Letters to the Editors

Calcium pyrophosphate disease and polymyalgia rheumatica: association or coincidence?

Comment on "Ultrasound shoulder assessment of calcium pyrophosphate disease with suspected polymyalgia rheumatica" Ottaviani *et al*.

Sirs,

We read with interest the article "Ultrasound shoulder assessment of calcium pyrophosphate disease with suspected polymyalgia rheumatica", recently published in *Clinical and Experimental Rheumatology* (1).

Among the 52 enrolled patients fulfilling the 2012 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for polymyalgia rheumatica (PMR) (2), Ottaviani *et al*. identified 25 (48.07%) with a diagnosis of calcium pyrophosphate disease (CPPD). The authors concluded that EULAR/ACR criteria do not allow excluding CPPD as PMR-mimicking disease, because all patients affected with CPPD fulfilled these same classification criteria. They also proposed that expanding ultrasound (US) examination in patients with suspected PMR to include acromion-clavicular (AC) joints might provide better diagnostic accuracy.

Their conclusions are very relevant in clinical practice. CPPD can be a PMR-mimicking disease. Indeed, patients with CPPD may present with proximal involvement (3), and CPPD can cause an inflammatory neck pain when a crowned dens syndrome is present (4). Moreover, the treatment of both CPPD and PMR is anti-inflammatory, however different concerning colchicine and different glucocorticoids (GCs) regiments. Therefore, if Ottaviani's report is confirmed in multicentric, large-sized studies, the possibility that PMR patients without GC-free remission can have an overlapping CPPD should be considered.

Two questions need to be discussed. Firstly: Can CPPD always be considered an exclusion diagnosis in older persons with suspected PMR?

The prevalence of CPPD increases with age. Therefore, random coexistence with PMR is probable. According to some research groups, CPPD is an infrequent PMR-mimicking condition (3, 5, 6). In particular, in Pego-Reigosa's prospective study in 2005, the evidence of ankle arthritis, tibiofemoral osteoarthritis and tendinous calcifications were identified as predictive factors for the diagnosis of the so-called "pseudo-PMR pattern" of CPPD (3).

In a clinical practice, determining whether patient suffers from PMR or CPPD is not always easy, and the possibility that one condition could be the trigger factor for the other cannot be excluded.

Our 59-year-old female patient was diagnosed with PMR, presenting classical manifestations, fulfilling the 2012 EULAR/ACR classification criteria, after exclusion of rheumatoid arthritis and connective tissue diseases. Good control of PMR enabled gradual withdrawal of GCs within one year. However, in the next 9 years she developed two episodes of effusive knee joint arthritis. Knee joint ultrasound showed prominent synovitis and cartilage calcifications. Joint fluid aspirate showed the presence of positively birefringent CPP crystals by polarised light microscopy. Colchicine 1mg per day brought resolution of symptoms, however without normalising of CRP. After three further months, she complained of arm and pelvic girdle pain with general malaise. Induction of low dose CS brought fast and complete resolution of her symptoms.

The second question is: what is the value of US examination of AC joints in distinguishing CPPD from PMR?

To answer this question, we re-evaluated a bi-centric US database of confirmed PMR cases according to US CPPD criteria proposed by Ottaviani *et al*. All examinations were performed between 2014 and 2020 using a predefined protocol based on protocols by Jiménez-Palop *et al*. (7) and Falsetti *et al*. (8). Among 204 patients with 208 pictures of AC joints (minimum one picture for patient) available, we identified only one case meeting these criteria, and further 22 possible, however doubtful pictures. No diagnosis of CPPD had previously been made in these patients.

In conclusion, we are grateful to Ottaviani *et al*. for allowing us to critically revise our clinical perspective (9, 10). We agree that the possibility of underestimated CPPD should be considered at every stage of PMR. We also agree that expanding standard shoulder examination in PMR patients to include AC joints might be of clinical relevance. However, the question remains whether to consider PMR and CPPD accompanying or randomly associated diseases.

Informed consent: all patients gave their informed consent in line with the specific national provisions.

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