenic infarct and current superior mesenteric artery occlusion were thought to be secondary to systemic embolisation of vegetations with possible focal thrombus formation. Literature shows case reports of *Streptococcus cristatus* presenting with thrombotic events like splenic infarcts and ischemic colitis.[2]

## CONCLUSION

This case underscores the importance of ruling out infective endocarditis in a patient with fever, arthralgia and erythema nodosum, along with positive ANCA results, before starting long term immunosuppressive therapy. It also highlights the importance of giving attention to rare presentations like erythema nodosum and thrombotic events in infective endocarditis. This case also adds more scientific evidence on the capacity of *Streptococcus cristatus* to produce serious infections like endocarditis.

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