CASE REPORT

A case of bronchiolitis obliterans organising pneumonia associated with SAPHO (synovitis-acne-pustulosis-hyperostosis-osteitis) syndrome

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SUMMARY

A 57-year-old woman with SAPHO (synovitis-acne-pustulosis-hyperostosis-osteitis) syndrome presented with recurrent episodes of pneumonia. She was treated with multiple courses of antibiotics with no success. The transbronchial biopsy undertaken via bronchoscopy revealed organising pneumonia (OP). She was treated with steroids and responded well with full clinical recovery and normalisation of her chest X-ray. To our knowledge, this is the first reported case of OP in association with SAPHO syndrome. This case report highlights the importance of considering OP in patients with SAPHO syndrome who present with chest infection.

BACKGROUND

SAPHO (synovitis-acne-pustulosis-hyperostosis-osteitis) syndrome is a rare condition with a prevalence in Caucasians of 1 per 10 000 characterised by cutaneous and osteoarticular manifestations. It usually presents as synovitis, acne, pustulosis, hyperostosis and osteitis. It has unclear pathogenesis and is diagnosed by taking into account clinical, laboratory and radiological investigations. It

is usually treated with non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, immunosuppressants and sometimes antimicrobials. To the best of our knowledge, so far no association of SAPHO syndrome and organising pneumonia (OP) has been described in the literature. Writing up this case report will highlight a rare association and facilitate timely diagnosis and treatment of OP in patients with SAPHO syndrome.

CASE PRESENTATION

A 57-year-old woman with SAPHO syndrome initially presented to her general practitioner with cough, breathlessness and fleeting areas of consolidation on chest X-ray (CXR) (figure 1). She was treated for a presumed infectious pneumonia with successive courses of amoxicillin, doxycycline and clarithromycin, but despite taking three courses, her symptoms persisted and CXR changes did not resolve.

At this point, she was referred to Respiratory Outpatient Clinic and subsequently had further tests including CT thorax, bronchoscopy, autoimmune screening and lung function test. The CT thorax showed worsening bilateral dense opacities (figure 2).

In her relevant medical history, she suffered from SAPHO syndrome that was diagnosed on basis of clinical and radiographic features. Her clinical features at the time of diagnosis were scalp psoriasis, pain in the lower back and upper anterior thoracic spine as well as a bony prominence on left clavicle and right mid tarsal joints. The lumbar spine X-ray showed sclerosis of L3, L4 and L5 vertebrae. The CT scan confirmed the X-ray findings and also showed erosive changes of left manubrio sternum and clavicle. The radiographic findings were consistent with the diagnosis of SAPHO syndrome. She was taking NSAIDs for pain relief. She was not on immunosuppressants or any other medication with the potential to cause pneumonitis. She was an ex-smoker with a 30-pack-year history with no obvious evidence of airway disease.

INVESTIGATIONS

Her blood tests showed white blood cells 9.5×10^9 , C reactive protein 84 mg/L, negative autoimmune screening tests and negative HIV test. CT thorax showed right lower lobe extensive consolidation and atelectasis in the left lung (figure 2). Her lung

Figure 1 Chest X-ray on presentation: bilateral dense opacities typical of organising pneumonia.

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Figure 2 CT scan thorax on presentation: bilateral dense opacities typical of organising pneumonia.

function test showed mild obstructive defect on spirometry (Forced Expiratory Volume in one second (FEV1) 117%, Forced Vital Capacity (FVC) 153%, FEV1/FVC 65%) and normal gas transfer (transfer factor of the lung for carbon monoxide (TLCO) 88%, gas transfer ability per unit of the lung (KCO) 75%). She underwent bronchoscopy and had bronchial washings and transbronchial biopsy undertaken. Bronchial washings culture was negative for bacteria, acid-fast bacilli and fungi. Differential cell count of bronchial washings showed neutrophils

Figure 3 Chest X-ray after oral steroid treatment: complete resolution of bilateral opacities.

50%, macrophages 40%, lymphocytes 10%, eosinophils 0% and no malignant cells.

Her biopsy showed characteristic histopathological features of OP, including the presence of Massons bodies.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses included infectious pneumonia and other forms of acute interstitial lung diseases.

She was initially treated as community-acquired pneumonia but no response to antibiotics and persistent fleeting shadows on CXR raised suspicion of OP. The transbronchial biopsy showed characteristic histopathological findings. In the context of her clinical presentation and characteristic CXR changes, we elected to treat for OP, rather than proceed to surgical biopsy.

TREATMENT

She was treated with a tapering course of oral corticosteroids that she tolerated quite well. Her body weight was 50 kg and she was given oral prednisolone 30 mg per day for 2 weeks, reducing by 5 mg a month over a 6-month period. Within 2–3 weeks, she noticed a significant improvement in her exertional breathlessness. Her follow-up CXR at 6 weeks from the start of corticosteroids treatment showed significant resolution of opacities (figure 3). She was advised to seek medical help in case of relapse of symptoms while on tapering regimen.

OUTCOME AND FOLLOW-UP

She successfully came off oral corticosteroids. She was well after 1 year of follow-up with no further episodes of pneumonia and no respiratory symptoms.

DISCUSSION

SAPHO syndrome is a rare rheumatological condition characterised by cutaneous and osteoarticular manifestations. It is not known to involve the lung parenchyma. Its pathogenesis is not clear but bacterial infections, immune dysfunction and certain genetic factors have been proposed as potential triggers of inflammatory process that causes SAPHO syndrome.

