# Correspondence

INSTRUCTIONS FOR LETTERS TO THE EDITOR

Editorial comment in the form of a Letter to the Editor is invited; however, it should not exceed 800 words, with a maximum of 10 references and no more than 2 figures (submitted as camera ready hard copy per Journal Guidelines) or tables and no subdivision for an Abstract, Methods, or Results. Letters should have no more than 3 authors. Full name(s) and address of the author(s) should accompany the letter as well as the telephone number, fax number, or E-mail address.

*Contact.* The Managing Editor, The Journal of Rheumatology, 920 Yonge Street, Suite 115, Toronto, Ontario M4W 3C7, CANADA. Tel: 416-967-5155; Fax: 416-967-7556; E-mail: jrheum@jrheum.com Financial associations or other possible conflicts of interest should always be disclosed.

## Why "Spondylodiscitis," Why "SAPHO Syndrome"?

*To the Editor:*

I read the recent article by Dr. Akisue and colleagues[1] concerning their experience with lumbar spondylodiscitis in SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis) with great interest, and would like to offer my opinion on this case.

German rheumatologists and radiologists see this problem differently, based on longterm and extensive experiences with the SAPHO syndrome and its inflammatory effect on the spine.

We clinically, radiologically, and histopathologically surveyed 144 cases corresponding to the criteria of the SAPHO syndrome[2]. Our cohort, moreover, documents the nosologic heterogeneity of the SAPHO syndrome, which is not a uniform entity[3]: 64 cases (44%) clearly belong to the "chronic recurrent multifocal osteomyelitis" (CRMO) category. Their assignment to all age classes with a peak between 15 and 20 years of age (mainly female) became possible due to the definition of this acquired, sterile inflammatory disease of the bone marrow as an "adult CRMO"[4]. In our cohort these are represented by 23 cases, 13 female, between 18 and 60 years of age.

We define the CRMO syndrome as primarily a chronic polyosteomyelitis that also occurs monostotically and that immunopathogenetically is likely a form of "reactive osteomyelitis." Hypovirulent commensal germs like *Propionibacterium acnes* are considered as likely antigens. This osteomyelitis proceeds histopathologically in 3 stages as a lympho-plasmacellular process that begins as edema of the bone marrow, which can be seen on magnetic resonance tomography, and limits itself after several years of sclerosing, or often hyperostosing. We have described the accompanying ossifying periostitis and inflammatory surrounding paraosseous resp. perivertebral soft tissue edema with possible neural and vascular complications[5].

The manifold osteoarticular panorama can be subdivided in accord with the clinical dominance of the disease into various types, whereas the pediatric-metaphysial type affects mainly the lower extremities, with sympathetic arthritis; the pelvic type with sympathetic coxitis from acetabular inflammation; the inflammatory anterior chest wall syndrome, often with primarily chronic osteomyelitis of the clavicula; and the vertebral type (spondyloarthropathies) are the most frequent locations of the bone marrow process. The association with pustular dermatoses, that is, mainly the palmoplantar type of pustular psoriasis, increases with the manifestation age from 30% to 70% of the respective age group. In our cohort these are represented by 32 cases (50%).

In our CRMO cohort 22 cases (33%) had spinal involvement, and 8 of these cases were young women with the palmoplantar type of pustular psoriasis. The radiological and histopathological substrate is sterile lymphoplasma cellular spondylitis, which primarily occurs as an inflammatory edema of the bone marrow. Similar changes were seen in the case described by Akisue, *et al* in a 22-year-old woman with the affected 5th lumbar vertebra with typical signal intensity in the magnetic resonance T-T2 sequence or after the administration of a contrast medium. In our cohort of 22 patients we observed the involvement of 72 vertebral bodies from C3 to L5, 15 times multisegmentally, and 7 times deforming, and in 2 cases it was destructive up to the vertebrae plana.

Akisue, *et al* in their report describe the inflammation of the bone marrow (Figure 3), initially in stage I also erosive (Figures 1 and 2) in this way resembling a spondylodiscitis. In the vertebral manifestation of CRMO we believe the spondylodiscitis is always a secondary complication, the primary manifestation being chronic osteomyelitis, i.e., sterile spondylitis. This is also nosologically more understandable, because the sterile primary spondylodiscitis is an inflammatory enthesopathic symptom of the spondyloarthropathies, as seen in the psoriatic form with ossifying enthesitis. CRMO, however, in our view, is based on a primary inflammation of the bone marrow, in the case of the spine primarily a spondylitis, which may be confused with a spondyloarthropathy with secondary spondylodiscitis, making for a very difficult differential diagnosis. We have described these manifestations in the largest cohort to date[2].

Our therapy has been successful in 28 patients with combined longterm medication using azithromycin (as immunomodulator) and (osteotrope) calcitonin[2,6].

In summary, we would classify this case as a vertebral type of the CRMO syndrome. In our view it is primarily a chronic osteomyelitis (spondylitis) of the 5th lumbar vertebrae with secondary spondylodiscitis and typical prevertebral edema.

