Rare disease

SAPHO syndrome with bacillus Calmette-Guérin (BCG) immunotherapy for bladder cancer

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Summary

The authors describe a case of SAPHO syndrome with bacillus Calmette-Guérin (BCG) immunotherapy for bladder cancer. The patient had undergone transurethral resection (TUR) and was treated with BCG immunotherapy following TUR. Two years after treatment for bladder cancer, the patient had palmoplantar pustulosis, and in the past 1 month suffered from pain localised to the anterior chest wall. The bone scintigraphy showed a strong focal enrichment in the right chest wall, suggesting spondyloarthropathy rather than malignant disease. On the basis of clinical and scintigraphy findings, SAPHO syndrome was diagnosed. The patient was treated with topical therapy and non-steroidal anti-inflammatory drugs and symptoms improved. The authors suggest that SAPHO syndrome might be caused by an association with BCG immunotherapy.

BACKGROUND

SAPHO syndrome is a rare disease, and is an acronym for synovitis, acne, pustulosis, hyperostosis and osteitis.¹ This disease affects both skin and bones, mainly in the costal area and anterior chest wall. The aetiology of SAPHO syndrome seems to involve genetic, infectious and immunological components. Treatment of the SAPHO syndrome is predominantly conservative. On the basis of aetiology, the treatment of SAPHO syndrome should include non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids,² antibiotics,³ bisphosphonates,⁴ tumour necrosis factor α (TNF α) antagonists^{5 6} and a combination of isotretinoin and pamidronate.⁷ Surgery is the ultimate treatment. There has been no report of SAPHO syndrome with cancer. Our patient had a history of bladder cancer. We performed the procedure to rule out metastasis and diagnosis of SAPHO syndrome was made on the basis of characteristic bone scintigraphy findings and skin manifestations. Therefore, we suggest that the SAPHO syndrome might be considered as differential diagnosis in patients with cancer with treatment including immunological component. An awareness of SAPHO syndrome is important to avoid unnecessary treatment and repeated invasive procedures.

During the past three decades, BCG immunotherapy has been used successfully to treat superficial bladder cancer.⁸ It is proposed that a scoring model be used to stratify the risk of recurrence and progression in patients treated with BCG.⁹ Patients without recurrence had greater increased urothelium expression of antigen-presenting molecules and chemokines after BCG immunotherapy. These parameters might, therefore, serve to predict and monitor the efficacy of BCG immunotherapy.¹⁰ Correlation between interleukin (IL)-8 secretion rate and recurrences in induction BCG immunotherapy following TUR in cases of primary non-muscle-invasive bladder cancer was suggested. Besides numerous other prognostic factors that have been suggested so far, IL-8 levels after BCG immunotherapy

appears to be a good predictive factor for successful outcome in BCG immunotherapy following TUR.¹¹ An aetiology of SAPHO syndrome seems to involve immunological components. For example, SAPHO syndrome was associated with elevated IL-8 and IL-18 plasma levels.¹² Unfortunately, a limitation of our study is that measurements at the immunological component level, after treatment of BCG for bladder cancer, were not available. However, there might be an association between onset of SAPHO syndrome and BCG immunotherapy.

CASE PRESENTATION

We present the case of an 80-year-old woman with a 10-year history of hypertension, arrhythmia, ischemic heart disease, hyperlipidaemia, neuritis and gastritis. She had been treated with amlodipine besilate, pilsicainide hydrochloride, ubidecarenone, dipyridamole, nitroglycerin, simvastatin, mecobalamin, tocophenol acetate, etizolam and nizatidine. In 2006, she experienced frequent urination. A detailed examination was conducted and she was later diagnosed with bladder cancer. She had undergone TUR and adjuvant treatment with BCG immunotherapy. Post-treatment, the patient is stable without recurrence of disease.

She had experienced palmoplantar pustular skin lesions in October 2008 (figure 1) and received topical therapy that included tacalcitol and diphenhydramine laurylfate. In the past 1 month, she additionally complained about progressive breath- and movement-dependent pain of the sternum.

