

Poncet's disease: a symmetric seronegative polyarthritis with enthesopathy refractory to therapy

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ABSTRACT

Poncet's disease is a reactive polyarthritis associated to active tuberculosis (TB), with excluded presence of mycobacterium in the joints and bones affected, and no other cause for the clinical arthritis. It is a frequently forgotten entity, especially in countries with low tuberculosis prevalence. It is described a case report of a man of Guinea-Bissau that presented symmetrical generalized polyarthralgias and hands swelling, clinical sacroiliitis and multiple enthesopathies. Serum and urinary biochemical testing were normal. Immunologic studies were negative and serum levels of angiotensin-converting enzyme and calcium were normal. Sexual transmitted diseases were excluded. The initial diagnose was undifferentiated polyarthritis or reactive arthritis. A persistent and refractory monoarthritis of the right wrist demanded a direct and cultural exam of the synovial fluid, synovial biopsy and protein chain reaction for TB that were negative. After he developed right wrist arthritis with purulent synovial fluid positive to TB in the direct exam and the detection of *M. tuberculosis* in the cultural exam. Granula was found in his chest radiograph. He was diagnosed a Poncet's disease reactive to a pulmonary TB infection.

Keywords: Reactive arthritis; Sacroiliitis; Tuberculosis.

INTRODUCTION

The tuberculosis (TB) infection can be presented by a wide range of different manifestations¹. The musculoskeletal system is the fourth most common extra pulmonary target, after pleural, lymphatic and genitourinary systems². In the musculoskeletal TB mainly affects

large weight-bearing joints, but can also occurs as a spondylitis-like involvement, reactive arthritis, septic arthritis, tenosynovitis, bursitis, osteomyelitis and soft tissue abscesses¹. These findings are encountered in 1 to 3% of the patients with a TB infection and 50% of these are associated with pulmonary TB¹. Franco-Paredes et al³ also defined 4 different categories: direct musculoskeletal involvement of *M. tuberculosis*; *M. tuberculosis* as an infectious pathogen in rheumatic diseases (anti-TNF α users); anti-mycobacterium drug-induced rheumatologic syndromes (tendinitis, lupus); reactive immunologic phenomena caused by TB (reactive arthritis, erythema nodosum).

The two principal species of the *M. tuberculosis* complex responsible for the human disease are *M. tuberculosis* and *M. Bovis*. INF- γ and TNF- α are the main components of the granuloma formation. Virulence factors present in the *M. tuberculosis* membrane are highly immunogenic in human-like heat shock protein (HSP65)¹. TB spondylitis is characterised by a marked kyphotic deformity, where is relevant the differential diagnosis with pyogenic spondylitis. Peripheral joint involvement is frequently insidious and occurs in one or two joints. TB soft tissue abscesses, bursitis (frequent in the hip) and tenosynovitis (frequent in the tendon sheaths of the hand and the wrist) are rare (1% of musculoskeletal TB) and its pathological mechanism can be explained by the bacilli entrance in the blood stream and/or direct inoculation, and its deposit in highly vascular areas around the joint structures⁴.

Joint TB is a health concern in endemic areas, but some developed countries have documented a new wave of joint TB cases, mainly due to immunosuppressive diseases, drug-resistant TB species and the use of anti-TNF α drugs⁵. TB infection can also present itself as a reactive arthritis (Poncet's disease), somewhat different from the classical ones.

Non-TB reactive arthritis can be defined as a sterile joint inflammation that develops following a distant in-

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fection, whether enteric, urogenital or upper respiratory tract, and preferentially affecting young adults⁶. Positive serology to *Yersinia*, *Campylobacter*, *Salmonella* or *Chlamydia* is pathognomonic. The typical manifestations are enthesopathy, tendinitis and asymmetric oligoarthritis, although it is necessary to look for other complaints, such as (symptoms of skin and mucous membranes, gut inflammation, carditis, nephritis, urogenital symptoms and ocular lesions)⁶. Sometimes, at the early stages of the arthritis process, it is difficult to ascertain the differential diagnosis with bacterial aetiology. In both the acute phase is similar with blood and synovial fluid leukocytosis, and bacterial components or viable bacteria have been found in joints during a reactive arthritis^{6,7}. In contrast to non-TB reactive arthritis, Poncet's Disease (PD) presents different characteristics (Table I)^{7,8}.

Human leukocyte antigen (HLA)-B27 is closely associated with reactive arthritis and PD by unknown mechanisms^{9,10}. Different models suggest that HLA-B27 expression modulates the host-microbe interaction, and Vähämiko et al⁹ reported that monocytes expressing HLA-B27 have less capability to resist to the intracellular replication of *Salmonella*, thus HLA-B27 might enhance the monocytes/macrophages TNF α production induced by the *Salmonella* lipopolysaccharide (LPS). PD, a non-infectious immunologic reaction through T-lymphocytes action, can be mediated by association with HLA-B27¹¹, although most of the reported cases are HLA-B27 negative.

