

# Acute Form of Sarcoidosis: Löfgren's Syndrome

## Akute Form der Sarkoidose: Löfgren-Syndrom

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### Bibliography

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### Abstract

▼ Löfgren's syndrome, an acute form of sarcoidosis, is the combination of bilateral hilar lymphadenopathy (BHL), erythema nodosum (EN) and polyarthralgia or arthritis. Unlike sarcoidosis, Löfgren syndrome has good prognosis and a lower relapse rate. A 58-year-old woman was admitted to our

department complaining of arthralgia, rashes on the pretibial region and other nonspecific symptoms such as fever, cough and weakness. Based on clinical symptoms, radiological and histological findings we diagnosed Löfgren's syndrome. The patient was treated with Prednisolone 0,5 mg/kg/day for six months and acute arthralgia as well as erythema nodosum disappeared.

### Case Report

▼ A 58-year-old woman was admitted to our hospital with a dry cough, weakness and fever. She had a history of acute arthralgia and erythema nodosum 3 weeks before admission. At home, she was using non-steroidal anti-inflammatory drugs (NSAIDs) and amoxicillin, but there was no effect. Clinical examination showed symmetrical erythema nodosum lesion on the pretibial region (● Fig. 1) and mild swelling in both ankles. Laboratory findings showed non-iron deficiency anaemia, thrombocytosis, elevated level of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), 158.95 mg/l and 66 mm/h, correspondingly. angiotensin-converting enzyme (ACE), liver enzymes, creatinine and glucose test were revealed no pathological results. Blood and urine cultures, immunological laboratory findings of systemic connective tissue diseases were negative. Chest radiography and thoracic computed tomography (CT) (● Fig. 2) revealed bilateral hilar lymphadenopathy. A biopsy specimen of mediastinal lymph nodes revealed a non-caseating granuloma with giant cells. Histopathology of skin lesions demonstrated subcutaneous inflammatory infiltration, swollen vascular endothelium with nucleus debris (● Fig. 3). Based on clinical symptoms, radiological and histological findings we diagnosed Löfgren's syndrome. The patient was treated with Cefuroxime 4,5 g/day intravenously, Ibuprofen 1,2 g/day, Prednisolon 0,5 mg/kg/day and clobetasol ointment 0,05% once daily.

After six months weakness, acute arthralgia and erythema nodosum receded.

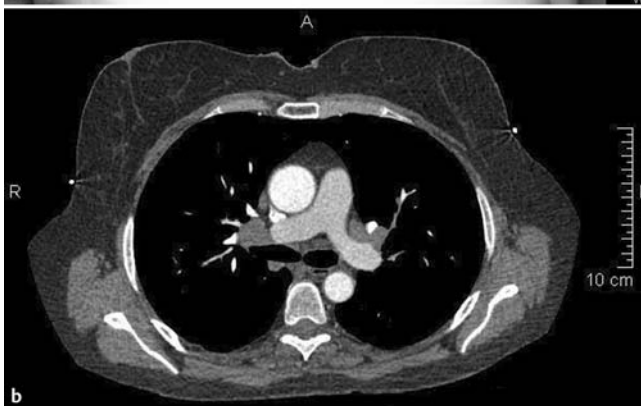
### Discussion

▼ Sarcoidosis is an inflammatory disorder presenting with granuloma formation, most commonly in the lungs (88%), lymph nodes, eyes and skin [1]. Löfgren's syndrome is an acute subtype of sarcoidosis presenting with the classical triad: bilateral hilar lymphadenopathy (BHL), erythema nodosum and polyarthralgia or arthritis [2]. Some studies have shown that 35% of all sarcoidosis cases are Löfgren's syndrome [12]. The main feature is erythema nodosum, which according to Mañá J et al. occurs in approximately 93% cases [3], with a predominance amongst women (67%) compared with men [4]. BHL and symmetrical self-limited polyarthralgia occur in 22% of the Löfgren's syndrome cases [2]. Polyarthralgia usually is symmetrical, involving ankles (more than 90% of the cases), knees and small joints of the hands or feet, wrists and elbows (15% to 40%) [5]. Chronic or iterative arthritis in Löfgren's syndrome is rare, affecting 1% to 4% of patients [6]. Periarticular inflammation of the ankles or ankle arthritis without erythema nodosum is mostly seen in men [5].

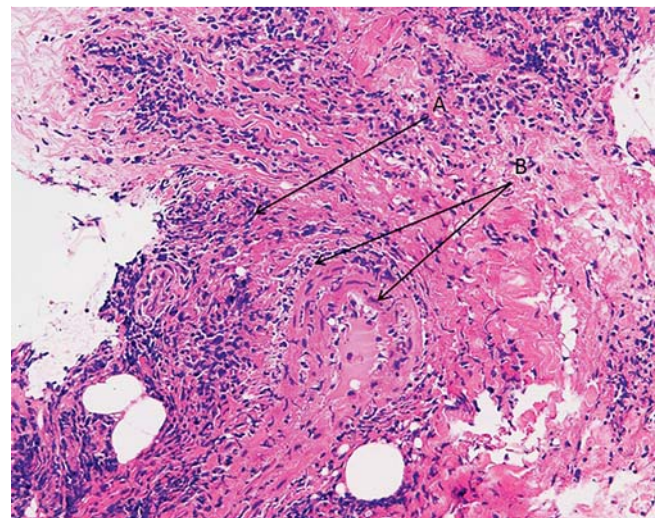
In a case of Löfgren's syndrome chest X-ray shows the BHL or pulmonary infiltration, serum calcium level might and serum ACE might be increased in 50% of cases, ESR or CRP level is elevated in more



