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# Letter to the editor: Rheumatoid arthritis or parvovirus B19 arthritis?

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Dear editor,

Adult patients with new onset polyarthritis may present a diagnostic challenge; differential diagnosis between primarily rheumatic conditions with viral arthritis such as those caused by parvovirus (PV)-B19 is one of the concerns.

Infection by PV-B19, a single stranded DNA virus, is very common, affecting more than 50% of adults in the United Kingdom and with a prevalence that rises with age reaching 75% in individuals older than  $50^{1,2}$ . In children the characteristic skin rash (slapped face) is common and articular involvement is rare following the pattern of large joints oligoarthritis<sup>1</sup>. In adults the rash is usually absent and articular symptoms are common (80%) taking a polyarticular pattern that involves wrists, metacarpophalangeal and interphalangeal joints symmetrically<sup>1</sup>. So, in adults the differential diagnosis with early rheumatoid arthritis (RA) is mandatory. Moreover, these patients may present important morning stiffness<sup>3</sup> and develop autoantibodies such as rheumatoid factor and antinuclear antibody at low titers creating further difficulties1. The polyarticular PV-B19 arthritis has usually a self-limited pattern but can also become chronic developing erosions as well<sup>2</sup>. This has led to the question of whether PV-B19 chronic arthritis is a persistent infection with articular involvement or a trigger for RA in genetically predisposed individuals. A study done in Taiwan, in 100 patients with RA and 94 controls showed that RA patients had more PV-B19 infections (24% IgM anti-B19 in RA vs. 16% in controls; and 34% of B19DNA in serum or synovial material of RA patients versus 6.4% in control sera) showing a possible link between these two entities4. The same observation was done in a study in

RA patients from Taiwan, which also showed that RA patients HLA-DR4 positives had higher prevalence of HP-B19 infections than those HLA-DR4 negatives suggesting a synergistic effect between HLA-DR4 and PV-B19 infection.

From the practical point of view, being able to differentiate these two situations helps the clinician to choose a treatment: while in chronic PV-B19 infections immunoglobulin has been used, in RA synthetic disease modifiers and/or biologics are indicated.

Herein we describe a patient that illustrates the difficulties in the differential diagnosis between these two situations and that responded well to antimalarials and methotrexate.

She was a 55-year-old woman, smoker of 10 packsyear, with a negative past medical history that came with a trigger first left finger and bilateral wrist arthritis. At that time the investigation showed C-reactive protein of 0.17 mg/L, erythrocyte sedimentation rate of 18 mm and a positive IgM for PV-B19 with negative IgG. Antinuclear antibodies (ANA), anti-CCP and rheumatoid factor (RF) were negative; complements were normal. Serology for syphilis, HIV, and HTLV I and II, hepatitis B and C; cytomegalovirus, Epstein-Barr, and herpes simples 1 and 2 were negative. Hand X-Rays were normal. She was treated with a single injection of betamethasone depot and with antimalarials and became asymptomatic. A follow-up visit done 1 year later showed that she was well and the IgM HPV-B19 was absent with positive IgG. The patient remained well using antimalarial until 4 years later when she developed bilateral synovitis of all metacarpophalangeal and proximal interphalangeal joints with flexors tenosynovitis confirmed by ultrasound. ANA, RF and anti CCP remained negatives. Methotrexate (15 mg/week) was added to treat-

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ment with good response. She is currently on a 1-year follow-up after starting methotrexate and in remission.

This patient's initial presented picture pointed to HP-B19 infection. Then, she had a 5-year period of remission and the later manifestations of the disease were highly suggestive of seronegative RA. It is possible she had the two diseases or that the HPV-B19 became chronic, being quiescent during 5 years because of antimalarial use. It is also thinkable that the HPV-B19 triggered the later appearance of a true RA. While a definite answer seems impossible, it is interesting to note that the patient answered to methotrexate. The literature suggests immunoglobulin use in cases of chronic HP-B19 infection, but it is also worthwhile to note that, in other viral infections triggered arthritis such as of chikungunya, methotrexate and antimalarial have been used with success<sup>1,6</sup>.

Further studies in the role of viral infections in autoimmunity are needed to clarify this fascinating link between PV-B19 infections and RA.

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The authors declare that he followed the World Medical Association Declaration of Helsinki in this study. An informed consent was obtained from the patient for publication of her case.

# **CONFLICT OF INTEREST:**

The authors declare that they have no conflict of interests.

# **REFERENCES**

- Marks M, Marks J. Viral Arthritis. Clin Med 2016; 16: 129-134
- Woolf AD, Cohen BJ. Parvovirus B1 9 and chronic arthritiscausal or casual association? Ann Rheum Dis 1995; 54: 535-536.
- Vassilopoulos D, Calabrese LH. Virally associated arthritis 2008: clinical, epidemiologic, and pathophysiologic considerations. Arthritis Res Ther 2008; 10: 215.
- Kozireva SV, Zestkova JV, Mikazane HJ, Kadisa AL, Kakurina NA, Lejnieks AA, et al. Incidence and clinical significance of parvovirus B19 infection in patients with rheumatoid arthritis. J Rheumatol 2008; 35: 1265-1270.
- Chen YS, Chou PH, Li SN, Tsai WC, Lin KH, Tsai KB, Yen JH, Liu HW. Parvovirus B19 infection in patients with rheumatoid arthritis in Taiwan. J Rheumatol 2006; 33: 887-891.
- Amaral JK, Bingham CO 3rd, Schoen RT. Successful methotrexate treatment of chronic Chikungunya arthritis. J Clin Rheumatol 2020; 26: 119-124.