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Casi clinici

Case reports

Acute pericarditis and myocarditis by *Toxoplasma gondii* in an immunocompetent young man: a case report

Un caso di pericardite e miocardite da Toxoplasma gondii in un giovane immunocompetente

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INTRODUCTION

Toxoplasmosis is the most frequent protozoan infection among human beings. Primary acquired infections in immunocompetent hosts are usually asymptomatic or may cause only slight, self-resolving and not pathognomonic symptoms, as fever, cervical lymphadenopathy and tiredness.
Severe diseases due to *Toxoplasma gondii* are quite infrequent because the parassitemia is short-lasting and the immune response forces the protozoa to hide in tissue cysts, and they survive as latent forms (bradizoites) inside muscles, heart and brain. On the contrary, immunocompromised hosts often experience a life-threatening involvement of one or more organs during primary infections or can suffer reactivation of pre-existing tissue cysts, due to deficiency of the immune system [1, 2].

CASE REPORT

A white 32-year-old man was admitted to the Emergency Room of Cardarelli Hospital, Naples, on July 24, 2006.
He presented with chest pain described as severe and intermittent, which worsened by deep breathing and lying down and radiated to left arm. The pain had risen up after three days moderate fever and arthralgia, which were treated with acetylsalicylic acid (ASA). He was complaining asthenia and bilateral neck limphadenopathy since 2 weeks. Anamnesis was negative for use of recreational drugs and use of other medications than ASA, assumption of alcohol or cigarette smoking, unprotected sex, trips abroad. No relevant diseases in his past history. He was married, had two kids and worked as a civil servant.
On clinical examination the patient appeared alert, feverish (37.3°C), with normal blood pressure, 95 rhythmic heartbeats per minute, harsh vesicular murmur, no painful abdominal points, no cyanosis, no hepato-splenomegaly, body mass index of 23.14 (optimal weight). Electrocardiogram showed unspecific abnormalities in ventricular repolarization but major seric cardiac enzymes were elevated: troponin I counted 3.75 ng/ml [reference values 0-0.06], creatine phosphokinase 338 IU/L [r.v. 15-180], lactate dehydrogenase 570 IU/L [r.v. 227-450], alanine aminotransferase 49 UI/L [r.v. up to 40]. C-reactive protein (CRP) was also elevated [22.30 mg/L, r.v. 0-5] and erythrocyte sedimentation rate (ESR) resulted normal [6 mm/h, r.v. up to10 mm/h].
Anti-inflammatory (ASA 500 mg three times a day per os) and antibiotic therapy (ceftizoxime 1 g e.v. twice a day) was promptly started. Echocardiogram displayed moderate pericardial effusion, hyperechoic pericardium slightly detached in the back side and hypokinetic apex with estimated ejection fraction of 50%; therefore an antiarrhythmic drug was added to the therapy (bisoprolol 12.5 mg/die). Chest X-ray was negative for broncho-pneumonic foci and

