

COMPLEX POLYPATHOLOGY INFECTIOUS, RHEUMATOLOGICAL, NEUROLOGICAL AND ORTHOPEDIC – REAL CHALLENGE FOR FUNCTIONAL REHABILITATION - CASE REPORT

Libu Cristiana^{1,2}, Iliescu Mădălina Gabriela^{1,2}, Bohe Zoe Maria^{1,3}, Arghir Oana Cristina^{1,4}, Bilous Dana-Maria⁵, Ionescu Ana-Maria¹, Obadă Bogdan¹, Albadi Irina^{1,3}, Oprea Doinita^{1,2}

¹ University "Ovidius" of Constanta, Faculty of Medicine

² Balneal and Rehabilitation Sanatorium of Techirghiol

³ Clinical Emergency Hospital Constanta County "Sfântul Apostol Andrei"

⁴ Pneumology Hospital of Constanta

⁵ University of Medicine and Pharmacy Carol Davila

Mădălina Iliescu

email: iliescumadalina@gmail.com

ABSTRACT

Introduction. Infectious and autoimmune rheumatic diseases (ARDs) are closely linked. Apart from the challenging, sometimes differential, diagnosis between these conditions, it is recognized that microbes play an important role in the pathogenesis of the latter. Material and method. We present the case of a 45-year-old female patient from our rehabilitation department, with complex pathology (infectious, neurological, rheumatological and orthopedic pathology) that began more than 15 years ago. The patient's pathological history began insidiously at the age of 30 when she was diagnosed with neurotoxoplasmosis. She received anticoagulant, antiepileptic, steroidal, antibiotic and antihelminthic treatment. After four years, the patient shows insidious onset of inflammatory pain in the large joints and in 2010 is diagnosed with seropositive rheumatoid arthritis, according to American College of Rheumatism/European League against rheumatism (ACR/EULAR) criteria with symmetric impairment of the large joints (shoulder, elbow, hip, knee, ankle). Despite the treatment with disease-modifying anti-rheumatic drugs (DMARDs) received, in the following years she needed 4 arthroplasties in the large joints due to osteonecrosis. Conclusions. On clinical grounds, infections, especially chronic infections, can cause a plethora of autoimmune phenomena, thus mimicking ARDs. Therefore, the differential diagnosis between ARDs and infectious diseases is sometimes challenging as they often display similar clinical manifestations. It is highlighted that the immune system can be our friend or our foe considering that its function and dysregulation are the common denominators in autoimmune and infectious diseases. In the era of new drugs and new therapeutic strategies, safety of the patients should always be our first concern.

Keywords: autoimmune rheumatic diseases, therapeutic strategies

Introduction

Starting from the phrase „there are no diseases but there are patients”, differential diagnosis and comprehensive treatment run by a multidisciplinary team should take precedence in modern medicine. The existence of an inflammatory or mixed pain that occurs in a patient with associated risk factors (long-term treatment with corticosteroids, consume excessive alcohol, have sickle cell disease, infections, hyperbaric events, storage disorders, marrow infiltrating diseases, coagulation defects, and some autoimmune diseases) must raise a high level of suspicion among clinicians of aseptic

osteonecrosis of bone in earliest stages (1,2).

Case report

A 45 year old female, from urban area, recently retired due to illness, presents to the Techirghiol Balneal and Rehabilitation Sanatorium for mixed vertebro-peripheral pain accompanied by morning stiffness of about one hour with a complex history of infectious, neurological, rheumatological and orthopedic pathology that began more than 15 years ago. The patient's pathological history began insidiously at the age of 30 with headaches, severe physical asthenia, myalgias and paresthesia in the lower

limbs, symptoms that evolved for several months and worsened with partial left motor crises with secondary generalization for which she was admitted as an emergency and was initially diagnosed with meningitis with hemorrhage outbreaks.

Since the patient's condition was precarious, with the appearance of fever, worsening of tonic-clonic seizures and tetraparesis, an magnetic resonance investigation - MRI (Figure. 1) and angio-MRI were performed, showing multiple oval and round focal lesions in different sizes, in both front and parietal lobes, with polymorphic cystic appearance and important protein content being specific to infection-type of focal lesions and having suggestive appearance of thrombophlebitis of cerebral venous sinuses.

