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LETTER TO THE EDITOR

Does prolonged blood culture incubation improve microbiological diagnosis of HACEK and slow-growing bacteria infective endocarditis?

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We were very interested with the publication by Lindell et al. and the letter by Fida et al. describing cases of infective endocarditis due to *Cutibacterium acnes* especially on prosthetic valves [1, 2].

C. acnes are large described anaerobic bacteria part of cutaneous flora and involved in deep infections. Many studies report cases of bone and joint infections, meningitis, infective endocarditis (IE), or endovascular infections [3, 4]. It is well known that prolonged cultures are necessary to detect *C. acnes*, because they are slow-growing bacteria detected after several days especially on cultures under anaerobic atmosphere.

IE is a disease characterized by a high rate of morbidity and mortality. The in-hospital mortality rate is up to 20%, with a one-year mortality ranging between 25 and 40%. According to French and European guidelines, prolonged cultures of blood cultures are recommended in case of suspicion of IE.

In Saint Joseph Hospital, Paris, France, the cardiologic unit handles the management of IE. All patients with a suspicion of IE are discussed on a multidisciplinary staff with cardiologists, infectious diseases specialists, microbiologists, and pharmacology specialists.

We evaluated all the blood cultures registered between 2012 and 2018 with a suspicion of IE. According to French and European guidelines, routine subcultures are not recommended. Routine terminal Gram staining is also not recommended [5]. For each patient with a suspicion of IE, at least 2 bottles of an aerobic and anaerobic blood culture are punctured and incubated for 14 days (Bactalert, Virtuo, Biomérieux, France). In case of positive signal, a direct examination is performed, and the blood bottle isolated on blood and chocolate agar during 5 days at 37 °C in CO_2 and under anaerobic atmosphere. When the direct examination is negative, the curve on the machine is systematically controlled and a specific fungal coloration is performed. The positive blood bottle is also isolated on blood and chocolate agar for 5 days.

During the period 2012–2018, we registered 9181 positive aerobic bottles and 8394 positive anaerobic bottles. On the positive aerobic bottles, 6206 were detected positive (40.4%) in less than 5 days, 2973 (19.3%) between 5 and 10 days, 2 (1.3×10^{-4}) between 10 and 14 days. Subcultures on these two bottles found a *C. acnes and Staphylococcus hominis*. These bacteria were considered as cutaneous contaminants during sampling because no symptom of infection was reported.

Three patients were positive on the aerobic bottle with HACEK group bacteria, *Haemophilus influenzae*, *Haemophilus aphrophilus*, and *Cryptosporidium hominis* in less than 5 days. These positive cultures were associated to IE.

On the positive anaerobic bottles, 7939 (51.7%) were detected positive in less than 5 days, 449 (2.9%) between 5 and 10 days, and 6 (3.9×10^{-4}) between 10 and 14 days. Subcultures on the 6 bottles showed one *Staphylococcus epidermidis* and 5 *C. acnes*. These microbiological results were considered as contaminants too.

For one patient, positive culture was significant in 10 days on aerobic and anaerobic culture to *C. acnes* but no diagnosis of infection was reported after clinical, radiological, and microbiological analysis.

The totality of IE on native or prosthetic valves was found on blood cultures between one and 10 days. HACEK group bacteria were detected on aerobic blood cultures in less than 5 days. These results are in accordance with other previous studies [6, 7].

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Regarding the results found in Lindell et al. study, 50 cases of *Cutibacterium sp.* IE were reported in 21 years amounted to 2.5 cases/year. These findings are in accordance with the results reported in Fida et al. study with 1 case/year. Endocarditis involving *Cutibacterium* species remain rare and are almost reported in male patients with a prosthetic valve. These reports are very interesting but the extended cultures, subcultures, or direct examination on all blood cultures for patients suspected of IE are very time-consuming. The cost effectiveness of these technics seems very limited in relation to the impact on the care of the patient. It may be accurate to focus on patients with risk factors by collecting the main clinical information: male gender, suspicion of IE, presence of prosthetic valve in order to perform the extended cultures on these cases specifically. The role of multidisciplinary discussions between clinicians and microbiologists appears to be essential in this context.

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