Lofgren's syndrome

Introduction

Lofgren's syndrome is an acute and usually benign form of sarcoidosis affecting younger adults. It is characterized by the coincident features of ankle swelling, with or without erythema nodosum and bilateral hilar adenopathy (Perruquet et al, 1984). Uveitis, parotitis and fever may also occur but parenchymal pulmonary and hepatic involvement is less common (Mana et al, 2007). It is believed to be a CD4 positive T cell-mediated response to an unknown antigen with characteristic non-caseating granulomatous inflammation typically with giant cells (Spilberg et al, 1969). Women often present with erythema nodosum, while men more often exhibit bilateral ankle swelling (Grunewald and Eklund, 2007) as a result of synovitis, tenosynovitis or periarticular inflammatory oedema (Arnold, 1993). This case is presented to make clinicians aware of the acute sarcoid presentation and to avoid incorrect diagnosis.

Discussion

Acute sarcoid (Lofgren's syndrome) has an estimated prevalence rate of 10–12 per 100 000 population with a slight predominance of females and a peak incidence between 20 and 39 years of age which increases in the spring (Badrinas et al, 1989). The highest annual incidence of all cases of sarcoidosis has been observed in northern European countries (5–40 cases per 100 000 population), where the highest incidence of Lofgren's syndrome is also found, in contrast to the very low frequency in subjects of African origin living either in Europe or North America.

Symptoms of Lofgren's syndrome may be restricted to ankle swelling alone, especially in young men, and other diagnoses are often considered first. If erythema nodosum becomes confluent it may be misdiagnosed as an infective cellulitis. The condition is usually self-limiting but may run an indolent course.

Lofgren's syndrome (acute sarcoidosis) varies in severity and distribution from single to multisystem inflammation. In the majority of cases it resolves spontaneously within 12 months, but in a small proportion of cases, 6% in one follow-up study over 5 years, it may progress to chronic sarcoidosis with severe functional impairment of one or more organs. An overall mortality rate for sarcoidosis of up to 4.8% was reported from one large referral centre (Reich, 2002).

The combination of erythema nodosum or bilateral ankle periarthritis and radiological evidence of bilateral hilar adenopathy, with or without an elevated serum angiotensin-converting enzyme level, is usually sufficient to make a diagnosis if other causes can be reasonably excluded, e.g. tuberculosis or lymphoma. Non-invasive tests include a negative tuberculin skin test (mantoux) and a gallium-67 scan which may be positive when the chest radiograph is normal or equivocal. Tissue biopsy is only required when clinical features are insufficient alone.

The presentation of Lofgren's syndrome with ankle swelling (Hedfoss and Lindstrom, 1983), bilateral hilar adenopathy and erythema nodosum represents 9–34% of all cases of sarcoidosis (Stiltzbach et al, 1974). Fatigue, night sweats and weight loss are common. Erythema nodosum is observed predominantly in women, and more commonly in caucasian women rather than those of Asian or African ethnicity. Ankle joint involvement is a common presentation of acute sarcoidosis (Berkman, 1985). Two thirds of all sarcoidosis patients have a remission within a decade of diagnosis with few or no consequences. Unfortunately up to one third of patients have unrelenting disease, leading to clinically significant organ impairment.

Most cases are diagnosed by clinical and radiographic manifestations. In addition to chest radiography, measurement of pulmonary function, including total lung capacity and diffusion capacity, should be performed. The classic radiological assessment of sarcoidosis remains the routine chest roentgenogram (Hunninghake et al, 1999). Serum angiotensin-converting enzyme levels, when elevated, will help confirm suspected cases but when normal may indicate a self-limiting disease course. Other non-invasive tests, e.g. gallium scanning and mantoux testing, may be useful but tissue biopsy is rarely required.

The condition usually remits spontaneously with a low percentage of recurrence and may not require any treatment. Non-steroidal anti-inflammatory drugs are often needed but corticosteroids are rarely required for uncomplicated acute Lofgren's except when parenchymal lung disease, parotitis, uveitis or significant hepatic involvement is present. Chronic disease treatment depends upon disease activity and severity. Corticosteroids, hydroxychloroquine and, less frequently, immunosuppressive agents such as methotrexate, ciclosporin or azathioprine are required. Rarely in refractory sarcoid, anti-tumour necrosis factor agents or cyclophosphamide are used.

Conclusions

Lofgren's syndrome is an acute presentation of sarcoid. It involves young people with combination of hilar adenopathy, sym-

Dr K Sanyal *is Speciality Registrar in Clinical Rheumatology and Internal Medicine and* **Dr BE Bourke** *is Consultant Rheumatologist in the Department of Rheumatology, St George's Hospital and University, London SW17 0QT*

Correspondence to: Dr K Sanyal (ksanyal01@doctors.org.uk)

Case Report

A previously fit 24-year-old Caucasian woman presented with a 4-week history of painful swollen ankles with fatigue. There was no history of cough or breathlessness. Clinical examination revealed multiple lesions of erythema nodosum on the lower legs with bilateral erythematous ankle swelling. Chest and general examination was normal with no lymphadenopathy. Laboratory investigations included erythrocyte sedimentation rate 31 mm/hr (normal range 1–10 mm/hr), C-reactive protein 21.7 mg/litre (normal range 0–5 mg/litre), adjusted calcium 2.39 mmol/litre (normal range 2.1–2.55 mmol/litre), serum angiotensin-converting enzyme level 61 U/litre (normal range 8.0–52.0 U/litre) and a thrombocytosis (platelets 508 000/mm^3). Chest X-ray showed evidence of bilateral hilar adenopathy. The diagnosis of Lofgren's syndrome was confirmed by the symptoms, signs and chest X-ray findings.

metrical polyarthritis, eye inflammation and erythema nodosum. It is mostly self-limiting and has a good outcome. **BJHM**

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LEARNING POINTS

- In younger adults presenting with bilateral ankle pain and swelling, a chest X-ray is essential.
- The condition may occur in the overt absence of erythema nodosum, especially in young men.
- Lofgren's syndrome almost always follows a benign course to total remission.