Tc-99m Pyrophosphate Myocardial Scanning in Chagas' Disease

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Chagas' disease is a serious protozoan infection affecting up to 20% of populations in some endemic areas. Myocarditis and cardiomyopathy occur in 50% of patients who go on to develop chronic Chagas' disease. We have studied a patient with no overt cardiac symptoms who revealed intense myocardial uptake of Tc-99m pyrophosphate. The significance of this finding in relation to early detection and progress of therapy is explored.

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Chagas' disease (South American trypanosomiasis) is an infection caused by *Trypanosoma cruzi*. The disease is transmitted by reduviid bugs, primarily those of the genera *Triatoma*, *Panstrongylus*, and *Rhodnius*, and occurs in a large area from Mexico to Argentina, the main foci being in Argentina, Brazil, Chile, Uruguay, and Venezuela. In Brazil several states are considered endemic regions. It is estimated that 20% of people living in these areas are infected, totalling nearly 4,000,000 people. In the United States, animal infestations have been detected in wild rats, opossums, and mice, but only a handful of clinically apparent indigenous human cases have been reported from Texas.

The bugs hide in the cracks and thatch of poorly constructed rural dwellings. They attack people at night, usually biting the face at the mucocutaneous junction (hence the common name "kissing" or "assassin" bug). Human infection results from contamination of the wound by the bug's feces, which contain the flagellated trypanosomes.

The disease is manifested by both acute and chronic forms. The acute form is initiated by the appearance of trypanosomes in the general circulation. This occurs after an incubation period of 2 wk, during which the organisms multiply within the *chagoma* at the site of the bite. This stage, which may range in intensity from subclinical to prostration, is characterized by recurrent fever, generalized lymphadenopathy, hepatosplenomegaly, urticarial rash, and acute myocarditis. The pathogenesis of these symptoms appears to be an autoimmune inflammatory reaction involving mesenchymal tissues.

The late manifestations are neuropathy caused by destruction of ganglionic nerve cells, and diffuse myocarditis with associated cardiomegaly, arrhythmias, and heart failure.

The use of radionuclide scanning techniques to study myocardial disease was introduced largely by Bonte et al. in 1974, using Tc-99m pyrophosphate for the diagnosis of myocardial infarction (*1*,*2*). Experience since then has shown that myocardial concentration of pyrophosphate is found in several conditions (Table 1) (*3*). We have recently studied a patient with Chagas' disease with intense myocardial uptake of pyrophosphate. To our knowledge no previous cases have been reported.

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CASE REPORT

A 48-year-old man from the state of Minas Gerais in central Brazil was referred for radionuclide bone scanning because of spinal pain with normal bone radiographs. The total-body bone scan was performed using 20 mCi of Tc-99m stannous pyrophosphate and a scintillation camera. No bony abnormalities were detected, but the heart showed 4+ (greater than rib intensity) myocardial concentration (Fig. 1). The patient had no symptoms of cardiac disease and the ECG was normal. Because of the patient's origin, a serum complement-fixation test was performed and was found positive for Chagas' disease.

DISCUSSION

The mechanism by which Tc-99m pyrophosphate, a bone-seeking tracer, concentrates within damaged myocardium is not

TABLE 1. CONDITIONS ASSOCIATED WITH MYOCARDIAL UPTAKE OF Tc-99m PYROPHOSPHATE

1. Angina pectoris
2. Cardiomyopathy
3. DC cardioversion
4. Malignant effusions
5. Myocardial infarction
6. Myocardial irradiation
7. Pericarditis
8. Trauma
9. Ventricular aneurysm

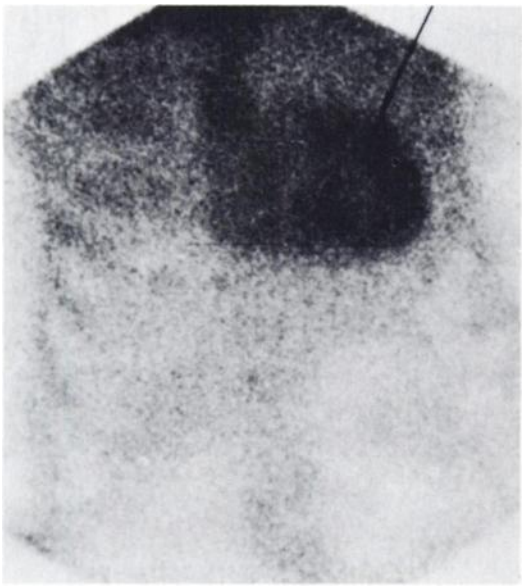

FIG. 1. Anterior scintiphoto of thorax 2 hr after administration of 20 mCi Tc-99m stannous pyrophosphate. Arrow indicates diffuse, intense myocardial uptake.

well understood. Because radiolabeled phosphates are known to concentrate in areas of high calcium turnover, calcium binding has been postulated as the mechanism. Electron micrography has shown that in irreversibly injured muscle cells calcium deposits within mitochondria in the form of apatite-like spicules or as fine granular particles (*4–6*). Direct binding of the phosphate moiety to the apatite structures may occur.

Wrogamann and Pena have postulated a condition of mitochondrial calcium overloading as a pathologic feature of all muscle-cell necrosis (*7*). Up to 50 times normal concentration of calcium may be found in individual mitochondria. They suggest that such mitochondrial overload leads to loss of cellular energy, hypercontraction of muscle fibers, and cell necrosis. Buja et al. found elevated calcium in experimental myocardial infarction and related the uptake of pyrophosphate to this mechanism (*8*).

We have found no histochemical studies concerning myocardial calcium concentrations in Chagas' disease, but the histopathologic changes have been well described (*9*). Involved muscle cells are diffusely distributed throughout the heart. Intracellularly there is mitochondriosis, vacuolization, and increase of intramitochondrial granules; lysis of myofibrils; rupture of the sarcoplasmic reticulum; and protrusion and thickening of the sarcolemma. In the interstitium, large numbers of lymphocytes, plasmacytes, and histiocytes surround the infected cells. The degree of fibrosis is related to the severity and duration of the disease.

The myocarditis of Chagas' disease is caused by direct myocardial invasion of the trypanosomes, leishmanial multiplication, and intracellular pseudocyst. When the pseudocysts rupture, releasing the newly formed leishmanial and trypanosomal forms, an intense inflammatory response results (*10,11*). In the untreated patient, the chronic nature of the myocarditis is ensured by repeated release and invasion of the trypanosomes. The importance of detecting myocardial involvement is underscored by its high incidence in chronic Chagas' disease (as high as 50% of infected individuals, and as many as 10% of rural populations) and the serious disability and mortality that result if the disease is not checked (*10,11*). Considerably more patients will need to be studied to determine the incidence and variability of scan findings in Chagas' disease. Those in the patient presented here, who had no overt cardiac symptoms, suggest that positive scan findings may precede clinical manifestations.

The detection of chronic Chagas' disease is accomplished with substantial reliability by complement fixation (Machado-Guerreiro test) and hemagglutination tests (*12*). The diagnosis of functional cardiac abnormalities can be made by a variety of radiographic and echographic techniques (*13*). These tests, however, do not reveal specific tissue injury, nor do they indicate disease activity. Pyrophosphate scanning, on the other hand, is known to outline specific regions of myocardial necrosis (*14*), and scan intensity may relate to the evolution of tissue injury and recovery (*3*). It is possible, then, that in Chagas' disease myocardial scanning may be useful in identifying not only the early presence of Chagas' myocarditis, but also its progress with therapy.

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