Preschool Sarcoidosis

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Abstract

Sarcoidosis is a multisystemic granulomatous disorder of unknown etiology, most commonly affecting young adults and presenting most frequently with bilateral hilar lymphadenopathy, pulmonary infiltration, and skin or eye lesions. Sarcoidosis in children under the age of 4, preschool sarcoidosis, is rare and has very different clinical mainfestations characterized by the typical triad of skin, eye and joint involvement without lung disease. Diagnosis is established when compatible clinical findings are supported by histological evidence of widespread noncaseating epithelioid-cell granulomas in more than one organ or a positive Kveim-Siltzbach skin test. This report describes a 2-year-old Thai girl with typical clinical manifestations of preschool sarcoidosis. The histopathological studies of tissue specimens and the laboratory investigations support the diagnosis of sarcoidosis. The patient responded to systemic corticosteroid therapy.

Key word : Preschool Sarcoidosis, Sarcoidosis

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Sarcoidosis is a chronic, multisystemic, granulomatous disorder of unknown etiology which mainly affects young adults between the ages of 30 and 40. It is relatively uncommon in children and most child cases occur between 9 and 15 years of age. The clinical features vary according to age. The disease in older children and adults usually presents with a combination of lung, lymph node and eye involvement[1-5]. Sarcoidosis in children under the age of 4, preschool sarcoidosis, has very different clinical manifestations characterized by the typical triad of skin, eye and joint involvement

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without lung disease[6-8]. Sarcoidosis is worldwide in distribution and the prevalence varies by geographic region, both between and within countries. Prevalence is high in Sweden, Scandinavia, the United Kingdom and the United States[9,10]. Up to now, only about 60 cases of early onset sarcoidosis have been reported and the youngest patient was a 2-month-old boy[11,12]. Epidemiologic data are not complete for the Far East except for Japan [13,14]. Sarcoidosis is very rare in Thailand and nearly all cases reported have been adults[15]. There have been only 2 pediatric cases in Thailand, a 12-year-old boy presenting with generalized massive lymphadenopathy[16] and a 3-year-old girl with hypertensive encephalopathy[17].

In this report, we describe a typical case of preschool sarcoidosis in a young girl.

CASE REPORT

A 2-year-old Thai girl from Nonthaburi Province was admitted to the Department of Pediatrics, Siriraj Hospital, in June 1997 because of skin rash and joint swelling. She was well until 4 months of age, when she developed pruritic dry erythematous rash on her trunk and extremities which was diagnosed as atopic dermatitis and treated successfully with topical emoillient and steroids. At age 8 months, she had swelling of her wrist, ankle and knee joints with mild tenderness and limitation of movement. The skin lesions changed to small brownish papules. Her physical growth and development were normal but she refused to walk because of discomfort in the legs.

Physical examination on admission revealed generalized dry skin with brownish red, flat-topped papules on her extremities, trunk and neck (Fig. 1). Her fingers were fusiformly swollen (Fig. 2). The wrist, knee and ankle joints were swollen without signs of inflammation, which caused significant limitation of movement. Generalized lymphadenopathy was present in the cervical, axillae and inguinal areas. The liver and spleen were enlarged and extended below the costal margin 4 and 2 cm, respectively. Ophthalmoscopic examination by slit-lamp microscope revealed bilateral corneal opacity and synechiae. The remainder of her physical examination was normal.

Initial laboratory studies showed a hemoglobin level of 10.6 g/dL, a hematocrit level of 33.4 per cent, and a white blood cell count of 13,000 cells per mm^3 with 55 per cent polymorphonuclear leukocytes, 34 per cent lymphocytes, 5 per cent monocytes and 6 per cent eosinophils. Liver function tests revealed elevated alkaline phosphatase 163 U/L (normal 39-117) and globulin 3.9 g/dL (normal 2.5-3.5). Serum protein electrophoresis showed polyclonal hypergammaglobulinemia. The Westergren erythrocyte sedimentation rate was 45 mm/h and the c-reactive protein was positive. Radiograph of the chest did not demonstrate pulmonary infiltration or lymph node enlargement. Bone radiograph showed subarticular osteoporosis of both hands. The tuberculin skin test with purified protein derivative 10 IU was repeatedly negative with the presence of BCG scar. Serum angiotensin converting enzyme (ACE) level was 13.92 IU/ml (normal value 6.3 ± 2.7 IU/ml). Other laboratory examinations which were normal or gave negative results included serum calcium level, 24-hour urinary calcium excretion, creatinine clearance, $CD_4 : CD_8$ T-lymphocyte

