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Special Articles

Cardiac Manifestations of Parasitic Infections Part 3: Pericardial and Miscellaneous Cardiopulmonary Manifestations

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Summary

This is part three of a three-part series discussing parasites of the heart. In this section, we present an overview on parasitic diseases involving predominantly the pericardium and other miscellaneous cardiopulmonary manifestations such as some pulmonary hypertension syndromes and endomyocardial fibrosis.

Key words: heart, parasites, Chagas disease, pericardium, myocardium

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Pericardial Disease Secondary to Parasitic Infections

Amoebiasis

Amoebiasis is caused by a protozoan *Entamoeba histolytica* transmitted by the fecal-oral route.[1,2] It has a worldwide distribution but is mainly found in developing countries. In the United States, amoebiasis is seen in immigrants and travelers returned from endemic countries.[2–5] The ability to invade tissues distinguishes *Entamoeba histolytica* from the morphologically identical *Entamoeba dispar*.[4]

Extraintestinal amoebic disease is mainly localized in the liver.[2,3] Involvement of the pericardium is very rare but is considered a serious complication of amoebiasis.[2,3] The suppurative feature of amoebic pericarditis may cause it to be confused with tuberculous pericarditis.[2,3] Amoebic pericarditis can result from rupture of an amoebic liver abscess, and rarely from the lungs or pleura, into the pericardium causing acute tamponade physiology, chest pain or heart failure.[1–3] Amoebic pericarditis has been more frequently described among pediatric populations in which the association of concomitant intestinal amoebiasis maybe as high as 20%.[1,2] The diagnosis is usually established by serology. However, a distinguishing factor between tuberculous and amoebic pericarditis, is that there is a predominance of neutrophils in patients with amoebiasis.[2,3]

Treatment of pericardial amoebiasis requires a combination of surgical drainage and metronidazole.[1,3]

Cysticercosis

Ingestion of the eggs of *Taenia solium* may produce cerebral cysticercosis as the most serious complication. The condition can also present as ocular, spinal, cutaneous, muscular or cardiac lesions.[6,7]

Cardiac involvement in cysticercosis is extremely rare, but autopsy studies have shown prevalence of 20–25%

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in patients with concomitant documented neurocysticercosis.[6–8] Cardiac cysticercosis is often asymptomatic and discovered during cardiac surgery or at autopsy. Cysticerci are usually multiple and randomly distributed in cardiac tissues including the subpericardium, subendocardium, and myocardium.[7,8] The inflammatory response can be variable; granuloma formation can be present as well as fibrosis, leading to arrhythmias and conduction abnormalities.[6–8]

The role of albendazole and praziquantel or surgery in cardiac cysticercosis is still unclear.[6–8]

Echinococcosis

Human infection with the metacestode form of any one of the four species of *Echinococcus* (*E. granulosus, E. multilocularis, E. vowels,* or *E. oligarthrus*) may result in echinococcal disease.[9–11] *Echinococcus granulosus* causes cystic echinococcosis, the form most frequently encountered. Humans become inadvertent intermediate hosts when they ingest eggs from the feces of infected dogs or other canids. Hydatid cysts develop over months to years. Most of them will remain asymptomatic but some of them become large enough to cause symptoms.[10,11] Cysts are mainly located in the liver and the lung and only 10% can occur in the rest of the body.[9]

Cardiac hydatid cysts have been described in 0.5–3% of echinococcosis cases and are usually univesicluar.[12–20] Clinical presentations of cardiac echinococcosis include arrhythmias, myocardial infarction, cardiac tamponade, pulmonary hypertension and sudden cardiac death.[13–20] *E. multilocularis* has been reported to infect the pericardial cavity without disclosable liver involvement.[16–18] However, most cases of pericardial echinococcosis may be due to spread from an initial location at the liver dome.[14,15,17,18] The diagnosis relies on positive serologic testing and radiographic findings.[9–11]

The drug of choice for the treatment of echinococcosis is albendazole and or praziquantel.[21,22] Surgery, when feasible, is the most common form of treatment for echinococcosis.[21,23]

Miscellaneous Cardiopulmonary Manifestations Associated to Parasitic Diseases

Schistosomiasis

Involvement of the myocardium or pericardium by *Schistosoma* species is considered a rare event and is usually is due to accumulation of *Schistosoma* eggs inducing a granulomatous response, which may lead to myocarditis or pericarditis.[24–26] However, chronic schistosomiasis may lead to severe liver fibrosis secondary to hepatosplenic schistosomiasis.[26,27] This process involving portal hypertension may be associated with a hepatopulmonary syndrome manifested as dyspnea on exertion, right ventricular hypertrophy and ultimately *cor pulmonale*.[24–27] In addition, endothelial damage in the pulmonary circulation results from shunting of *Schistosoma* eggs through portosystemic shunts. The ability of *Schistosoma mansoni* to survive during its residence in the pulmonary circulation is due to molecular masking by coating with the ABO blood group glycolipids and MHC molecules derived from the human host.[24–26] *Schistosoma* induced pulmonary hypertension carries a grave prognosis since it usually denotes an advanced stage of hepatosplenic schistosomiasis.[24,27] In addition, thrombosis *in situ*, particularly, of the right pulmonary artery may occur, as well as cardiac arrhythmias and sudden cardiac death syndromes.[26,27]

