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Unusual manifestation of cutaneous toxoplasmosis in a HIV-positive patient

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Abstract. We report a case of unusual cutaneous toxoplasmosis manifestation in a HIV-positive patient. He presented with hard and painful nodular lesions on the arms, hands and chest. Serology tests for anti-*Toxoplasma* antibody were negative. However, histopathologic examination of the lesion revealed foci of macrophages containing crescent-shaped organisms resembling the zoites of the protozoan parasite *Toxoplasma gondii*. Ultrastructure examination under electron microscopy and PCR confirmed the organism as *T. gondii*.

INTRODUCTION

Toxoplasmosis is a widespread infection which is caused by the obligate intracellular parasite *Toxoplasma gondii*. It has been estimated that one-third of the human population is infected with this parasite. The infection is generally asymptomatic in healthy or immunocompetent individuals. Symptoms, if appear, resemble those of infectious mononucleosis such as lymphadenopathy, fever, fatigue, muscle pain, sore throat and headache. In pregnant women, toxoplasmosis may pose problem because congenital infection may lead to neonatal malformations, neurological damage, blindness or fetal death. In immunosuppressed individuals, the disease may provoke severe symptoms such as brain abscesses, encephalitis, pneumonia and disseminated infection (Montoya & Liesenfeld, 2004).

Cutaneous manifestation of toxoplasmosis, however, is rarely encountered. In 1941, Pinkerton and Henderson described the first documented cases of acute toxoplasmosis with prominent cutaneous manifestations (Pinkerton & Henderson, 1941). Reviews reveal that the incidence of cutaneous toxoplasmosis is <10% (McCabe *et al*., 1987). There is great variability in the gross appearance of the lesions in cutaneous toxoplasmosis. Rash, maculopapular, papular-nodular, purpuric, papulopustular, lichenoid, and erythema-multiforme-like lesions have been described (Mawhorter *et al*., 1992). In this paper, we report a patient who developed a form of cutaneous lesion which is different from those previously reported.

Case report

The patient was a 49-year-old HIV-positive Chinese male who was diagnosed as having HIV infection many years ago. Despite treatment with highly active antiretroviral therapy with good virological response, as evidenced by repeatedly undetectable HIV RNA levels, he failed to respond immunologically with CD4 cell level which was persistently below 100 cells/mm^3. He presented with multiple hard

and painful nodular lesions on both arms, hands, and a few on the chest. The nodules were non tender, and variable in size (0.5 to 3 cm in diameter, Figure 1A). Other parts of the body were not affected, and no skin ulcers were observed. Serological tests for anti-*Toxoplasma* IgG and IgM were negative. Histopathology examination of the lesions showed numerous foci of macrophages with intra– and extracellular organisms in the underlying dermis (Figure 1B). These organisms were crescent-shaped, resembling the zoites of *T. gondii*. The skin biopsy also showed granulomatous inflammation. The histology slide was examined under electron microscopy, and *T. gondii* was identified on the basis of ultrastructural features of the zoites (Figure 1C). The organism was confirmed when the skin biopsy was subjected to a nested polymerase chain reaction (PCR) which successfully amplified a 96-base pair region (Figure 2) of the *T. gondii* B1 gene (Burg *et al.*, 1989). The origin of the *T. gondii* infection was uncertain. It is likely that the patient might have a previous latent infection that was reactivated resulting from the HIV infection. Another possibility is that the patient acquired the *T. gondii* infection, after the HIV infection. Humoral immunity of the patient might have been affected as evidenced by the absence of anti-*Toxoplasma* antibody response. Despite treatment with standard anti-*Toxoplasma* drugs which included sulphadiazine and pyrimethamine, the lesions failed to resolve. The patient continues to develop new lesions whilst on therapy.

DISCUSSION

Prior to our report, there was one documented description of cutaneous toxoplasmosis in an acquired immuno-

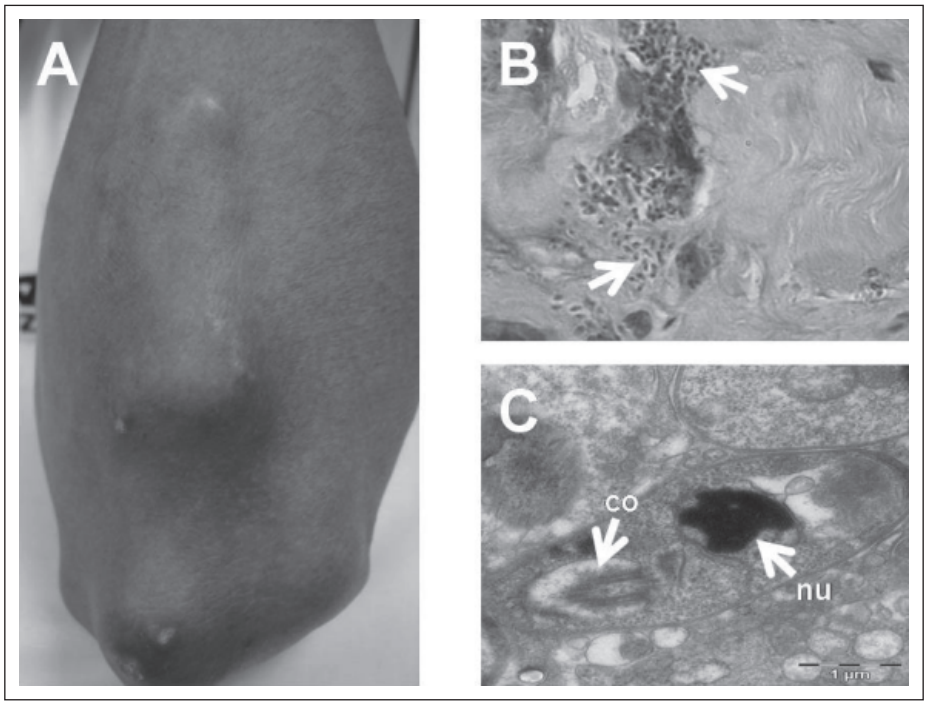

Figure 1. A, Large nodules (1-3 cm) on lower left arm of the patient. B, Skin section of dermis showing foci (*arrows*) of macrophages with intra- and extracellular *Toxoplasma gondii* zoites, x1000. C, Electron micrograph showing typical ultrastructures (*co: conoid; nu: nucleus*) of a zoite, x7000