Laboratory examination revealed no inflammatory reaction, C-reactive protein level of 0.04 mg/dl (normal: <0.05 mg/dl) and white blood cell count of 5600/mm³ (normal: 3900–9000/mm³). Biochemistry results were as follows: aspartate aminotransferase, 18 IU/l (normal: <32 IU/l); alanine aminotransferase, 19 IU/l (normal: <34 IU/l); γ -glutamyl transpeptidase, 7 IU/l (normal: 8–60 IU/l); lactic

Figure 1 Skin lesion on the hand.

dehydrogenase, 176 IU/l (normal: 250–450 IU/l); alkaline phosphatase, 299 IU/l (normal: 93–271 IU/l); and creatinine, 0.72 mg/dl (normal: <1 mg/dl).

We performed a bone scintigraphy (figure 2), which showed abnormal uptake in sternocostoclavicular joint. She typically presented with a musculoskeletal complaint, frequently localised to the anterior chest wall, and skin involvement occurred simultaneously with bone manifestation. On the basis of the results of the physical and radiographic examination, SAPHO syndrome was diagnosed.

The patient received physical therapy that included NSAIDs for chest pain and topical therapy for skin involvement. Treatment was successful, and after 6 months, there were no clinical symptoms.

INVESTIGATIONS

We describe a patient with SAPHO syndrome, who underwent treatment with BCG immunotherapy for bladder cancer. We performed the procedure to rule out metastasis, and a diagnosis of SAPHO syndrome was made based on the characteristic bone scintigraphy findings and skin manifestations. An accurate diagnosis of SAPHO syndrome requires careful clinical and radiological examinations. Awareness of SAPHO syndrome is necessary to make an accurate diagnosis and to prevent inappropriate and unnecessary treatment.

The aetiology of SAPHO syndrome is uncertain and seems to involve genetic, infectious and immunological components, including elevated IL-8 and IL-18 plasma levels and IL-8 and TNF α production. BCG immunotherapy is the most effective therapy for bladder cancer. Numerous

prognostic factors, including IL-8, have been suggested. There might be an association between the onset of SAPHO syndrome and BCG immunotherapy.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis includes chronic, recurrent, multifocal osteomyelitis; infectious osteomyelitis; arthritis; primary or metastatic tumours; and Paget's disease. The diseases with systemic manifestations may mimic conditions.

TREATMENT

Based on aetiology, treatment of SAPHO syndrome should include NSAIDs, corticosteroids, antibiotics, bisphosphonates, TNF α antagonists and a combination of isotretinoin and pamidronate. Treatment of the SAPHO syndrome is predominantly conservative. In this case, the patient had only symptomatic relief, and treatment consists of topical therapy and NSAIDs for skin involvement and chest pain.

OUTCOME AND FOLLOW-UP

The patient runs a protracted course, with remissions, but without serious disability. However, we have to observe the clinical course, especially intermittent relapses, due to the immunological component of the SAPHO syndrome.

DISCUSSION

SAPHO syndrome is a rare disorder and there has no report of this with cancer. In this study, the patient had a history of bladder cancer and was treated with BCG immunotherapy.

Figure 2 Bone scintigraphy of whole body showing abnormal uptake in the sternoclavicular joint, especially strong accumulation in manubrium of sternum and mild accumulation in sternocostoclavicular joint.

We performed the procedure to rule out metastasis, and diagnosis of SAPHO syndrome was made on the basis of characteristic bone scintigraphy findings and skin manifestations. SAPHO syndrome should be included in the differential diagnosis in cases undergoing treatment for cancer. An awareness of SAPHO syndrome is important to avoid unnecessary treatment and repeated invasive procedures.

A relationship between the efficacy of BCG immunotherapy and immunological reaction, especially IL-8, is reported. The aetiology of SAPHO syndrome seems to involve immunological components. We suggest that the cause of SAPHO syndrome might be related to BCG immunotherapy for bladder cancer.

Learning points

- In the cases with pustulosis, we have to consider skeletal lesions of chest wall (clavicle, sternum and sternoclavicular), and a diagnostic procedure should be undertaken.
- The patients being treated for malignant tumour, wherein the treatment enhances immunological activity, might be diagnosed with SAPHO syndrome.
- In patients with cancer being treated with immunological components, the SAPHO syndrome should be considered as differential diagnosis.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Matsumaru K, Nagai K, Murakami T, Andoh K. SAPHO syndrome with bacillus Calmette-Guérin (BCG) immunotherapy for bladder cancer. *BMJ Case Reports* 2010;10.1136/bcr.12.2009.2591, date of publication

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