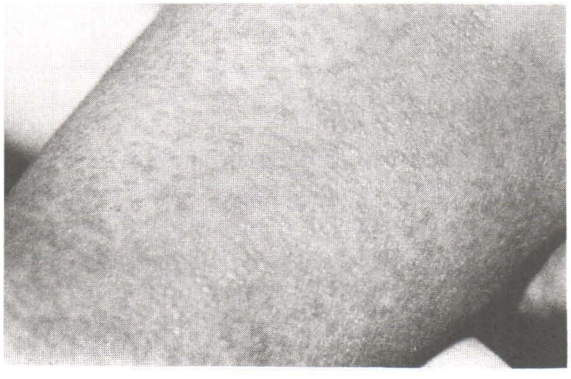

Fig. 1. Flat-topped papules on the forearm.

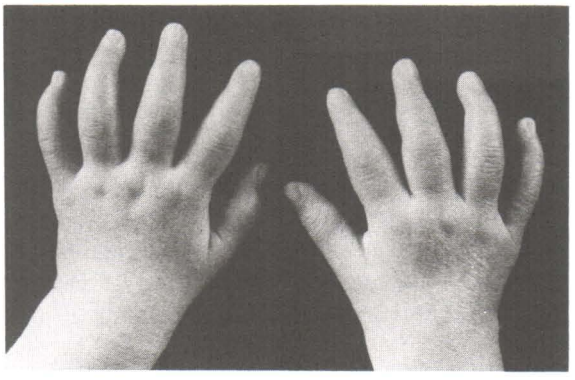

Fig. 2. The fingers were fusiformly swollen.

ratio, urinalysis, antinuclear antibody, rheumatoid factor, bone marrow aspiration, gastric wash for acid fast bacilli and plain film of the KUB system. The Kveim-Siltzbach test was not performed because there was no antigenic suspension available.

Histopathological study of skin biopsy taken from lesions on the forearm demonstrated non-caseating tuberculoid granulomas composed of epithelioid cells and multinucleated giant cells in both upper and lower dermis (Fig. 3). Some granulomas were associated with follicular structures or in the vicinity of hair follicles. There were Schaumann's bodies in some giant cells. The epidermis as well as nerve and arrector pilorum muscle appeared normal. Liver biopsy also demonstrated multiple non-caseating tuberculoid granulomas. Special stains of both skin and liver biopsies were negative for bacteria, fungus and mycobacteria. There was no evidence of any foreign body. Cervical lymph node biopsy showed prominent lymphoid follicles consistent with reactive hyperplasia. There was no granuloma in the lymph node but the skin overlying the lymph node did show non-caseating granulomas. Cultures and polymerase chain reaction from all tissue specimens were negative for mycobacteria, fungus and bacteria.

Sarcoidosis was diagnosed and therapy with prednisolone 1 mg/kg/day was given because of the eye lesion. Swelling of the joints, the skin lesions and opacity of the eyes dramatically resolved within a few weeks. The hepatosplenomegaly decreased and could not be palpated. After 4 months of therapy, attempts to taper off the prednisolone dosage were made several times, but each time the joint symptoms recurred within a week.

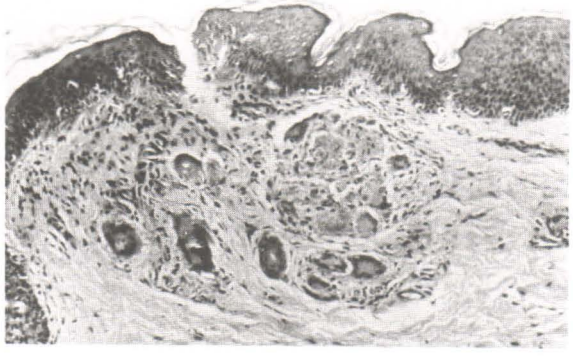

Fig. 3. Non-caseating granuloma in the dermis.

DISCUSSION

Preschool sarcoidosis is a rare disorder and diagnosis is often made at a much later stage of the disease in children than in adults[18]. The incidence and prevalence of sarcoidosis in Thailand are unknown[19]. Almost all children with sarcoidosis are symptomatic. The symptoms are usually secondary to local tissue infiltration and injury by pressure and displacement by granulomas[20]. They are often vague and non-specific, including weight loss, fatigue, lethargy, anorexia and less commonly, fever[5,7]. Other symptoms are related to specific organs or systems involved. Our patient had no constitutional symptoms, but she had papular rash. Maculopapular eruptions are the most common dermatologic finding[21,22]. The joint symptoms in very young children have early appearance and insidious onset[23]. Fusiform swelling of the fingers, as in our patient, is common[24]. Involvement of the eye is an extremely important cause of morbidity because of its association with blindness. Chronic granulomatous uveitis is the most common ocular manifestation of sarcoidosis[25]. Hepatosplenomegaly and generalized peripheral lymphadenopathy occur in many sarcoidosis patients and confirm the systemic character of the disease[26,27]. Renal manifestation occurs infrequently in children [17,28]. Other organs that may be involved include cardiovascular system, nervous system, salivary glands, ears, tonsils, thyroid gland, larynx, gastrointestinal tract, muscle, bone marrow and genitourinary tract[3].

