



Commentary

Commentary on "Systemic candidiasis and cytomegalovirus infection in the setting of artificial cardiac device deployment"

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Citation: Huaman, M. (2015).
"Commentary on "Systemic candidiasis and cytomegalovirus infection in the setting of artificial cardiac device deployment"

The VAD Journal, 1. doi:
<http://dx.doi.org/10.13023/VAD.2015.14>

Please see the paper by
Thangam M et al
<http://dx.doi.org/10.13023/VAD.2015.13>

Editor-in-Chief: Maya Guglin,
University of Kentucky

Received: August 23, 2015

Accepted: August 30, 2015

Published: August 30, 2015

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Funding: Not applicable

Competing interests: Not applicable

Keywords

Ventricular assist device; heart failure; infection; immune function

Thangam and associates [1] report the case of an unfortunate elderly male with history of coronary artery disease who developed an acute myocardial infarction due to occlusion of the right coronary artery. This was complicated by the development of a ventricular septal defect and refractory heart failure requiring implantation of cardiac devices including intra-aortic balloon pump, ventricular assist device (VAD) and ultimately total artificial heart (TAH). Despite all efforts, the patient expired ~3 months after the AMI event.

The patient developed candidemia and retinitis attributed to cytomegalovirus (CMV) disease during his complicated hospital course. The authors postulate that these severe opportunistic infections were, in great part, a result of host immune defects related to VAD and TAH implantation.

Local and systemic effects on host immune responses have been described after VAD implantation. Most studies were conducted in the pulsatile VAD pump era [2], but similar immune defects may be present with continuous flow pumps [3]. Dysfunctional systemic immune responses appear to be related to interactions between the circulating immune system and the endovascular surface of the implanted device. Biodegradation and leaching of device components may also contribute in the long-term [4]. Thus, abnormal activation of monocytes and other presenting cells leading to impaired phagocytic function, aberrant antigen presentation and excessive costimulatory signals have been described. This leads to aberrant activation of T cells that express CD95 and therefore become



more susceptible to induced cell death resulting in overall impairment of cellular mediated responses [2].

VAD recipients have shown lower expression of pro-inflammatory cytokines such as interleukin (IL)-2, tumor necrosis factor-alpha, and higher expression of suppressive IL-10 and T regulatory cells during in vitro antigenic challenge, compared to non-VAD advanced heart failure patients [4]. Dysfunctional activation of B cells after VAD implantation has also been described. This may induce autoimmunity and production of autoantibodies [2]. Most studies of immune responses in VAD recipients have had important limitations including small samples size, cross-sectional design, suboptimal selection of control groups with unbalanced confounders, and lack of correlation with clinical outcomes. Therefore routine assessment of cellular or humoral immune responses or use of universal antimicrobial prophylaxis in recipients of VAD is not currently recommended [5].

Overall the authors of this case report are to be commended on their effort in reminding us of the negative effects of VAD implantation on host immune responses. However, although host immune defects described in the setting of VAD implantation may have contributed to pathogenesis, there is a myriad of factors that may have increased the risk of candidemia and CMV reactivation in the critically-ill patient presented here.

Examples of risk factors for candidemia in this patient include the presence of a central venous catheter, exposure to broad spectrum antibiotics, pancreatitis, prolonged stay in intensive care unit, recent abdominothoracic surgery, among others. In addition, the ocular findings described as likely CMV retinitis may have been related to endogenous fungal endophthalmitis in the setting of candidemia, rather than related to CMV disease. The presence of CMV viremia is not surprising in this critically-ill patient and may just represent CMV reactivation not necessarily related to his ocular disease. For example, a recent study showed that the rate of detectable CMV viremia in a cohort of critically ill septic patients was 24% [6]. Having said this, CMV retinitis is certainly possible, and just the presence of CMV viremia in critically-ill patients may be a marker of poor outcomes including increased 90-day mortality [6]. A pathogenic role of VAD/TAH implantation on CMV reactivation is plausible in this case, but the patient had several other factors related to his critical illness and complications that most likely contributed to impaired immune responses and increased risk of reactivation of herpes viruses such as CMV.

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