**Fig. 1** a,b Erythema nodosum. A nodular eruption with an erythematous appearance.



**Fig. 2** Chest radiography (a) and computed tomography (b): bilateral hilar lymphadenopathy.



**Fig. 3** Dermatohistopathology: **A**, septal subcutaneous inflammation (panniculitis) containing neutrophils, eosinophils, and lymphocytes as well as fibroblast proliferation. **B**, vascular endothelium swelling, visible nucleus debris.

than 80% of patients with acute polyarthritis [3]. Some authors state that lymph node biopsy is a safe and economical diagnostic method [7], while others note that histologic confirmation is not required unless there are atypical features [3]. The differential diagnosis of BHL includes lymphoma, fungal infection, tuberculosis, lung cancer [8] and others. Polyarthralgia is often observed in various collagen diseases, including rheumatoid arthritis. Erythema nodosum can be also caused by other diseases e.g. infection (*Streptococcus* spp., tuberculosis, mycoplasma, cellulitis [9]), drugs, inflammatory bowel disease, non-Hodgkin's lymphoma and others [10].

The acute form of sarcoidosis was originally described by Sven Halvar Löfgren (1910–1978), a Swedish clinician. In 1953, Löfgren characterized 212 adult patients with BHL who were diagnosed with sarcoidosis on the basis of absence of tuberculosis. Löfgren demonstrated that erythema nodosum was present at the onset of the disease in 113 cases in which articular symptoms were common [5].

Löfgren's syndrome is more frequent amongst young white women, especially from Scandinavian countries and Ireland, but is less common in black people [3]. Sarcoidosis can appear at any age, but typically develops between ages of 20–29 [11]. According to some previous studies there is a second morbidity pike in women over the age of 50, especially in Scandinavian countries and Japan [12]. The syndrome is rare between young children and teenagers and elder people over the age of 70 [13]. Females are three times more likely to have Löfgren's syndrome than males [14], significantly frequent in springtime compared to wintertime [15].

Past studies suggest, that environmental, occupational factors, contacts with dust or chemicals may trigger the disease [16]. A large US-based case-control study identified several exposures associated with sarcoidosis risk, including insecticides, agricultural employment, and microbial bioaerosols such as molds and mildews [16]. Terčelj M et al. report that fungi play a role in the pathogenesis of sarcoidosis, because peripheral blood monocytes from patients show higher reactivity to fungal cells [17]. Metal-working-fluid can cause sarcoidosis due to the bacterial or fungal contamination of the fluids and aerosols during the work [17].

Also genetic factors influence the risk for the disease. Genes localized to the human leukocyte antigen (HLA) region on the chromosome 6 are very important. In patients with Löfgren's syndrome the absence of HLA-DRB1\*03 increases the risk for extrapulmonary manifestations of the skin or enlarged lymph nodes and in 49% of the cases developed a non resolving disease, while almost every DRB1\*03-positive patient had a resolving disease during 2 years [18]. Also the influence of various polymorphisms in the C-C chemokine receptor 2 (CCR2) gene on chromosome 3 was investigated. Studies show that one particular haplotype (CCR2) is related to an increased risk of Löfgren's syndrome [19]. Löfgren's syndrome does not show any specific biomarkers, consequently the diagnosis is based on clinical manifestation and a good self-limiting prognosis with spontaneous remission [3]. The treatment of most patients with Löfgren's syndrome is symptomatic, usually, with the use of anti-inflammatory drugs, oral corticosteroids and in severe cases systemically acting drugs (methotrexate, thalidomide, cyclophosphamide and azathioprine) [2].

### Conflict of Interest

The authors declare no conflict of interest.

### Zusammenfassung

#### Akute Form der Sarkoidose: Löfgren-Syndrom

Eine spezifische akute Form der Sarkoidose – Löfgren-Syndrom – manifestiert als Kombination aus bilateraler Hiluslymphadenopathie (BHL), Erythema nodosum und Polyarthralgie oder Arthritis. Im Gegensatz zur Sarkoidose hat das Löfgren-Syndrom eine gute Prognose. Eine 58-jährige Frau wurde in unsere Klinik wegen Arthralgie, akutem prätibialem Erythema nodosum, Fieber, Husten und allgemeiner Schwäche aufgenommen. Basierend auf den klinischen, radiologischen und histologischen Befunden wurde ein Löfgren-Syndrom diagnostiziert. Die Patientin wurde mit Prednisolon 0,5 mg/kg pro Tag sechs Monate lang behandelt. Alle Krankheitssymptome zeigten eine Remission.

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