Case report

CHILDHOOD SARCOIDOSIS: A CASE REPORT

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ABSTRACT

Childhood sarcoidosis is a rare multisystemic granulomatous disorder of unknown etiology. The diagnosis is often delayed due to lacking of recognition of clinical features.

We report a 23 month-old boy who presented with multiple pinkish papules and painless cystic swellings in his ankles and wrists. A skin biopsy showed multiple sarcoidal granulomatous lesions. He was treated with steroids and had a good response. Childhood sarcoidosis is characterized by arthritis, uveitis, and cutaneous involvement. Glucocorticoids remain the first choice therapy for children with multisystem involvement. The prognosis of early-onset childhood sarcoidosis varies in different studies due to the rarity of the disease.

Keywords: *Childhood sarcoidosis, granulomatous disorder, arthritis, uveitis*

I. INTRODUCTION

Sarcoidosis is a systemic granulomatous disorder of unknown cause characterized by the presence of non-caseating granuloma. Its clinical features are protean, with a disease expression ranging from symptomatic in dividuals with abnormal chest radiographs to multiorgan failure. Although many organ systems can be involved, the lung is most commonly affected and accounts for the majority of morbidity and mortality from the disease. Sarcoidosis is well recognized in adults and is most commonly diagnosed between the ages of 20 and 40 years, but it can also occur in children. Although sarcoidosis in children maybe underdiagnosed, it is in fact quiter are in the pediatric age [1].

The diagnosis is often delayed because of the lack of awareness and unfamiliarity with its clinical features. The clinical triad of this rare disease is skin rash, arthritis and uveitis, whereas the typical presentation of hilar lymphadenopathy, pulmonary infiltration and systemic involvement in late-onset type, as well as adult type, is rarely seen [2]. The prognosis of early-onset childhood sarcoidosis varies in different studies due to the rarity of the disease. The choice of treatment of childhood sarcoidosis is corticosteroids.

II. CASE PRESENTATION

A23-month-old boy visited our hospital with multiple pinkish papules and some confluence into papular plaques with scales. Lesions were symmetrically distributed over both cheeks, forearms, back, shanks. He also presented with painless cystic swelling inankles and wrists **(Figure 1)**.

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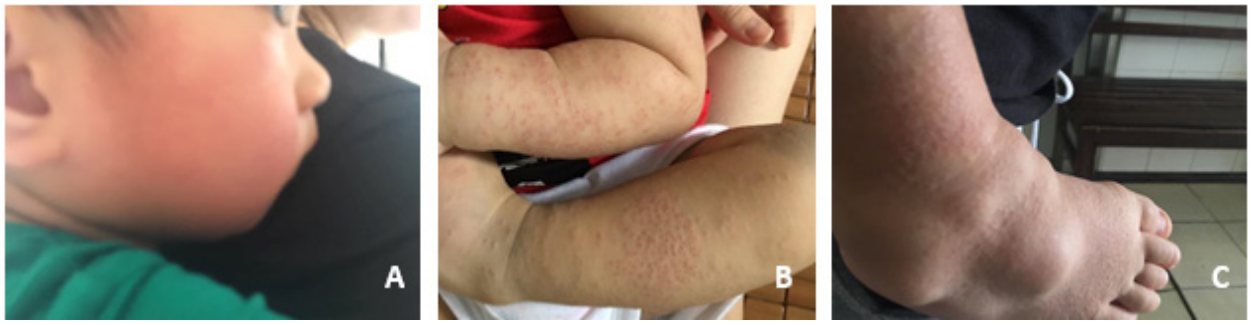

Figure 1: Multiple pinkish papules and some confluent papuloplaques with scaling distributed over cheeks (A), shanks (B). Cystic swelling in ankles (C)

About his clinical history, at the age of 7 months, the patient had multiple erythematous papules, distributed over the trunk and extremities and swelling in ankles. He was diagnosed with synovitis, got low dose corticoid and the rash improved but the swelling ankles did not disappear. However, the swelling ankles were painless so that he stopped getting corticoid. After that, the rash appeared many times, his mother gave him corticoid without a doctor's examination.

16 months later, he came to our hospital with papular plaques with scales over cheeks, trunk, shanks and cystic swellings in ankles and wrists. His mother noticed that he had red eyes. He had no fever, well feeding, no joints pain, no diarrhea, no cough.

A series of examinations were performed during this period. Chest X-ray examination, abdominal ultrasound showed normal. Ankles ultrasound revealed thickened synovium, hydrarthrosis, tendon sheath effusions. Complete blood count, electrolytes, liver function, renal function were normal. Tests for antinuclear antibody and rheumatoid factor were negative, and assays for complement components C3 and C4 were within normal ranges.