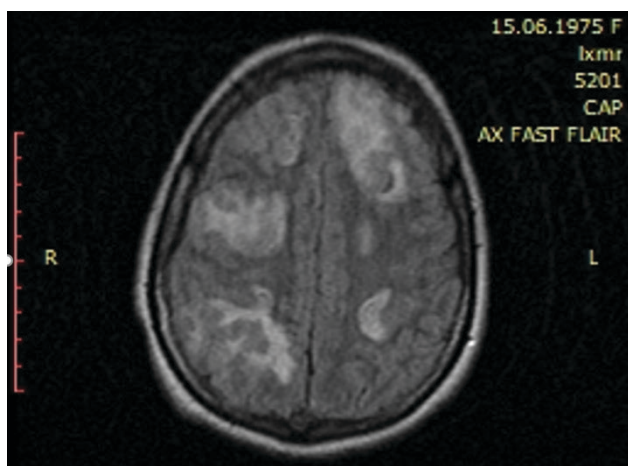


Figure 1 Axial Fluid attenuated inversion recoveryweighted imaging showing multiple isointense corticomedullary junction lesions surrounded by vasogenic edema.

After weeks of suitable treatment, the patient's condition improves and is discharged with anticoagulant, antiepileptic, steroidal, antibiotic and antihelminthic treatment, but continued to have recurrent epileptic seizures due to sequelae cerebral lesions (Figure 2) that did not yield to any proposed treatment.



Figure 2 Contrast enhanced brainComputed Tomography showing dot and ring-like calcifications at corticomedullary junction suggestive of previous neurotoxoplasmosis.

In 2009, after four years, the patient shows insidious onset of inflammatory pain in the large joints and in 2010 is diagnosed with seropositive rheumatoid arthritis, according to ACR/EULAR criteria with symmetric impairment of the large joints (shoulder, elbow, hip, knee, ankle), with low-moderate activity, with absence of erosions and no signs of local inflammation, for which she has undergone treatment with Methotrexate, Sulfasalazine and Hydroxichloroquine.

At the same time, the diagnosis of antiphospholipidic syndrome has been ruled out, that had been taken into account due to some of spontaneous miscarriages in the past. Due to severe pain in the coxo-femoral joints a computer tomography - CT (Figure 3 and Figure 4) and MRI is performed that showed aseptic osteonecrosis of the both femoral head bones for which total hip arthroplasty (Figure 5) was performed on the left one in 2010 and on the right one in 2012.

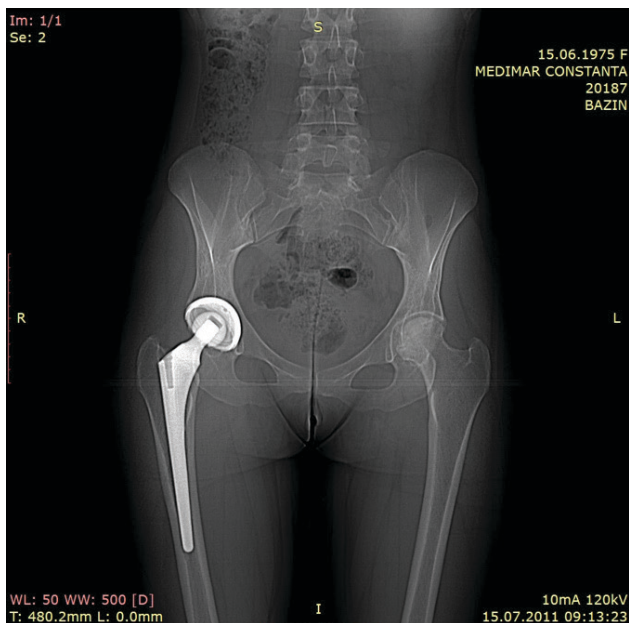


Figure 3 Frontal Computed Tomography Scout shows right total hip replacement arthroplasty and mild collapse of left femoral head with sclerosis.

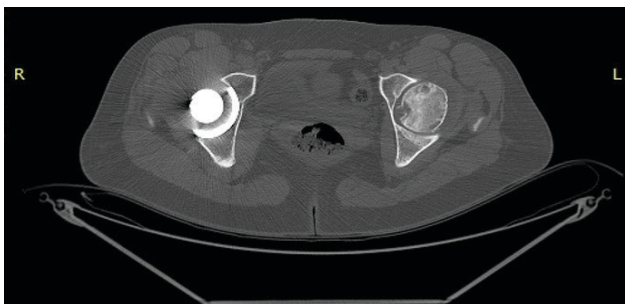


Figure 4 Axial Computed Tomography shows right total hip replacement arthroplasty and patchy areas of bone lucency and sclerosis with crescentic subchondral lucency.



