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Commentary

Tropheryma whipplei Endocarditis Diagnosed by Tissue 16S rRNA Gene Sequencing: A Commentary

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About the study

Infective Endocarditis (IE) is a serious disease. Finding the causative pathogen is very important for successful treatment. However, in many cases, standard blood cultures are negative. This condition is called Blood Culture-Negative Endocarditis (BCNE) and it is a major diagnostic challenge.

Many things can cause BCNE, such as prior antibiotic administration or infection with fastidious organisms. *Tropheryma whipplei* is one of these fastidious pathogens. This bacterium is known for causing Whipple's disease, which often includes symptoms like arthralgia, fever, weight loss, diarrhea and malabsorption. Identifying *T. whipplei* as a cause of IE has been difficult. However, the appearance of new molecular biology techniques has changed this situation.

Our case report is a clear example. A 66-year-old man presented with intermittent fevers and arthralgia for many months. His valvular disease progressed, and echocardiography showed vegetations on the mitral valve. We performed 14 sets of blood cultures, but no causative pathogens were identified. This was a case of BCNE. Because his valve regurgitation progressed, he needed double-valve replacement surgery. The diagnosis was only confirmed after surgery. We used 16S rRNA gene sequencing on the excised valve tissue, and the test identified *Tropheryma whipplei*.

This case highlights the limitations of conventional diagnostic pathways. *T. whipplei* is an organism that is exceptionally difficult to culture in the laboratory. Therefore, reliance on blood cultures will always fail. Other tests, like PCR on duodenal biopsy, may not be useful if the patient does not have clear gastrointestinal symptoms. This leaves molecular analysis of the affected valve tissue as the most definitive diagnostic method.

Broad range 16S rRNA gene sequencing of valvular biopsies is a powerful and essential tool. This modern molecular approach can find the pathogen's gene directly from the tissue. We do not need to wait for a culture to grow. As recent guidelines suggest, this technique has a greater sensitivity and specificity than conventional cultures for identifying pathogens in surgically managed endocarditis. For our patient, this molecular diagnosis was the pivotal event that changed his treatment.

The therapeutic implications are profound. Empirical antibiotic therapy for BCNE, which often targets HACEK organisms or Bartonella, is not effective against *T. whipplei*. This pathogen requires a specific, long-term regimen. Our patient was successfully treated with ceftriaxone followed by one year of oral Trimethoprim-Sulfamethoxazole (TMP-SMX). Without the definitive diagnosis, he would have received an inadequate course of antibiotics, leading to a high risk of relapse.

This case also brings a related clinical dilemma into sharp focus: The timing of empirical antibiotics. We know that prior antibiotic administration can reduce the sensitivity of both cultures and molecular tests on excised valve tissue. In our patient, we made the decision to withhold preoperative empirical antibiotic therapy. This was possible because his vital signs were stable and imaging showed no evidence of embolism. This difficult decision was key to securing the final diagnosis. Doctors must carefully balance the risk of clinical deterioration against the immense diagnostic value of sterile tissue.

Conclusion

In conclusion, clinicians should consider *T. whipplei* in patients presenting with BCNE, especially those with a background of fever of unknown origin or chronic arthralgia. Our case reinforces that a definitive diagnosis is often impossible without advanced molecular tools. The integration of 16S rRNA gene sequencing of surgical specimens into routine clinical practice is a clinical necessity for improving the detection and treatment of fastidious pathogens.