There is no single laboratory test or group of tests diagnostic for sarcoidosis. The Kveim-Siltzbach test has long been the traditional method of diagnosing sarcoidosis[29]. This test was not performed in our patient because a standardized reagent was not available. An elevated ACE level produced by epithelioid cells of the granulomas is used to confirm diagnosis of sarcoidosis, evaluate disease activity, and measure a response to therapy. Most patients with active systemic sarcoidosis have elevated ACE levels, but this is not specific[30]. Values for erythrocyte sedimentation rate and c-reactive protein parallel the clinical disease activity[7]. Pulmonary function test in sarcoidosis mostly indicates restrictive disease of the lung[20]. Our patient was too young to perform this study. Hypercalcemia, hypercalciuria and nephrocalcinosis were absent in our patient. Biopsy provides the best supporting

evidence for diagnosis and the site is determined by abnormalities noted in accessible organ systems such as skin and peripheral lymph nodes. This is a useful and non-invasive diagnostic procedure. The hallmark of sarcoidosis is the formation of non-caseating granulomas consisting of epithelioid cells and multinucleated giant cells surrounded by lymphocytes in the involved organs(5). The diagnosis of sarcoidosis is based on the presence of a compatible clinical picture, laboratory tests, characteristic histologic appearance on organ biopsy with negative stains and culture for mycobacteria and fungi, and exclusion of other granulomatous diseases (4,5,31).

Sarcoidosis should be treated when there are significant symptoms or evidence of progressive damage to the involved organs. The indications for therapy include progressive pulmonary impairment, progressive renal impairment, persistent hypercalcemia or hypercalciuria, disfiguring cutaneous lesions, ocular, cardiac and neurologic involvement. Systemic corticosteroid is the most effective and remains the treatment of choice. The prognosis of children with early onset sarcoidosis is not well known due to the rarity of the disease and to the lack of long term follow-up studies(11). Physical examination, work-up for systemic sarcoidosis and long term follow-up should be undertaken in all suspected patients. Early diagnosis and prompt treatment in children are important to prevent many of the complications such as blindness, renal impairment and pulmonary insufficiency(18).. Most of the mortality is due to cardiac and pulmonary complications (32-34).

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โรคซาร์คอยโดสิส ในเด็กก่อนวัยเรียน

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sarcoidosis เป็นโรคเรื้อรังที่เกิดจากการมีก้อนแกรนูโลม่าในอวัยวะต่าง ๆ ของร่างกายโดยไม่ทราบสาเหตุ ส่วนใหญ่โรคเกิดในผู้ใหญ่ sarcoidosis ในเด็กเล็กอายุน้อยกว่า 4 ปีที่เรียกว่า sarcoidosis ในเด็กก่อนวัยเรียนนั้นพบได้น้อยมาก และมีอาการแสดงแตกต่างจากโรคที่พบในผู้ใหญ่และเด็กโต โดยพบมีลักษณะเฉพาะร่วมกัน 3 ประการคือ มีความผิดปกติที่ผิวหนัง ตาและข้อ แต่ไม่มีอาการทางปอด หลักการวินิจฉัยโรคอาศัยลักษณะทางคลินิกที่เข้าได้กับโรค ร่วมกับลักษณะทางพยาธิวิทยาที่พบก้อนแกรนูโลม่าประกอบด้วยเซลล์ที่มีลักษณะคล้ายอิพิทีเลี่ยมและไม่มีเนื้อเยื่อตายที่มีสภาพคล้ายเนยแข็งในอวัยวะต่าง ๆ ของร่างกายมากกว่า 1 แห่ง หรือทำการทดสอบผิวหนังด้วยวิธีของ Kveim-Siltzbach แล้วได้ผลบวก รายงานนี้นำเสนอผู้ป่วยเด็กหญิงไทยอายุ 2 ปีที่มีอาการและผลการตรวจทางห้องปฏิบัติการเข้าได้กับโรค sarcoidosis ผู้ป่วยมีอาการดีขึ้นอย่างชัดเจนเมื่อให้การรักษาด้วยการรับประทานยาคอร์ติโคสตีรอยด์

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