Besides many controversies, PD is defined as a non-suppurative reactive polyarthritis associated with active extra-articular TB (with no other mycobacterial involvement or cause for the arthritis)⁸.

CASE REPORT

A 44-year-old man from Guinea-Bissau was referred to our rheumatology outpatient clinic with three month long symptoms of symmetrical generalized arthralgias and swelling of both hands. The patient had previously been diagnosed with pernicious anaemia, bilateral optic neuropathy due to vitamin B12 deficit, monoclonal gammopathy of undetermined significance (MGUS), and erosive corneal scarring.

Physical examination revealed metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints arthritis, and all of the Disease Activity Score 28 joints, plus the tibiotarsal joints were tender.

Clinical sacroiliitis was reported but without radiographic signals. No other abnormalities, including erythema nodosum, wheezing or crackles in his chest or lymphadenopathies were detected. Serum and urinary biochemical testing were normal, as well as the immunologic studies, including HLA-B27, that was negative. Serum levels of angiotensin-converting enzyme and calcium were normal. Sexual transmitted diseases were excluded. On X-ray of the hands, feet, hips and lumbar spine there were no abnormalities. With an initial diagnosis of undifferentiated polyarthritis or reactive arthritis, prednisolone 7,5mg/day and naproxen 1000mg/day were administered, with moderate joint pain relief.

After four months the patient presented right wrist synovitis and both tender tibiotarsal joints with no other systemic complaints. Prednisolone 10 mg/day was prescribed, without relieve and three months after multiple entesopathies had developed: right epicondylitis and epitrocleitis, and bilateral Achilles ten-

TABLE I. CLINICAL FEATURES OF REACTIVE ARTHRITIS AND PONCET DISEASE

Reactive arthritis	Poncet disease
Onset of symptoms weeks before the arthritis	Onset of symptoms months before the arthritis
Frequently associated to sacroiliitis	Rarely associated to sacroiliitis
Resolution of the arthritis weeks after the treatment	Resolution of the arthritis days after the antituberculous therapy
Some with chronic evolution	Chronic evolution has never been reported
In both	
Pathogenetic mechanism: a CD4+ and bacterial antigens migration to the joints after the infection	
HLA-B27 can either be positive or negative	
Enthesopathic symptoms	

donitis. A right wrist arthrocentesis was performed, and synovial fluid cultures and synovial biopsy were made. The microbiological study of the synovial fluid and the synovial membrane were negative (Gram, Ziehl-Nielsen and Löwenstein-Jensen) and the polymerase chain reaction (PCR) assay of the synovial fluid was negative for *M. tuberculosis* complex. The synovial biopsy showed an unspecific synovitis. The wrist magnetic resonance imaging (MRI) reported an exuberant multifocal extensor tenosynovitis in the wrist and carpal area and bone erosions.

Two months after the invasive procedures the patient returned with an abscess of the wrist and with one week of evening fever, without other systemic symptoms. Subsequent arthrocentesis yielded a purulent synovial fluid compatible with caseum, whose sample revealed a Ziehl-Nelsen positive analysis. The joint underwent surgical debridement and joint lavage. Chest X-ray showed miliary TB (no chest X-ray was performed previously to the symptoms) but the bronchofibroscopy did not find endobronchial lesions and the direct examination by Ziehl-Neelsen and Löwenstein-Jensen culture of bronchial mucus were negative. The chest computerized tomography showed right axillar lymphadenopathies and multiple pulmonary nodules at the upper lobes. Standard blood and urine cultures for TB were negative. Fundoscopy exam did not find granuloma. The tuberculosis treatment consisted in isoniazid, pyrazinamide, rifampicin and ethambutol in the first 2 months, followed by rifampicin and isoniazid in the following 6 months. Joint pain and enthesopathies resolved after 5 days treatment, but wrist synovitis persisted and further surgical procedures were required. After 60 days of synovial fluid's Löwenstein-Jensen culture, the result was positive for *M. tuberculosis*.

DISCUSSION

This case reports a primer undifferentiated symmetric, seronegative polyarthrititis with axial symptoms, associated with entesopathies that evolved towards persistent wrist arthritis. The culture exams, the synovial biopsy and the nucleic acid amplification techniques were negative until chest granula was diagnosed. Joint symptoms improved after specific *M. tuberculosis* treatment. Further clinical investigation showed that the pulmonary TB was not bacilliferous and that there were no other infections. TB pulmonary infection was diag-

nosed after the refractory wrist arthritis, as the patient had no others systemic complaints. It is therefore likely that the patient had the pulmonary infection for a long time before the diagnosis had been made.

This case demonstrates that active TB may be associated to a reactive arthritis that rapidly improved with the TB treatment. We suggested the diagnosis of Poncet's Disease. However a lot of controversy has been associated with PD because in some situations it is unclear whether the patient has active TB or sterile arthritis¹².