Treatment of schistosomiasis (all species) is with praziquantel or alternatively oxamniquine for *S. mansoni*.[24,25]

Zoonotic Filariasis

Dirofilaria spp. are the cause of the pathology associated with "heartworms" in dogs.[28,29] *Dirofilaria immitis*, a common parasite of dogs and other canids prevalent in many areas of the world can occasionally affect humans. In the dog, the parasite undergoes its early development in the subcutaneous tissues for about 3 months before migrating to the right side of the heart.[29–31] Once injected by a mosquito vector the adult worms live in the right chambers of heart where they can induce myocarditis.[28,29] Although adult *D. immitis* worms have been found on several occasions in the heart and major vessels of humans at necropsy, the usual finding is for immature worms to be located in partially or completely occluded by small pulmonary arteries, where the obstruction has produced a pulmonary infarct and eventually a well-circumscribed coin lesion containing the parasite.[28] These lesions are usually identified in asymptomatic individuals undergoing routine chest radiographs. Other filariae species such as the lymphatic-dwelling human filariae (*Wuchereria spp., Brugia spp.)* may be also identified as pulmonary nodules similar to those where *Dirofilaria immitis* may cause.[28–31] The occurrence of severe, and occasional lethal, myocardial involvement that often occurs in dogs and other canids has not been described in humans.[29,30]

Tropical Pulmonary Eosinophilia

Tropical pulmonary eosinophilia is caused by a hypersensitivity response to microfilariae of the lymphatic-dwelling filarias *Wuchereria bancrofti* and *Brugia malayi*.[32–35] This process, manifested as chronic pulmonary infiltrates with eosinophilia, may result in permanent deficits in pulmonary function.[34,35] Eosinophils located in the lung as a response to the presence of filaria in the pulmonary circulation may degranulate and lead to the production of toxic oxygen radicals that contribute to a chronic pulmonary inflammatory process.[33,35,36] These

restrictive pulmonary function deficits may result in pulmonary hypertension that subsequently may lead to *cor pulmonale*.[33–36]

Tropical Endomyocardial Fibrosis

Helminth induced hypereosinophilia has been associated with tropical endomyocardial fibrosis. The clinical presentations of tropical endomyocardial fibrosis are similar to those of the idiopathic hypereosinophilic syndrome when it involves the heart.[37–39] The proposed immunopathogenesis suggests that when eosinophilia is persistent, blood eosinophils many undergo characteristic changes that have been associated with cellular activation and eosinophil-induced tissue damage.[38,39] This results in endomyocardial fibrosis that may be manifested clinically as restrictive cardiomyopathy.[39] This process leads to endomyocardial fibrosis, mural thrombus formation, arrhythmias, and pericarditis with effusion in some cases. Filariae and schistosomiasis are the most frequent nematodes inducing chronic eosinophilia with consequent endomyocardial fibrosis.[37,39]

Summary of the Three-part Series

Parasitic infections previously seen only in resource-constrained settings can be currently diagnosed anywhere in the globe due to travel, immunosuppression, HIV/AIDS; organ transplantation and blood transfusion. Some parasites may directly or indirectly affect various anatomical structures of the heart manifested as myocarditis, pericarditis, or pulmonary hypertension. Chronic persistence of some parasites in the heart constitutes an important immunopathogenic mechanism of cardiac injury.

The overall magnitude of the biomedical burden of parasitic infections is the reason behind the increased interest in further characterizing their molecular and clinical features. Therefore, parasitic infections should be included in the differential diagnosis of myocardial and pericardial disease anywhere in the globe.

Specific chemotherapy for many of the parasitic diseases discussed in this review are far from satisfactory since most of the currently available drugs carry significant toxicity, have limited clinical efficacy. Few drugs for the treatment of most of these parasitic diseases are currently in development. Furthermore, some pharmaceutical companies have withdrawn existing antiparasitic drugs from the market due to insufficient financial return.[40] The lack of effective vaccines, effective chemoprophylaxis, or successful pharmacologic therapies to control many of the parasitic diseases of the heart, in particular Chagas' disease, makes it one of the most important public health challenges of our time.

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