Sarcoidosis in Japanese and American Children*

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A study of sarcoidosis among Japanese and American children suggests that there are more than the previously suspected number of children with asymptomatic sarcoidosis. The annual chest roentgenogram in Japanese school children detected the majority of these cases, while in the United States, where the annual chest roentgenogram is not required, the majority of children had sarcoidosis diagnosed through symptomatic complaints.

Sarcoidosis is a chronic systemic granulomatous disease, the cause of which is unknown. The disease appears to be relatively rare in children. In a review of the world literature to February 1953, McGovern and Merritt were able to document only 104 cases in children 15 years of age and younger. To these, they added nine others, all diagnosed in Washington, DC area hospitals. Since that time, most of the cases in children have been reported in Japan and in the United States. The present report includes two groups of children with sarcoidosis, one from Japan and the other from the United States (the Research Institute for Tuberculosis and Cancer, Tohoku University, Sendai, Japan, which includes patients from that area, and the Medical College of Virginia, Health Sciences Division, Virginia Commonwealth University, Richmond, with patients primarily from Virginia and including 33 previously reported cases*).

Case Reports

Age, Sex and Race

Except for one three-year-old in the United States series, all the patients in both series were in the pre-adolescent and adolescent age group (8 to 15 years). In the Japanese series, there were 18 girls and 27 boys, while in the United States group, there was almost equal sexual distribution with 21 girls and 19 boys. All the Japanese patients were Orientals. In the United States group, 29 (72 percent) were black and 11 (28 percent) were white.

Symptoms

In Japan, three patients presented with eye disorders; the remaining 42 were asymptomatic and were discovered in mass chest roentgenographic surveys. On the other hand, in the United States group, 35 of the 40 patients were symptomatic at the time of diagnosis. Among these, there was no pattern of symptoms specific for sarcoidosis. The most common complaint, grouped together as fatigability, malaise, or lethargy, occurred in approximately one-third of the United States patients. Cough, fever, and dyspnea were next in frequency, and weight loss and adenopathy followed in that order.

Organ and System Involvement

Bilateral hilar lymph node-lung involvement is the hallmark of sarcoidosis in children; it occurred in 44 of 45 Japanese cases and in all of the United States patients. Only ocular disease was noted in the other Japanese patient.

Peripheral lymphadenopathy and eye lesions were the only other areas of involvement noted among the Japanese (Table 1). Blindness resulted in three of 15 patients, one Japanese and two Americans.

The presence of skin lesions in adults with sarcoidosis is presumed to be of bad prognostic import. The same may be true in American children. None of the Japanese in this study developed skin lesions. However, lesions were present in ten (25 percent) of the United States group. While there were only five (13 percent) persisting sequelae among the American cases, three of these appeared in patients who also had skin lesions; two of those with skin lesions developed blindness, and one showed severe restrictive lung disease. There was no instance of erythema nodosum.

Hepatosplenomegaly was common among the United States patients (Table 1). In two instances, the liver and spleen were palpable at the level of the iliac crest. No hepatosplenomegaly was observed in the Japanese group.

Osseous lesions, appearing as punched-out areas of hyperlucency, were present in a few (10 percent) of the Americans. Such lesions are usually noted in the metacarpals, metatarsals, and phalanges, but one patient in this group showed such a lesion in the femoral metaphysis. No bone lesions were present in the Japanese study.

Results

Laboratory Study

The most common abnormal laboratory finding in the United States group was hyperglobulinemia.
Table 1—Childhood Sarcoidosis*

<table>
<thead>
<tr>
<th>Childhood Sarcoidosis Under 15 Years</th>
<th>Japan</th>
<th>USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td>Tissue confirmation</td>
<td>41 (91)</td>
<td>40 (100)</td>
</tr>
<tr>
<td>Positive Kveim</td>
<td>4/4 (100)</td>
<td>0/0</td>
</tr>
<tr>
<td>Race</td>
<td>Oriental</td>
<td>29 (73) Black</td>
</tr>
<tr>
<td>Age group</td>
<td>8-15 yrs (med 12 yrs)</td>
<td>3-15 yrs (med 13 yrs)</td>
</tr>
<tr>
<td>Presenting symptoms</td>
<td>3 (6)</td>
<td>35 (87)</td>
</tr>
<tr>
<td>Bilateral hilar lymph nodes with parenchymal involvement</td>
<td>33 (73)</td>
<td>22 (55)†</td>
</tr>
<tr>
<td>Bilateral hilar lymph nodes with parenchymal involvement</td>
<td>11 (25)</td>
<td>18 (45)</td>
</tr>
<tr>
<td>Peripheral lymphadenopathy</td>
<td>18 (40)</td>
<td>30 (67)</td>
</tr>
<tr>
<td>Ocular involvement</td>
<td>6 (13)</td>
<td>9 (23)</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>0</td>
<td>10 (25)</td>
</tr>
<tr>
<td>Hepatoeleomeningaly</td>
<td>0 Liver 12 (30) Spleen 9 (23)</td>
<td></td>
</tr>
<tr>
<td>Bone cysts</td>
<td>0</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Hypergobulinemia</td>
<td>11/43 (26)</td>
<td>24/36 (67)</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>2/37 (5)</td>
<td>7/33 (21)</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>18/40 (40)</td>
<td>19 (47)</td>
</tr>
</tbody>
</table>