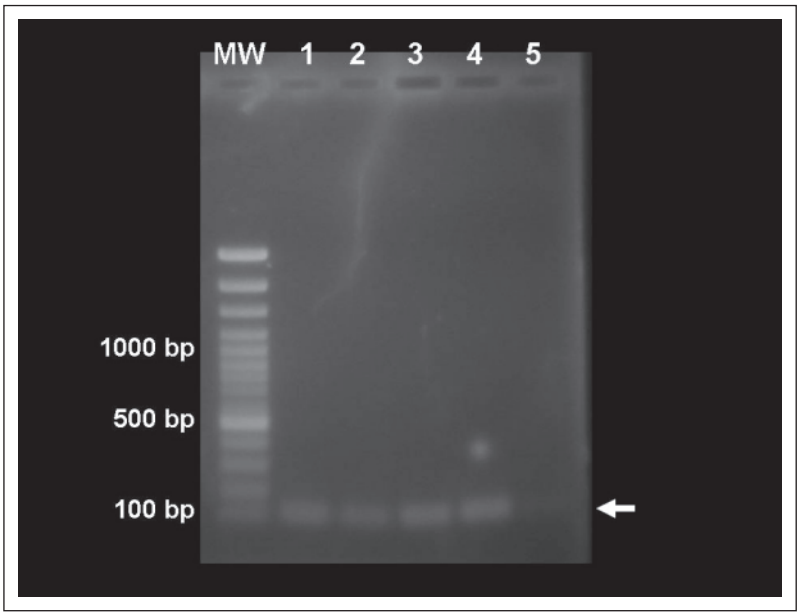

Figure 2. Nested PCR using primers specific for *Toxoplasma gondii* B1 gene. Lane 1 is the positive control using extracted *T. gondii* DNA as template. Lanes 2, 3 and 4 are PCR products from amplification of DNA extracted from the skin lesions, showing a positive band of 96 bp (arrow). Lane 5 is the negative control. Lane MW is the DNA molecular weight standards

deficiency syndrome (AIDS) patient (Hirschmann & Chu, 1988). Unlike the lesions seen in our patient, the AIDS patient developed disseminated reddish and slightly indurated papules. However, on histologic examination, *T. gondii* zoites were not demonstrated. After specific anti-*Toxoplasma* therapy with pyrimethamine and sulfadiazine, the cutaneous eruption disappeared. Recently, cutaneous toxoplasmosis was reported in two immunosuppressed patients who underwent bone marrow transplantation. Neither patient showed nodular type lesions. In the first case, the patient developed nonvesicular, pleomorphic papular skin lesions on the extremities, torso, abdominal wall, and face, and these lesions were discrete, with no accompanying induration. Skin biopsy showed multiple *T. gondii* zoites in the epidermis (Lee *et al.*, 2005). The second patient showed small scattered papules (0.5 to 0.8 cm in diameter) with mild hyperemia on the legs. Small 'cysts' containing tiny *T. gondii* zoites were seen singly in the epidermis, skin appendages including follicular epithelium and sweat glands and ducts. In addition, free parasites zoites were seen lying in the dermis (Amir *et al.*, 2008). Many years before, a case of cutaneous toxoplasmosis was reported in a male patient with chronic myelogenous leukemia who received bone marrow allograft but continued to have pancytopenia. Multiple 1-cm diffuse palpable purpuric nodules developed on the scalp, right forearm, back and groin areas three weeks after the transplant. Electron microscopy of the biopsy revealed *T. gondii* zoites within the cytoplasm of keratinocytes, Schwann's cell and macrophages in all levels of the epidermis (Leyva & Santa Cruz, 1986).

In immunocompetent hosts, cutaneous toxoplasmosis manifestations that have been seen include nodular prurigo, ulcerative purpuric telangiectatic dermatosis, erythema multiforme-like eruptions, lichenoid lesions, fleeting erythematous macules, heliotrope

periorbital edema and scaly erythematous plaques (Hirschmann & Chu, 1988).

The pathophysiological basis underlying these cutaneous manifestations of toxoplasmosis is still unclear. It is believed that the spectrum of manifestations is due to heterogeneous systemic immune responses rather than a direct response to the parasite. This is supported by the fact that only 50% of reported cases have the organism demonstrated in the skin (Binazzi, 1986). Furthermore, there are a variety of immune reactions in the lesions, regardless of whether the parasite is found at the site (Justus, 1972).

In conclusion, the manifestations of cutaneous toxoplasmosis vary greatly and are nonspecific in characteristic. Nonetheless, it is important to consider this disease in the differential diagnosis of patients with varied dermatologic presentations. In this context, relying solely on routine *Toxoplasma* serological tests may not be sufficient. Diagnosis should be augmented with more specific methods such as skin biopsy, immunohistochemistry, electron microscopy, and PCR.

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