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Case report

Polyomyositis and myocarditis associated with acquired toxoplasmosis in an immunocompetent girl

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Abstract

Background: Acquired toxoplasmosis more frequently goes unrecognized. Immunocompetent adults and adolescents with primary infection are generally asymptomatic, but symptoms may include malaise, fever, and lymphadenopathy. By contrast, immunocompromised patients may experience severe manifestations including encephalitis and multisystem organ failure.

Case presentation: We report a case of polymyositis and myocarditis in a 13-year old immunocompetent girl with toxoplasmosis. The patient presented with proximal muscle weakness, dysphagia, palms and soles rash and elevated serum levels of muscle enzymes, with liver and myocardial involvement. The diagnosis of toxoplasmosis was confirmed by serology. The patient was treated with prednisolone and had an excellent outcome. During a follow-up period of four years no relapses occurred and antibody levels to the *T. gondii* significantly decreased.

Conclusions: Although several previous cases of toxoplasmosis occuring in association with polymyositis have been described in the literature such a wide spectrum of acute toxoplasmosis is rather unusual in immunocompetent adolescents. The relationship between *T. gondii* and polymyositis remains obscure. Appropriate investigation should be performed in every case of polymyositis not only for the appropriate treatment but also for further elucidation of this relationship.

Background

Toxoplasma gondii is the most common cause of protozoan infections in humans. Cats are the definitive hosts which produce oocysts and sporozoites. Ingestion by a nonfeline leads to the formation of tachyzoites and further dissemination with the formation of cysts in skeletal muscle, heart muscle and central nervous system (CNS). The acquired disease can be transmitted in humans by ingestion of tissue cysts in inadequately cooked meat or by ingestion of uncooked food that have come in contact with contaminated meat. The infection is usually asymptomatic, however clinical manifestations do occur, ranging from mild, nonspecific febrile illness and lymphadenopathy to systemic disease in immunocompromised patients [1–3]. The severe form of the disease may present with muscle, heart, liver and central nervous system involvement. Significant organ involvement in immunocompetent individuals is uncommon but

some individuals have suffered significant morbidity [1,2].

Acquired toxoplasmosis has been associated with polyomyositis and myocarditis but it remains obscure whether this is a causal of coincidental relationship [4]. We report a case of myocarditis and polyomyositis associated with acquired toxoplasmosis in an otherwise well adolescent.

Case Presentation

A previous healthy 13-year-old Caucasian girl was admitted with a 3-week history of vomiting, daily fever up to 38,9°C, malaise, anorexia and a 3-kilogram weight loss. The history was unremarkable for tick exposure or for recent travel. On physical examination axillary temperature was 38,2°C, the systolic blood pressure 110 mmHg, and the pulse rate 120 beats per min. Her liver was tender and palpable 3 cm subcostally. A mild proximal muscle weakness was noted.

Laboratory investigation revealed hemoglobin; 10.6 g/dl, total leukocyte count; 4,600/mm^3, neutrophils; 2,300/mm^3, lymphocytes; 1610/mm^3, monocytes; 460/mm^3, band forms; 230/mm^3, and adequate platelets. The erythrocyte sedimentation rate was 45 mm/h and the C reactive protein 0.5 mg/dl. Total serum protein, albumin and globulin concentrations were slightly decreased. Elevated serum values were found for alanine aminotransferase (407 IU/L), aspartate aminotransferase (639 IU/L), gamma-glutamyltranspeptidase (120 IU/L), lactate dehydrogenase (478 IU/L), creatine kinase (407 IU/L) and aldolase (16,9 IU/L). Urinalysis and clotting studies were normal. No pathogens were detected in urine, stool and blood cultures. A Mantoux tuberculin test was negative. Abdominal ultrasonography revealed a round, not cystic liver lesion of a diameter of 2 cm. This finding was confirmed by abdominal computed tomography.

With a presumptive diagnosis of a bacterial liver abscess, intravenous ampicillin, amikacin and metronidazole were initiated. In the following days the patient dramatically deteriorated, with dysphagia, inability to walk and raise the arms, further weight loss, fine tremor of hands and a maculopapular rash on palms and soles. Visual symptoms suggestive of chorioretinitis were not found. At that stage creatine kinase, lactate dehydrogenase and aldolase levels reached to peak values of 607 IU/L, 935 IU/L and 43 IU/L respectively. Alpha-fetoprotein, urine vanilmandelic acid and liver Tc-99 scan were normal. Serology for *Salmonella typhi, Brucella melitensis, Mycoplasma pneumonia, Echinococcus granulosus, Trichinella spiralis,* Coxsackie, herpes and hepatitis viruses was negative. Toxoplasmosis was serologically confirmed by a serial two tube tenfold increase of antibody titer by haemagglutination test (titer of 1:150 for IgM and 1:1024 for IgG and four weeks later titer of 1:150 for IgM and IgG: 1:109,350). Electromyogram was compatible with subacute inflammatory myopathy with brief polyphasic motor units of decreased amplitude as well as a few fibrillations during the voluntary contraction of the muscle. Echocardiogram showed dilatation of the left ventricle with poor contractility, suggestive of myocardial involvement. Antinuclear, anti-DNA, anti-Jo-1, anti-RNP and ANCA antibodies were negative. Serum IgG was 1,771 mg/dl, IgA 229 mg/dl and IgM 195 mg/dl. Complement C3 and C4 serum levels were normal.