Figure 5 Frontal radiograph showing total hip replacement arthroplasty on both sides.

In 2013, after weeks of intense pain in the shoulders that doesn't yield to the administration of nSAID, with significant limitation of the motion amplitudes in all plans, the patient is admitted for re-evaluation to the rheumatology department,

where after paraclinical investigations (Figure 6) are conducted, the diagnosis of aseptic osteonecrosis of both humeral heads is made and are performed, over time, two cementless hemiarthroplasties, one in 2017 on the right shoulder (Figure 7), and one in 2019 on the left shoulder (Figure 8). After further evaluations, the prosthesis of both knees was also taken into account due to bone sequestrations discovered at this level.

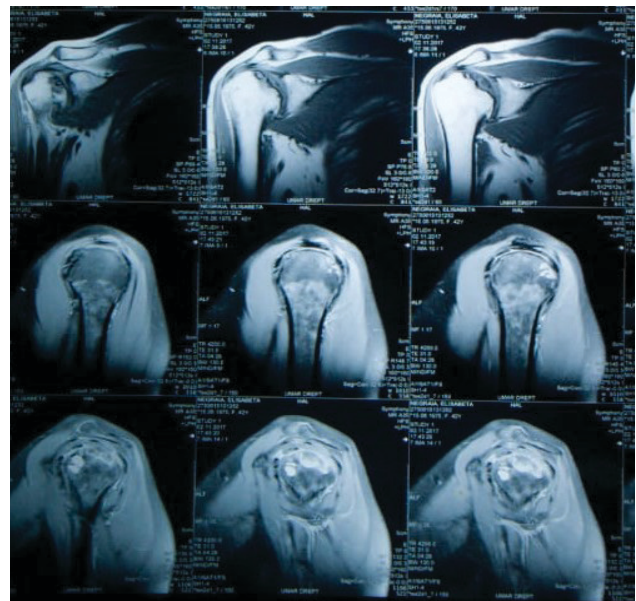


Figure 6 Coronal Proton Density and Sagittal Proton Density Fat Saturated weighted imaging show sclerosis and granulation tissue in right humeral epi, meta and diaphysis with surrounding marrow edema.

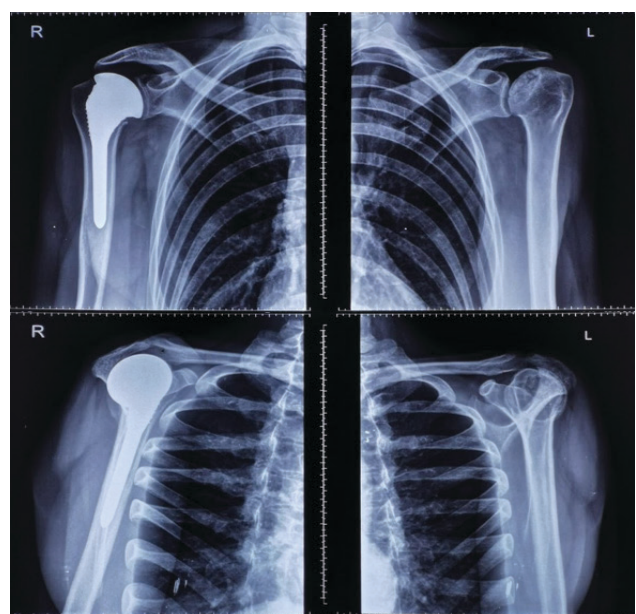


Figure 7 Anteroposterior and Anteroposterior with internal rotation shoulder radiographs show right humeral hemiarthroplasty.

