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LETTER TO THE EDITOR

Role of prolonged blood culture incubation in infective endocarditis diagnosis

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We read with interest the recent publication by Lindell et al. describing a large cohort of *Cutibacterium*/*Propionibacterium* prosthetic valve endocarditis (PVE) [1]. *Cutibacterium*/*Propioniobacterium* species are facultative anaerobes which are part of the normal skin microbiota and are increasingly recognized as a cause of endovascular infection, in recent reports, constituting 3.8–8% of PVE cases [1, 2]. As slow-growing organisms, *Cutibacterium*/*Propionibacterium* species may require prolonged durations of incubation for isolation. Accordingly, they may be missed with conventional durations of blood culture incubation. Prolonged blood culture incubation is frequently requested by the Infectious Diseases clinicians at our institution in cases of suspected endocarditis; however, the clinical value of this practice has been incompletely defined. Likewise, the clinical value of blind subcultures and terminal Gram or acridine orange staining of negative blood culture bottles in such situations is not clear [3]. Terminal subculture to chocolate agar is recommended by the Clinical and Laboratory Standards Institute (CLSI) for patients with suspected endocarditis who have negative blood cultures after 5 days.

Mayo Clinic Rochester is an endocarditis referral center. To evaluate the utility of prolonged blood culture incubation, blind subcultures, and terminal stains, we evaluated cases from December 2015 to December 2017, in which our clinicians specifically requested extended blood culture incubation for suspected endocarditis. During this time period, following such a request, blood cultures were incubated 10–14 days, subcultures were performed after 5 days of incubation, and terminal Gram and acridine orange stains were performed. Blood cultures were performed using the Becton Dickinson BD BACTEC FX™ platform with a typical blood culture set consisting of two BD BACTEC™ Plus Aerobic/F bottles and one BD BACTEC™ Lytic Anaerobic/F bottle. It is our routine practice to draw at least two blood culture sets per patient.

Extended incubation was performed on 116 blood cultures from 53 patients, with the incubation duration extended from the standard 5 days to 10 or 14 days for 8 and 108 cultures, respectively. In addition, bottles were briefly removed from blood culture instruments on day 5 of incubation, sub-cultured to chocolate blood agar, and returned to blood culture instruments to fulfill the extended incubation period. Subcultures were incubated for 5 days at 37°C in CO_2. Terminal blind Gram and acridine orange stains were performed on 105 negative cultures on the last day of incubation. Results of all blind subcultures, as well as all terminal Gram and acridine orange stains, were negative. Beyond 5 days of incubation, there were, however, five positive blood cultures in three patients, all with *Cutibacterium acnes* and all involving culture in anaerobic bottles. One patient had a single positive culture after 138 h of incubation, determined clinically to be a contaminant. The other two patients had two positive cultures each, after 153 and 168 h of incubation for one patient and 178 and 182 h of incubation for the other; both were men and had PVE, confirmed by histopathology, with findings compatible with *C. acnes* infection. No other bacteria, including no members of the HACEK group, were identified by prolonged incubation of blood cultures.

Results of this study add to other data showing that prolonged incubation of blood cultures in cases of endocarditis is useful for detection of *C. acnes*. Notably, the overwhelming majority of cases of *C. acnes* endocarditis have been reported in males (90–100%) with underlying prosthetic cardiac valves or devices (79–100%) [1, 2, 4]. The exact reason for male predominance is not known, however a similar trend has been described in osteoarticular infections [5].

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Although the CLSI recommends blind subcultures, similar to other studies [3, 6], we did not identify any additional pathogens with this approach. Therefore, we do not recommend routine blind subcultures in suspected endocarditis cases. Likewise, routine blind terminal Gram and acridine orange staining was not shown to be useful and is not recommended.

A standard 5-day incubation period for blood cultures on a continuously monitored blood culture system is adequate for almost all cultivable causes of endocarditis, including the fastidious HACEK organisms and other rare or fastidious bacteria. However, a 14-day "extended" incubation is clinically useful for recovery of *Cutibacterium*/*Propionibacterium* species (especially *C. acnes*) from blood cultures in endocarditis patients, because these organisms may be missed with a 5-day incubation protocol. Prolonged incubation of blood cultures should be considered in patients with suspected PVE when cultures are negative after 5 days of incubation.

References

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