cardiac enlargement. Complete blood count showed absolute and relative monocytosis (1380 cells/µL, that is 20% of 6680/µL WBC). On day 2 the patient was therefore hospitalised in the division of Cardiology.
Bacteriological and virological investigations and urine analysis were performed the day after. Urine analysis was negative. Antibodies versus *Human immunodeficiency*, *Hepatitis B, Hepatitis C, Coxsackie viruses, Mycoplasma pneumoniae, Epstein-Barr virus, Legionella pneumophila, Treponema pallidum, Leishmania spp., Echinococcus spp*. were all negative as well as Mantoux test, Vidal-Wright and Weil-Felix reactions. Acquired immunity versus *Varicella-Zoster virus, Cytomegalovirus, Measles and Rubella viruses* was established. However, ELISA analysis for anti-*Toxoplasma gondii* IgM showed an index of 1.64 [>1, positive] and for anti-*Chlamydia pneumoniae* IgA indicated a ratio of 1.8 [>1.1, positive]. To elaborate on these results, a second examination was performed seven days later (day 10). It was not observed any variation in regard to anti-*Chlamydia pneumoniae* IgA. On the contrary, anti-*Toxoplasma* IgM resulted increased of about 2.5 times (index, 4.26), whereas anti-*Toxoplasma* IgG were still absent.
During hospitalisation, patient's clinical condition improved and seric values slowly normalized. The patient was discharged on day 12 because global cynesis recovered and pericardium effusion disappeared on echocardiographical examination.
Only residuals of inflammation were visible on posterior layers and anterior portion of mitral valve, but without any regurgitation. Electrocardiogram showed sinus rhythm, although unspecific anomalies of ST were persisting. Treatment based on indomethacin 50 mg/die for 5 days, carvedilol 12.50 mg/die for 15 days, spiramycin 9 MU/die for 30 days and magaldrate 2.4 g/die for 30 days was prescribed. It was also advised to consult a specialist in infectious diseases.
The patient contacted us at the "Department of Infectious Diseases" of the Second University of Naples 10 weeks after discharge (mid-October 2006). We visited him and investigated the proceedings concerning the recent hospitalisation. He was not in pain and resulted healthy on physical examination, blood tests were done and turned out normal. We requested specific tests for toxoplasmosis which showed: IgG 800 UI/mL [positive, >8], IgM 3.16 index [positive, >0.65], IgG avidity 0.165 index [low avidity, <0.2] (ELFA-VIDAS assays), IgA 160 AU/mL [positive, >40] (ELISA). Electrocardiogram, echocardiogram and examination of ocular fundus, chest X-ray and abdomen ultrasound were normal too. Since the patient looked to be in good condition, he did not receive drugs for toxoplasmosis. However, he was invited to come back to our outpatient's department after 1 and 6 months. On the first check-up (mid-November 2006) patient was healthy, IgM anti-*Toxoplasma* were still present but IgG levels decreased to 362 UI/mL.
The patient did not attend the second check-up and did not get again in touch with us.

DISCUSSION

A large variety of infections, systemic diseases, drugs, and toxins have been associated with the development of myocarditis. Among the infections, the most common worldwide is the Chagas' disease or American trypanosomiasis by the parasitic protozoan *Trypanosoma cruzi*, endemic in rural Central and South America; *Toxoplasma gondii* is the second relevant pathogen in protozoan myocarditis [3, 4].
In 2000, Sano J. et al. stated that only 22 cases of toxoplasma pericarditis had been reported worldwide, 15 of them in absence of immunosuppressant disorder. They found that fever, dyspnea and chest pain were the usual symptoms at the onset while seven patients had then developed cardiac tamponade requiring pericardiocentesis [5].
Some of the case-reports found in medical literature are dated but well-conducted and described works: clinical manifestations of myocarditis by *Toxoplasma gondii* varied and several arrhythmias, including atrial fibrillation, ventricular arrhythmias and heart block, leading to cardiac insufficiency or presenting as myocardial infarction were reported [6-14]. Most of anomalies were however asymptomatic, complete heart blocks were only occasional and sudden deaths were rare [15-17].
In spite of such low number of cases of myocarditis by *Toxoplasma gondii*, many authors agree that toxoplasmosis should be considered in patients with myocarditis, pericarditis and/or polymyositis of unclear etiology, due to the effectiveness of specific therapies [18-23]. Thus, several drugs have been shown to be active against *Toxoplasma gondii* in past and recent years, both in vitro and in vivo: cotrimoxazole,

dapsone, sulfadiazine, pyrimethamine, macrolides, clindamycine, minocycline, trovafloxacin, atovaquone, artesunate, dihydroartemisinin [24-29]. Spiramycin is also effective and it is recommended in suspected or confirmed acute toxoplasmosis in pregnant women during the first 18 weeks of gestation [30]. Effectiveness of antiprotozoan therapy in acute pericarditis and myocarditis, however, requires an early diagnosis.

Although the gold standard for diagnosis of toxoplasmosis is represented by the biopsy of myocardium, Sano J. et al. also described the polimerase chain reaction (PCR) as method to detect the presence of *Toxoplasma gondii* in pericardial effusions for ethiological diagnosis [5]. However, this is instead usually based on both positive serology for acute toxoplasmosis and absence of another obvious cause, and isolation of parasite by direct examination or animal inoculation is very rare [18].