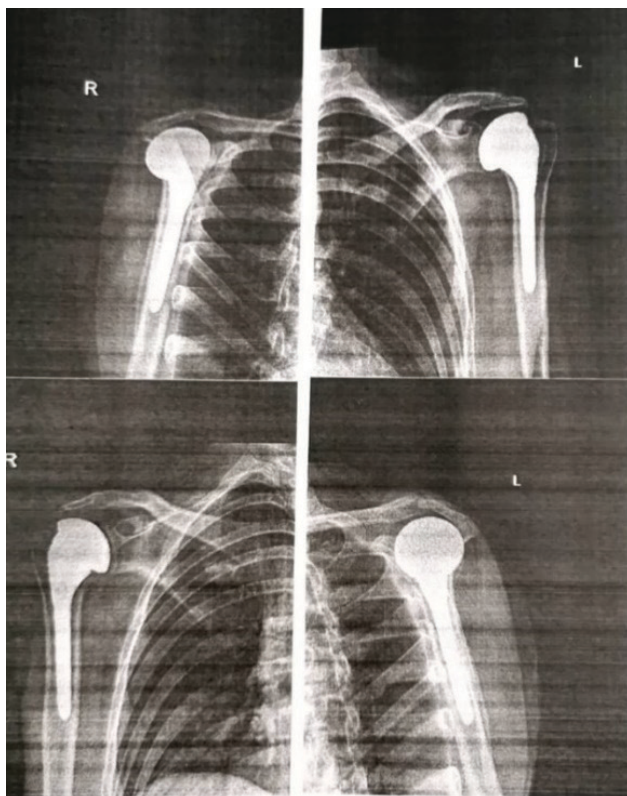


Figure 8 Anteroposterior and Anteroposterior with internal rotation shoulder radiographs show bilateral humeral hemiarthroplasty.

Genetic analyses were also carried out in 2018, revealing multiple mutations specific to hereditary thrombophilia.

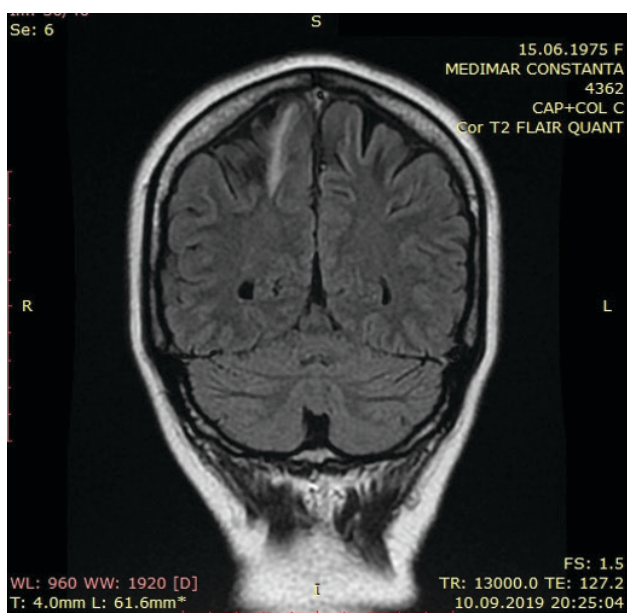


Figure 9 Cor T2 Flair shows area of hiperintensity at corticomedullary junction suggestive of gliosis.

Currently, the patient who still has tonic-clonic seizures due to the sequelae of infectious

brain injuries (Figure 9 and Figure 10) and is to undergo total knee arthroplasty, has a medium disabling status.

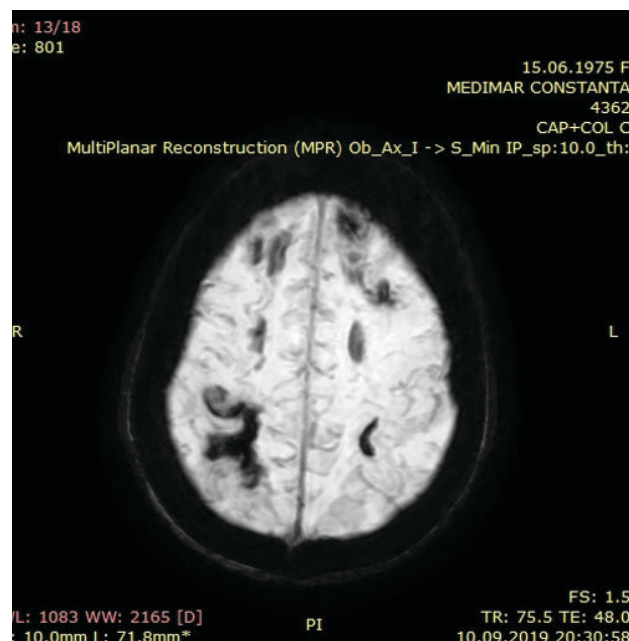


Figure 10 Axial Susceptibility weighted imaging showing regions of low-signal blooming artefact suggestive of hemosiderin deposition

Discussion

The term visceral larva migrans was for the first time used by Beaver in 1952 to describe any symptoms linked to a paratenic nematode larvae infection in patients with eosinophilia and long-term multi-system disease. Central nervous system involvement is usually rare, specially for *Toxocara*. The larvae are released after ingestion and penetrate the gut wall, from where they migrate via blood circulation to the liver, lungs, and left heart, from where they disseminate via the systemic circulation to eyes, brain and muscles. The larvae do not give symptomatology by mass effect because they don't grow, but through a collagenous reaction that encapsulates the antigen, manifesting as eosinophilic granuloma, and are metabolically active due to array of enzymes, waste products and cuticular components, which cause tissue damage, necrosis and a marked inflammatory reaction, with eosinophils as the major component (3).