Skin biopsy was performed and showed multiple sarcoidal granulomatous lesions without caseous necrosis, and Langerhans cells **(Figure 2)**. The fungal test was negative. Childhood sarcoidosis was diagnosed. Ophthalmologic examination was not performed because the patient did not cooperate.

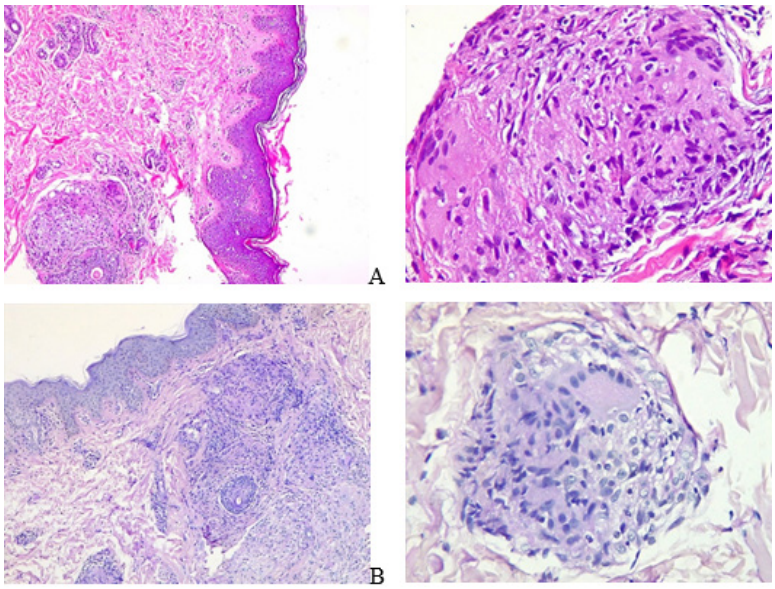

Figure 2: Tissue biopsy of the papular lesion showed noncaseating granulomas infiltrating the dermis. (A) hematoxylin and eosin, original magnification; (B) PAS (-)

After treatment with 20 mg/day (2mg/kg/day) prednisolone, the rash improved within 2 weeks and the cystic ankles, wrists disappeared after 5 weeks. The patient has been regularly followed up in our pediatric department, steroid dosage was recently tapered because of the stable clinical condition.

III. DISCUSSION

Childhood sarcoidosis is a rare entity with two distinct forms: early-onset and late-onset disease. Early-onset childhood sarcoidosis, with onset in the first 5 years of life differs from sarcoidosis in older children and adults and often poses a diagnostic challenge to the clinician. Typically presenting in the first year of life, patients with the early-onset disease exhibit unique clinical features characterized by the triad of arthritis, rash, and uveitis [3]. Hilar lymphadenopathy, the leading feature of late-onset forms [4], is rare in early-onset sarcoidosis. Uveitis, which occurs in more than half of the children with early-onset sarcoidosis, is relatively less common in patients with later-onset [3].

There is no laboratory test diagnostic of sarcoidosis, the World Association of Sarcoidosis and Other Granulomatous disorders (WASOG) only recommends dosing the serum angiotensin-converting enzyme (ACE). Its level is usually higher in children than in adults, but an increased ACE may help in the diagnosis [5]. The diagnosis of sarcoidosis is based on compatible clinical presentation and the gold standard is the typical epithelioid gigantocellular granuloma without caseating necrosis granuloma, from the biopsy of an affected organ. Other causes of granuloma such as mycobacterial, bacterial and fungal infection need to be ruled out.Childhood sarcoidosis is especially difficult to diagnose because of its variable presentation and ability to mimic other diseases [6].

Table 1: Histologic Classification of Cutaneous Granulomatous & Non - neoplastic Histiocytic Diseases [7]

Histologic Classification of Cutaneous Granulomatous & Non - neoplastic Histiocytic Diseases		
Necrobiotic/ Necrotizing - Granuloma annulare - Necrobiosis lipoidica - Rheumatoid nodules - Lupus miliaris disseminates faciel (variant of granulomatous rosacea) - Infections Mycobacterial Fungal Parasitic	Non - Necrobiotic/ Necrotizing - Sarcoidosis - Foreign body reactions - Melkersson - Rosenthal syndrome - Granulomatous rosacea - Elastolytic granuloma - Cutaneous Crohn disease - Granulomatous pigmented purpura - Interstitial granulomatous dermatitis - Lichennoid & granulomatous dermatitis - Blau syndrome Infections (mycobacterial, fungal…)	Histiocytic but non-granulomatous - Malakoplakla - Infections Leishmaniasis Histoplasmosis Lepromatous leprosy.