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## Dr. Akisue, *et al* reply

*To the Editor:*

We read with interest Dr. Schilling's comments about our article[1]. In 1987, Kahn and colleagues proposed the term SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis) to designate a group of conditions that showed peculiar bone lesions with or without dermatologic lesions[2]. It is still controversial whether the term should be used to designate these conditions, since clinical and radiographic manifestations are overlapped and combined in a condition where the etiology may not be uniform[3]. However, the term SAPHO syndrome has commonly been used in the English language literature, while another, acquired hyperostosis syndrome (AHYS), has also been proposed[3,4].

Dr. Schilling considers that SAPHO syndrome is not an entity with nosologic homogeneity and has proposed 5 distinct groups within SAPHO syndrome, of which chronic recurrent multifocal osteomyelitis (CRMO) is defined as type II. Based on the definition of CRMO by Dr. Schilling, our case may indeed be classified as a monostotic vertebral type of CRMO. However, CRMO was first described as a skeletal disorder with multiple bony lesions, usually affecting children and adolescents. Our case[1] was a 29-year-old woman presenting with a monostotic lesion. Therefore we do not believe that the term chronic recurrent multifocal osteomyelitis appropriately represents our case. In addition, we prefer to use the term CRMO when a patient meets the classic criteria proposed by King, *et al*[7]. Thus we stand by our diagnosis, based on the definitions of SAPHO syndrome by Kahn and colleagues[8,9].

The pathogenesis of SAPHO syndrome including CRMO remains unknown. Studies for vertebral lesions in SAPHO syndrome using magnetic resonance imaging (MRI) showed abnormal bone marrow signals, either focal or diffuse[10,11]. Focal abnormal signals have always existed in the endplates and the corners of the vertebral bodies[11]. In some cases, paravertebral soft tissues and intervertebral discs have also shown abnormal signal intensity, suggesting an inflammatory reactive lesion around paravertebral soft tissues and the intervertebral disc[11]. Nachtigal, *et al*[11] concluded that MRI findings were consistent with discitis and osteitis, namely spondylodiscitis. Dr. Schilling speculates that spondylodiscitis in our patient was a secondary complication and that the primary lesion was chronic osteomyelitis in the vertebral body. However, there is no evidence that strongly indicates the initial nosologic phenomenon in our patient occurred exclusively in the bone marrow. While we appreciate the hypothesis that spondylodiscitis in SAPHO syndrome is a secondary complication and that the primary lesion could be chronic osteomyelitis in the bone marrow, we believe that radiographic and histologic evaluations confirm spondylodiscitis in our patient.

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## *Mycobacterium tuberculosis* Infection of a Tophaceous Pseudogout Nodule

*To the Editor:*

I enjoyed the important case report by Santos-Ocampo, *et al*[1] showing supra-infection by mycobacteria of a calcific deposit in the finger. I would like to caution whether the calcific deposit was as definitely due to calcium pyrophosphate dihydrate (CPPD) crystals as described. The patient was young, had no family history of CPPD, had no risk factors described, and as a dialysis patient seemed more at risk for apatite [basic calcium phosphate (BCP)] deposition. Although CPPD can rarely cause tophus-like periarticular deposits[2], the radiographic pattern shown looks more like apatite. In addition, no typical cartilage calcifications were apparently noted. The microscopic examination described also raises concern, as the typical crystals were also noted to be associated with "lipid." Was this confirmed by fat stain? It seems possible that what were seen were the spherules typical of apatite, well described by McCarty and Gatter[3] and illustrated in the *Atlas of Synovial Fluid Analysis and Crystal Identification*[4]. Some apatite or other BCP clumps can also be angular and might be mistaken for CPPD, if the spherules were not recognized. Although usually non-birefringent, these clumps can be faintly birefringent.

The authors obviously had thought about apatite but did not have the special stains available. Most pathology laboratories can do calcium stains, but reference laboratories, such as ours or Neil Mandel in Milwaukee, are usually delighted to help with puzzling cases. Might another aspiration be done? None of this is to detract from the basic observation, but to try to be certain about the exact association. There may also be implications for treatment of the calcifications.

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## Dr. Santos-Ocampo replies

*To the Editor:*

We thank Dr. Schumacher for his interest in our case report. While we agree that basic calcium phosphate or apatite crystals could have contributed to the development of tophi in this patient, we also confirm that the aspirates of the right metacarpophalangeal and left elbow tophi did show an abundance of typical weakly positively birefringent rods consistent with calcium pyrophosphate dihydrate crystals. Certainly, both types of crystals could have coexisted in the same tophus. The lipids described in the fluid were not confirmed by fat staining. Most of the fluid obtained was sent for bacteriologic studies, and none are available for additional testing since the patient has died. We thank Dr. Schumacher for his generous offer to assist us in the future identification of apatite crystals. We will certainly request his assistance should a similar case present itself.

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