Cerebral nervous system involvement in *Toxocara* infection is manifested as encephalopathy with cognitive decline, meningo-

encephalitis, cerebral vasculitis, epilepsy, visual impairment, myelitis, radiculitis, cranial nerve involvement, or skeletal muscle affection (4,5). *Toxoplasma gondii* was discovered 110 years ago by scientists, and is described as a parasite capable of infecting all warm-blooded animals, including humans, making it one of the most successful parasitic organism worldwide. The soil ingestion is the primary way of human infection (5). Moreover, infection with one of the two sprouts makes the risk of infection with the other twice as high. Studies have shown that gardening, soil contact and poor hand hygiene are the risk factors for this infections (5).

The systemic factors that trigger avascular necrosis of bone (AVN) are not fully understood, but Pierre Lafforgue, in his article about this subject has described, as a possible mechanism, intraluminal obliteration of blood vessels by microscopic fat emboli, sickle cells, nitrogen bubbles or focal clotting due to procoagulant abnormalities (6). Also exposure to risk factors such as high-dose glucocorticoid therapy or femoral neck fracture can cause AVN after 1-6 months of treatment or incident (6). Our patient has two risk factors that could have caused aseptic bone necrosis, thrombophilia and a history of a long treatment with glucocorticoids, for which the trigger mechanism cannot be clearly stated.

Given that our patient has remained with multiple sequelae due to infectious and thrombotic pathology, but also due to the treatment followed, including epilepsy, we have raised the question whether it is closely correlated with the seropositive for *Toxoplasma gondii* and *Toxocara* sp.. The study of Ali Akyol et al. Shows that although specific IgG antibodies against *T. Gondii* and *Toxocara* sp. in 100 cryptogenic epileptic patients had had no history of epilepsy in their first degree relatives, no relationship between them was found (7).

Cerebral venous thrombosis diagnosed during cerebral co-infection was favored by multiple risk factors. In addition to late-diagnosed genetic thrombophilia, the use of contraceptives and local inflammatory status could have benefited their development (8).

There is a possibility that our patient may have been a healthy carrier of rheumatoid factor, and thus the delay in early diagnosis

and appropriate treatment may be responsible for advanced aseptic osteonecrosis of the bone and for which the only solution is arthroplasty, which cannot be proven with certainty because it met the ACR / EULAR criteria for diagnosing rheumatoid arthritis (RA).

Femoral head osteonecrosis is present in about 12% of patients with RA at hip arthroplasty, and occurs in 2 forms – classic avascular necrosis and degenerative necrosis. Both forms are significantly associated with corticosteroid use. „Lowdose” therapy does not protect patients against the development of osteonecrosis. Additionally, baseline prevalence of osteonecrosis of about 3% occurs in the absence of steroid use and may be related to the underlying inflammatory diseases. Despite its association with osteonecrosis the net effect of corticosteroid therapy on the natural history of rheumatoid hip disease remains unclear (9).

Osteonecrosis of the femoral head is easily misdiagnosed as lumbar disc herniation, hip synovitis, hip osteoarthritis, and rheumatoid arthritis. Patient history of corticosteroid use or alcohol abuse and MRI examination at the initial diagnosis may be protective factors for misdiagnosis. Hidden symptoms, physician title at the initial visit (as attending doctor or resident doctor), and only X-ray examination at the initial diagnosis may be risk factors for misdiagnosis (10).

Conclusions

The peculiarity of the case: Young patient with complex pluripathology, infectious, rheumatological, neurological, orthopedic, which requires a comprehensive approach in a multidisciplinary team for functional rehabilitation, a clear example that shows the complexity of our specialty (11,12,13)

The main objectives of the rehabilitation programme are pain relieving, preserving the mobility range and muscle force for both shoulders and hips, and preparing the patient for total knee arthroplasty, by strengthening the quadriceps muscle. All these measures will improve the patient's ability to perform all the daily living activities, and therefore, to prevent the patient from developing any kind of disability.

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