The SAPHO syndrome has an overlap with spondyloarthropathies (HLA-B27) and a positive connection with HLA-39 and HLA-61. This is also reflected by the fact that current treatment of SAPHO syndrome follows the therapy of spondyloarthropathies.

There are two diagnostic criteria for SAPHO syndrome that take into account clinical and radiographic features. The commonly used criteria proposed by Kahn require bone-joint involvement associated with either psoriasis vulgaris or acne. The isolated non-infectious hyperostosis/osteitis is also accepted for diagnosis in adults. The characteristic radiographic features are key in making the diagnosis in most cases. These include hyperostosis, sclerosis, osteitis and erosions. Rarely, bone and/or skin biopsy are done to rule out other conditions.^{1–3}

OP is a type of acute idiopathic interstitial pneumonia that is characterised by accumulation of inflammatory cells and collagenous plugs within the alveolar space. It is well known to be associated with connective tissue disorders but the association found with SAPHO has not previously been reported.^{4,5}

The fibrous exudate that develops in lung parenchyma in OP is also inflammatory in nature. Neutrophils were found in a high percentage in bronchial washings of our patient and their role has been described in pathogenesis of SAPHO syndrome as well.^{6,7}

Bacterial infection may be another trigger for both these conditions. It can cause OP if it remains unresolved and is also hypothesised to trigger the autoimmune process that gives rise to SAPHO syndrome. Different pathogens isolated from tissues in SAPHO are *Staphylococcus aureus*, *Haemophilus parainfluenzae* and *Actinomyces* whereas OP can be a consequence of any unresolved bacterial or viral chest infection.^{8–10}

Patients with both SAPHO and OP can present with relapses.

When it comes to treatment, both conditions respond to corticosteroids, immunosuppressants and sometimes antimicrobials.^{5 8 9}

Role of interleukins and tumour necrosis factor has also been established in both conditions.^{11 12}

It is unclear whether the OP in our patient was due to same abnormal and dysregulated inflammatory process underlying her SAPHO syndrome but there is good evidence in literature to suggest the common underlying pathogenic mechanisms.

Learning points

- ▶ The novel association of SAPHO (synovitis-acne-pustulosis-hyperostosis-osteitis) and organising pneumonia (OP) described in this case is of particular interest to respiratory physicians, rheumatologists, orthopaedic surgeons and general practitioners.
- ▶ In patients with SAPHO syndrome presenting with chest infection, there should be a high index of suspicion for OP, especially if there is poor or no response to initial antibiotics.
- ▶ Seeking early tissue diagnosis and timely treatment of OP in patients with SAPHO syndrome may reduce the morbidity associated with it.
- ▶ This case report will trigger further research for unusual presentations of SAPHO syndrome.

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REFERENCES

- 1 Khanna L, El-Khoury GY. SAPHO syndrome--a pictorial essay. *Iowa Orthop J* 2012;32:189–95.
- 2 Tlougan BE, Podjasek JO, O'Haver J, *et al.* Chronic recurrent multifocal osteomyelitis (CRMO) and synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome with associated neutrophilic dermatoses: a report of seven cases and review of the literature. *Pediatr Dermatol* 2009;26:497–505.
- 3 Hayem G. [SAPHO syndrome]. *Rev Prat* 2004;54:1635–1.636.
- 4 Lazor R, Vandevenne A, Pelletier A, *et al.* Cryptogenic organizing pneumonia. Characteristics of relapses in a series of 48 patients. The Groupe d'Etudes et de Recherche sur les Maladies "Orphelines" Pulmonaires (GERM"O" P). *Am J Respir Crit Care Med* 2000;162:571–7.
- 5 Lohr RH, Boland BJ, Douglas WW, *et al.* Organizing pneumonia. Features and prognosis of cryptogenic, secondary, and focal variants. *Arch Intern Med* 1997;157:1323–9.
- 6 Liao HJ, Chyuan IT, Wu CS, *et al.* Increased neutrophil infiltration, IL-1 production and a SAPHO syndrome-like phenotype in PSTPIP2-deficient mice. *Rheumatology* 2015;54:1317–26.
- 7 Travis WD, Costabel U, Hansell DM, *et al.* An official American Thoracic Society/European Respiratory Society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2013;188:733–48.
- 8 Rozin AP, Nahir AM. Is SAPHO syndrome a target for antibiotic therapy? *Clin Rheumatol* 2007;26:817–20.
- 9 Schilling F, Wagner AD. [Azithromycin: an anti-inflammatory effect in chronic recurrent multifocal osteomyelitis? A preliminary report]. *Z Rheumatol* 2000;59:352–3.
- 10 Poletti V, Cazzato S, Minicuci N, *et al.* The diagnostic value of bronchoalveolar lavage and transbronchial lung biopsy in cryptogenic organizing pneumonia. *Eur Respir J* 1996;9:2513–6.
- 11 Martinez JA, King TE, Brown K, *et al.* Increased expression of the interleukin-10 gene by alveolar macrophages in interstitial lung disease. *Am J Physiol* 1997;273:L676–83.
- 12 Hurtado-Nedelec M, Chollet-Martin S, Nicaise-Roland P, *et al.* Characterization of the immune response in the synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome. *Rheumatology* 2008;47:1160–7.

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