Skin lesions are the most common presentation in early-onset childhood sarcoidosis [7]. It occurs in 77% of early-onset sarcoidosis and 24-40% of late-onset cases [8]. The most typical skin eruption in early-onset childhood sarcoidosis is asymptomatic, discrete, macular and papular rash; it first appears on

the face and extremities and subsequently spreads to the trunk [9,10]. Soft, red to yellowish-brown, flat-topped papules appear most frequently on the face. Other skin eruptions including nodules, hyperpigmented or hypopigmented lesions, ulcers, and subcutaneous tumors can also be found [8,9].

Cutaneous sarcoidosis is usually an early manifestation of the disease, prompting the necessity to evaluate for systemic involvement, regardless of the percentage of skin surface affected. The skin is a convenient source for tissue and histologic diagnosis. The diagnosis of sarcoidosis is more rapid in patients with cutaneous sarcoidosis than other forms of the disease [7-9].

In our patient, the skin lesion first appeared when he was 7 month-old. The appearance and distribution of the skin lesion changed during treatment and adjustment of medication. Owing to the skin biopsy, we found the lesion granuloma without caseating necrosis, which suggested us sarcoidosis basing on the histologic classification of cutaneous granulomatous & non - neoplastic histiocytic diseases [7].

Uveitis or iritis is the most common ocular manifestation in 90% of cases of early-onset childhood sarcoidosis. However, early ocular involvement is asymptomatic, in our case, the boy had red eyes but the iritis was not confirmed because he had not cooperated for ophthalmologic examination. If left untreated, serious complications including blindness can occur [3].

Arthritis has been reported in 15% to 58% of children with sarcoidosis. Arthritis in early-onset childhood sarcoidosis is persistent, relatively painless, nondestructive, and affects predominantly the large joints. A good range of joint movement characterized by synovial proliferation and tendon sheath effusions is noted [11,12]. As in our patient, no destruction of joints and no limitation of movement is noted after long-term follow-up.

The diagnosis of early-onset childhood sarcoidosis should be distinguishable from juvenile rheumatoid arthritis, which is also characterized by a combination of skin, joint and eye manifestations [9]. Juvenile rheumatoid arthritis is characterized by painful joints with limitation of movements and destructive changes on radiographs. There is no method of distinguishing the uveitis that occurs in these two conditions; however, the antinuclear antibody test is positive in 88% of patients with juvenile rheumatoid arthritis but negative in sarcoidosis [12]. Skin changes may appear distinct between the two diseases at onset. The rash in juvenile rheumatoid arthritis is pink, evanescent and macular, whereas the eruption in early-onset childhood sarcoidosis is papules or plaques with scaling [11].

The current treatment of choice for childhood sarcoidosis with multisystemic involvement is corticosteroid. Cutaneous lesions and arthritis generally respond to therapy administered for systemic involvement but may recur after the treatment is discontinued [2].

The prognosis and natural history of sarcoidosis in children are unclear because of the rarity of the disease and the small number of reported cases [8]. In a Danish follow-up study, 80% of the subjects recovered completely without functional impairment [6,13].

In total, 46 ethnic Caucasian Danish children (aged,16 yrs, 24 males) with sarcoidosis were identified and median (range) clinical follow-up was 15 (3-23) yrs after onset of disease. At follow-up: 36 (78%) children recovered completely; 30 (65%) showed complete clinical regression at a median (range) 0.7 (0.6-5.9) yrs after onset of disease; two (4%) recovered with organ damage (unilateral loss of vision, abnormal chest radiograph); five (11%) still had chronic active disease with multiorgan involvement and impaired lung function; and three (7%) were deceased, due to central nervous system sarcoidosis and acute myeloid leukaemia probably caused by cytostatics. In Danish children,

sarcoidosis had a favourable prognosis; the majority recovered, 6 yrs after onset of disease. Some developed chronic active disease and impairment of pulmonary function, demanding continuous medical treatment. The prognosis was not related to the age at onset of disease. Erythema nodosum was associated with a good prognosis, and central nervous system involvement with a poor prognosis [13].

Blau syndrome and its sporadic counterpart, early-onset sarcoidosis, share an identical phenotype featuring the classic triad of arthritis, dermatitis, and uveitis and are associated with mutations of *CARD15* in 50-90% of cases. Further studies are required to understand better the long-term prognosis of this disease [7].

IV. CONCLUSION

Here, we presented a rare case of a typical presentation of early-onset childhood sarcoidosis. It is characterized by arthritis, uveitis, and cutaneous involvement. Notably, skin manifestations are very common in this type. This case reminds us to include childhood sarcoidosis in the differential diagnosis in pediatric patients who present with multiple papular eruptions along with systemic manifestations. It is necessary to perform skin biopsy to orient the diagnosis.

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