



Commentary

Tuberculous Pericarditis: A Complex Puzzle to Put Together



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Pericardial disorders constitute a relatively common cause of heart disease accounting for 0.1–0.2% of all hospital admissions (Kytö et al., 2014; Lange and Hillis, 2004). From a clinical point of view pericardial syndromes encompass acute pericarditis (including relapses in the setting of recurrent forms), chronic constrictive pericarditis and isolated chronic pericardial effusion (Imazio and Adler, 2015).

With specific respect to etiology, idiopathic and secondary forms are described, with the contribution of each form depending largely to the local epidemiology (Lazaros et al., 2009). Namely, in the Western world the great majority of acute pericarditis cases remain idiopathic (presumably viral), with secondary forms accounting for ~15–20% of the overall pericarditis cases (Imazio et al., 2010; Adler et al., 2015). On the contrary, in developing countries the most common etiology of acute pericarditis is tuberculous (TB) pericarditis. It represents 70–80% of cases in immunocompetent patients in certain regions such as sub-Saharan areas, rising to 90% in HIV-infected subjects (Imazio et al., 2010; Adler et al., 2015). The relevant percentage in the Western world is estimated at 4–5% (Imazio et al., 2010).

From all of the above, it is clear that in the diagnostic work-up in pericarditis cases, the local epidemiology should be strongly considered. However, in the specific context of TB, in recent years the high rates of immigration from regions with high prevalence towards Western Europe and North America, may alter local trends in acute pericarditis etiology, a circumstance that physicians should be aware of (Imazio et al., 2010).

TB pericarditis is a particular form of pericarditis for several reasons. First, regarding prognosis, it is associated with a high short-term mortality rates which approximates 16–40% in 6-month time period, a rate which only in malignant pericardial disease may be recorded (Mayosi et al., 2008; Lazaros and Stefanadis, 2013). Second, TB pericarditis is among the forms of pericarditis with the fastest evolution towards constrictive or effusive-constrictive forms. The rate of progression is 50% without treatment and it has been reduced to 17–40% upon the introduction of effective TB chemotherapy, including rifampicin-based treatment (Mayosi et al., 2008). Third, the most effective treatment of TB pericarditis is still a subject of controversy and intensive

research. Recently, two more interventions have been added to the standard therapeutic armamentarium of TB pericarditis, namely intrapericardial urokinase and corticosteroid therapy (Adler et al., 2015; Mayosi et al., 2008). The efficacy and safety of corticosteroid administration has been debated at length. This issue has been recently addressed in the IMPI trial, which included 1400 patients with either definite or possible pericarditis (Mayosi et al., 2008). The main findings of this trial were that although corticosteroids did not have a significant impact on the prespecified composite end point (including death, cardiac tamponade associated with hemodynamic compromise and chronic constrictive pericarditis development), prednisolone administration for six months resulted in a lower incidence of constrictive pericarditis and a need for hospitalization. Nevertheless, steroid administration resulted in a higher incidence of cancer mainly driven by an increase in HIV-associated cancer. Thus, corticosteroid administration should be reserved exclusively for immunocompetent patients.

Last but not the least, the diagnosis of TB pericarditis is a challenging issue. Current diagnostic criteria consider the diagnosis of TB pericarditis definite, in the presence of tubercle bacilli in biopsy specimens of pericardial tissue or in the pericardial fluid as detected by polymerase chain reaction or culture (Adler et al., 2015). Cases are considered possible in patients with unexplained pericarditis and either extrapericardial tuberculosis or elevated levels of adenosine deaminase, lysozyme and unstimulated interferon-gamma levels (any among them). A successful response to chemotherapy regimens in endemic areas constitutes an additional criterion. We emphasize that definite cases in the IMPI trial accounted for only 17% of the cases (Mayosi et al., 2008).

Although intense and high quality research focused on TB pericarditis has been accomplished in recent years, additional investigation is well-acknowledged. In particular, issues concerning diagnosis and treatment are required in the setting of both basic and clinical research. In this line, the paper published in this issue of the journal by Pasipanodya JG, is welcomed as a study that provides new and important insights at basic and clinical level (Pasipanodya et al., 2015). This investigation enrolled 70 patients with confirmed TB pericarditis included in the IMPI registry. The key messages of this study are summarized in three main findings.

The first finding is that even in the era of highly effective TB chemotherapy (namely the regimen used in the IMPI trial), the mortality of TB pericarditis is still high, with an overall mortality rate of 1.43 per

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100 person-months in a median follow-up of 11.97 months. The most plausible explanation for this finding derived from a highly adherent population, is the inadequate antibiotic concentrations in the pericardial fluid (especially rifampin and pyrazinamide), due to poor penetration (Shenje et al., 2015). Moreover, since severe immunosuppression was an independent predictor of death, deprivation of the inherent immune system defensive mechanisms offers an additional explanation.

The second finding and important novelty of this investigation, is that definite TB pericarditis may not constitute a paucibacillary disease as previously suggested. Thus, improvement on methodology to detect bacterial burden in the pericardial fluid is of paramount importance in order to improve diagnostic accuracy.

Finally, the third finding is that bacillary burden outranks well-established mortality predictors such as hypotension, constrictive pericarditis and effusive constrictive pericarditis. Accordingly, in an effort to reduce bacterial load, the administration of rapidly acting bactericidal drugs is particularly important for disease control.

In summary, TB pericarditis is a major cause of morbidity and mortality especially, but not exclusively, in developing countries. Additional research is urgently required to ensure an evidence-based approach of tackling the disease. In an effort to put all of these findings into perspective, of high priority in our treatment decisions should be the prompt reduction of the bacillary load, in order to prevent morbidity and mortality. Additional efforts should include preventive measures towards HIV infection spread. Administration of alternative chemotherapeutic regimens ensuring higher intrapericardial concentrations or modifications of the standard ones (concerning dosage and administration period), are prerequisites to put together the challenging puzzle of TB pericarditis.

Conflict of interest

The authors declare that they have no conflicts of interest.

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