Given the clinical and laboratory evidence of ongoing inflammation, and the heart involvement, intravenous prednisolone at a dose of 1,2 mg/kg daily, captopril at a dose of 25 mg twice daily, digoxin at a dose of 0.25 mg once daily were administered. Naproxen was added at a dosage of 750 mg daily a week later. The response to steroids was favorable. Fever subsided within two weeks and clinical and laboratory findings gradually improved. Steroid dosage was tapered to 1 mg/kg at discharge and treatment was continued with digoxin and captopril. Digoxin and captopril were continued until the normalization of echocardiogram two months later. Steroids and naproxen were weaned over a period of five and twelve months respectively. The rash on palms and soles subsided within three months and the liver lesion was no longer visible eighteen months after admission. *T. gondii* IgM serology converted to negative twelve months, whereas IgG antibodies remained at high levels (> 1:100,000) for eighteen months with a gradual decrease thereafter. A four-year follow up period was free of any symptoms or findings.

Discussion

Inflammatory muscle disease in children may be considered either acute or chronic. Most of acute inflammatory myopathies are usually associated with viral or bacterial infectious agents [4–6]. Chronic idiopathic myopathies comprise a diverse group of syndromes that have a common chronic muscle inflammation of usually unknown pathophysiology [5]. Skeletal muscle can be the site of inflammatory diseases that lead to muscle weakness, pain and increased myogenic enzymes [4,7].

Many bacterial, viral and parasitic pathogens can cause acute transient inflammatory myopathies, including *Staphylococci, Mycoplasmas,* Coxsackie group B and influentza viruses, trichinosis, toxoplasmosis, and cysticercosis [4–6,8]. Recent studies suggest that acute infectious polymyositis has a different course than the idiopathic one [4,5].

Table 1: Criteria for diagnosis of polymyositis in childhood (3 out of 4 required) [9].

	POLYMYOSITIS
Symmetrical proximal muscle weakness	+
Elevated muscle derived enzymes	+
Muscle histopathology	+
Electromyographic changes: inflammatory myopathy	+

The major symptom of chronic inflammatory myopathy in children is persistent and progressive proximal muscle weakness. Diagnostic criteria proposed by Bohan and Peter in 1975 are still used to establish the diagnosis of polymyositis in childhood (Table 1) [5,9]. The described case fulfilled two out of four polymyositis diagnostic criteria: Symmetrical proximal muscle weakness and elevated muscle derived enzymes. The electromyographic pattern was not typical for acute inflammation, however it was clearly abnormal and suggestive of subacute inflammatory process, hence it was considered as the third criterion. Muscle histopathology was not performed in the present case because of the patient's severe deterioration and the administration of prednisolone which could interfere with the results of the biopsy.

Toxoplasmosis may affect muscles, during either primary infection or reactivation and even cause multisystem disease, mainly in immunocompromised individuals [4,10]. Two forms of polymyositis following toxoplasmosis are known; an acute, responsive to antiprotozoal therapy and a chronic manifested by altered immune response and requiring treatment with steroids [10].

In our patient acute *T. gondii* infection was confirmed by both the presence of IgM and the rising titers of IgG antibodies [4]. Hence, it is likely that *T. gondii* directly caused the acute myositis and myocarditis. PCR for *T. gondii* was not available at that time. The liver lesion might be attributed to toxoplasmosis as well, since hepatic necrosis is a well-established complication of this infection. The impressive improvement following treatment with prednisolone was suggestive of immunological disturbances contributing to the development of inflammatory myositis. The presence of parasite in myofibers would be not enough to induce an inflammatory myositis with muscle cell necrosis. A potential mechanism for polymyositis might include an altered immune response leading to the production of autoantibodies and to muscular inflammation [4,7,10]. After the initial favorable response to steroids antiprotozoal agents were not considered as adjunct therapy.

We propose that polymyositis due to toxoplasmosis has two phases: an early one, usually self-limited and responsive to antiprotozoal therapy and a late one manifested by altered immune response requiring steroids. Clinical manifestations of late toxoplasmosis myositis may mimic those of idiopathic polymyositis, however the clinical course in immunocompetent patients is usually benign because of the generation of antibodies which will inhibit the growth of organism [10].

The complete recovery of the patient and the absence of any relapses suggest a recent toxoplasmic rather than a chronic idiopathic polymyosistis. Although such a wide spectrum of acute toxoplasmosis is not common in immunocompetent patients, several previous cases of toxoplasmosis in association with polymyositis have been described in the literature [10–13]. The presence of both polymyositis and myocarditis in the same patient with toxoplasmosis is uncommon and has been reported in autopsy and in a few cases in adults [14]. In patients with myocarditis, asymptomatic conduction abnormalities predominate with occasional complete right bundle block. These abnormalities often resolve with abatement of the disease activity [5]. Although the patient's *Toxoplasma* serology was consistent with acute infection, endomyocardial and skeletal biopsies might establish the definitive diagnosis of toxoplasmic myocarditis or myositis respectively [4,7,12,14,15].

In conclusion every case with polyomyositis and myocarditis should be investigated for toxoplasmosis. Although appropriate therapy may provide some clinical improvement at the early stages of acute toxoplasmosis, steroids seems to remain the cornerstone of management, especially when vital organ involvement is implicated [8,10,11].

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