Poncet's disease presumes an aseptic polyarthrititis, probably due to reactive mechanism, that develops in the presence of active TB elsewhere⁸. This immunological reaction, affecting mainly the wrists, elbows, knees and ankles^{13,14} can be associated with soft tissue manifestations. Both are considered due to a secondary immune response to *M. tuberculosis* infection¹³. Furthermore arthritis had been reported after intravesical instillation of *Mycobacterium bacillus* for bladder cancer¹². In a recent review⁸, 5 patients with oligo or polyarthrititis were reported having also a septic tuberculosis arthritis of one joint in addition to the other non-septic tender joints, and consequently it was admitted that septic tuberculous arthritis can be associated to reactive arthritis of other joints.

In the active TB infection, diagnosis can be made by bacteriological and nucleic acid amplification techniques. The diagnosis of latent TB is usually done by the history, i.e. previous contact with an infected patient, chest radiography compatible with previous TB infection and a positive tuberculin skin test. The later which may produce false positives by previous Baccille-Calmette-Guérin vaccination or false negatives due to immunosuppressive therapy¹⁵. To improve the reliability of the diagnosis of active or latent TB, there are essays to test for T-cell IFN- γ release (T-SPOT® and QFTG), which are more specific than the tuberculin skin test¹⁵.

Several arguments support the Poncet's Disease diagnosis:

- 1) Initial presentation of non-erosive seronegative polyarthrititis with axial complaints and tenosynovitis, resembling a reactive arthritis.
- 2) HLA-B27 negative. In accordance with most of the reported cases.
- 3) Common infectious agents causing reactive arthritis were excluded by serology.
- 4) Although blood and urinary cultures were negative, chest radiograph showed miliary TB and the previous non-septic wrist arthritis turned to be a *M. tu-*

berculosis arthritis.

- 5) Non-septic arthritis and enthesopathies quickly improved with antituberculous drugs, while septic TB arthritis responded slowly.

The patient initiated a combination of tuberculosis treatment drugs with secondary hyperuricemia. Clinical improvement took a few days, but the septic arthritis that usually takes 4 months to respond, took longer and it is still under orthopaedic surgical treatment. PD has usually a good prognosis and does not turn into chronic arthritis. Contrary septic arthritis can be complicated by erosive arthropathy, osteomyelitis and cutaneous fistula.

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REFERENCES

1. Weisman MH, Smolen JS. Infection-related rheumatic diseases. Mycobacterial, brucella, fungal, and parasitic arthritis. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH. *Rheumatology*. USA: Mosby;2008. p. 1029-38.
2. Bloch AB, Reider HL, Kelly GD, et al. The epidemiology of tuberculosis in United States. *Clin Chest Med* 1989; 10:297-313.
3. Ideguchi H, Tsukahara T, Kaneko T, et al. A case of Poncet's disease (tuberculous rheumatism). *Rheumatol Int* 2009; 29: 1097-1099.
4. Abdelwahab I, Bianchi S, Martinoli C, et al. Atypical extraspinous musculoskeletal tuberculosis in immunocompetent patients: part II, tuberculous myositis, tuberculous bursitis, and tuberculous tenosynovites. *Can Assoc Radiol J* 2006;57(5):278-286.
5. Vohra R, Kang HS, Dogra S, et al. Tuberculous osteomyelitis. *The Journal of bone and joint surgery* 1997; 79-B: 562-566.
6. Colmegna I, Espinoza LS. Recent advances in reactive arthritis. *Current Rheumatology reports* 2005; 7:201-207.
7. Pallazi C, Olivieri I, Salvarani C, et al. Artriti reattive: attualità in tema di diagnosi e terapia. *Reumatismo* 2002; 54: 105-112.
8. Kroot EJ, Hazes JM, Colin EM, et al. Poncet's disease: reactive arthritis accompanying tuberculosis. Two case reports and a review of the literature. *Rheumatology* 2007; 46:484-489.
9. Vähämäki S, Penttinen MA, Granfors K. Aetiology and pathogenesis of reactive arthritis: role of non-antigen-presenting effects of HLA-B27. *Arthritis research and therapy* 2005; 7: 136-141.
10. Hopkins GO. Multiple joint tuberculosis presenting as HLA-B27 disease. *Postgraduate Medical Journal* 1983; 59: 113-115.
11. Ozgul A, Baylan O, Taskaynatan MA, et al. Poncet's disease (tuberculous rheumatism): two case reports and review of the literature. *Int J Tuberc Lung Dis* 2004; 9: 822-824.
12. Cuende E, Almeida V, Portu J, et al. Poncet's disease and papulonecrotic tuberculid in a patient infected with the human immunodeficiency virus. *Arthritis and rheumatism* 1998; 41: 1884-1888.
13. Swahney S, Murray KJ. Isolated tuberculosis monoarthritis mimicking juvenile rheumatoid arthritis. *The Journal of Rheumatology* 2002; 29(4): 857-859.
14. Franco-Paredes C, Diaz-Borjon A, Senger MA. The ever-expanding association between rheumatologic diseases and tuberculosis. *The american journal of medicine* 2006; 119:470-477.
15. Valleala H, Tuuminen T, Repo H, et al. A case of Poncet disease diagnosed with interferon- γ release assays. *Nat. Rev. Rheumatology* 2009; 5: 643-647.