Here we have reported a case of acute pericarditis and myocarditis in an immunocompetent young man. Although neither biopsy of myocardium nor PCR analysis was performed, data indicate that acquired primary infection by *Toxoplasma gondii* triggered all the symptoms and signs reported of acute pericarditis and myocarditis. This is based on the following observations:

1. no other obvious cause of disease was present;
2. aetiological diagnosis and symptoms (fever, arthralgia, limphadenopathy) suggested an acute infection and resemble those described for toxoplasma pericarditis;
3. fast-growing seric levels of anti-*Toxoplasma* IgM were detected;
4. seroconversion for anti-*Toxoplasma* IgG and IgG low affinity for the antigen were proved [6-10].

Acute acquired infections by *Toxoplasma gondii* in immunocompetent patients, usually, do not need specific treatment unless severe or persistent symptoms or evidence of damage to vital organs are present: in that case a treatment with pyrimethamine plus sulfadiazine and folinic acid should be initiated [31, 32].

In the case reported here, the aetiological diagnosis, supported by serological tests positive for toxoplasmosis, recommended an anti-protozoan therapy as treatment and spiramycin (9 MU/day for one month) was administered in addition to anti-inflammatory and antiarrhythmic drugs. Since the recovery of the patient was complete, no relapse was observed, seric levels of anti-*Toxoplasma* IgM progressively decreased in the 4 months following primary detection and no further organ was involved, drugs more effective in organ toxoplasmosis than spiramycin were considered not to be necessary.

However, due to the fact that the patient did not come back for a second check-up, we could not determine how long the positivity for anti-*Toxoplasma gondii* IgM persisted in his serum and whether sequel appeared (e.g. late ocular involvement [33]).

In conclusion, infection by *Toxoplasma gondii* should be taken into account in the aetiology of unexplained pericarditis or myocarditis, because an early diagnosis could enable to promptly start an antiprotozoan therapy, which would in turn aloud a complete resolution of the morbid event.

***Key words*:** toxoplasmosis, pericarditis, myocarditis, *Toxoplasma gondii.*

SUMMARY

Infection due to protozoan parasite *Toxoplasma gondii* is highly prevalent among humans throughout the world. Acquired primary infection is seldom severe in immunocompetent people while it can be life-threatening in immunodeficient ones. We report a case of acquired toxoplasmosis in an immunocompetent healty 32-year-old man, presenting as acute pericarditis and myocarditis. The patient complained of intense chest pain, asthenia, arthralgia, low-grade fever, neck lymphadenopathy. Increased seric cardiac enzymes, electrocardiografic anomalies of repolarization and the presence of pericardic effusion on echocardiogram needed anti-inflammatory and anti-arrhythmic drugs and a close monitoring. The aetiological diagnosis, supported by serological tests positive for toxoplasmosis, recommended an antibiotic therapy as additional treatment (spiramycin 9MU/day for one month). Full symptoms remission and normalization of serological values suggested, however, that no more effective anti-protozoan treatment was needed. Thus, the infection by *Toxoplasma gondii* should be taken into account in the aetiology of either acute pericarditis or myocarditis, because a specific treatment is available, which can improve on the prognosis of the disease.

RIASSUNTO

L'infezione umana causata dal protozoo Toxoplasma gondii ha alta prevalenza in tutto il mondo.
L'infezione primaria è raramente severa quando acquisita nell'ospite immunocompetente mentre può essere fatale in caso d'immunodeficienza.Viene qui descritto un caso di toxoplasmosi acquisita presentatosi come pericardite e miocardite acuta in un giovane di 32 anni, immunocompetente ed in precedenza sano. Il paziente lamentava intenso dolore toracico, astenia, febbre moderata, artralgie, ingrossamento dei linfonodi del collo. Gli enzimi cardiaci risultarono incrementati, l'elettrocardiogramma mostrava anomalie della fase di ripolarizzazione ventricolare e l'ecocardiogramma versamento pericardico: veniva pertanto iniziata terapia antinfiammatoria ed antiaritmica, con stretto monitoraggio clinico. La diagnosi eziologica, supportata dalla positività di tests sierologici per toxoplasmosi, suggeriva l'aggiunta in terapia di un antibiotico (spiramicina 9MU/die per un mese). La guarigione completa e la normalizzazione dei parametri sierologici facevano ritenere non necessario iniziare un ciclo di terapia antiprotozoaria più efficace. L'infezione da Toxoplasma gondii dovrebbe dunque essere considerata nel percorso diagnostico di ogni pericardite o miocardite acuta, poiché disponiamo di farmaci in grado di migliorare la prognosi dell'evento morboso.

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