*Percentages given in parenthesis.
†One with questionable bilateral hilar adenopathy at time of diagnosis, later confirmed.

(> 3.5 g/100 ml). This was present in 24 of 36 (67 percent) Americans and in 11 of 43 (26 percent) Japanese patients. Other abnormal laboratory findings in both groups included eosinophilia (above 4 percent) and hypercalcemia (Table 1). Although the presence of an elevated alkaline phosphatase level is a corroboration diagnostic finding, retrospective interpretation of results is not easy since values may be reported in King Armstrong units, Bodansky units, or International units. Alkaline phosphatase levels were not determined in the Japanese group.

Corroborative Diagnostic Procedures

The routine tuberculin test (5TU) was positive in 6 (13 percent) of the Japanese; all 40 of the United States group were tuberculin negative.

The diagnosis of sarcoidosis was corroborated by biopsy specimens in 41 Japanese (29 lymph node, 5 lymph node and eye follicle, and 7 eye follicle); the other 4 had a positive Kveim test. An organ biopsy specimen compatible with sarcoidosis was obtained in all 40 of the American patients. Included among the biopsy specimens were lymph node alone (34 patients); lymph node and skin (3 patients); skin (1 patient) and lung (1 patient); and lymph node and testis (1 patient).

Pulmonary Function

Pulmonary function studies were performed in all 45 Japanese children at the first visit or soon after detection. In four patients the results were indicative of restrictive lung disease with vital capacity below 80 percent of the predicted value and normal FEV1. In the American study, pulmonary function studies were carried out on only 16 children during the acute stage of the disease. In 13 patients, the results were indicative of restrictive lung disease with reduced vital capacity and normal FEV1. In three instances, results were normal.

Therapy and Prognosis

Corticosteroid therapy often effects prompt disappearance of clinical manifestations of disease, eg, skin lesions, parenchymal infiltrates on chest roentgenogram, etc. Whether or not corticosteroid therapy is effective in improving the prognosis has not been established.

In the American series, prednisone, 1 mg/kg of body weight per day, was instituted at onset (20 patients treated) and gradual reduction in the dosage was initiated as soon as clinical manifestations of the disease disappeared. Attempt was made to provide a maintenance dose of prednisone (15 mg every other day) until the patient received a six-month course of treatment. One of the American group has had progressive pulmonary disease after three separate six-month courses of corticosteroid, and two of the Japanese group (12 received corticosteroid therapy) are still under treatment after seven and three years, respectively. Chest roentgenograms returned to normal in 38 of 43 (88 percent) Japanese children with or without adrenocorticosteroid therapy after one to two years; one patient in the group developed blindness. Among the United States patients, two developed blindness and three have restrictive lung disease. The chest roentgenogram returned to normal in the other 37 Americans.

Discussion

The major difference between sarcoidosis in Japanese and American children appears to lie in the case-finding method. In Japan, the school child receives an annual chest roentgenogram. In 42 of the 45 Japanese children, the disease was diagnosed in this manner. Only three were symptomatic, and each of these visited a physician because of an ocular
disorder. In the United States, school children do not receive routine chest roentgenograms; 35 of the 40 American patients were symptomatic at the time of diagnosis, albeit with a varied symptomatology. The most common complaint (fatigability, malaise, lethargy) occurred in only one-third of the United States patients.

If this logic is pursued, it would appear that there are probably many undiagnosed cases of sarcoidosis in children in the United States. Certainly, the presence of such clinical manifestations as peripheral lymphadenopathy, noted in 40 percent of the Japanese patients, was not sufficient provocation to suggest the diagnosis of sarcoidosis until a routine chest roentgenogram showed the presence of bilateral hilar lymphadenopathy. Corroborative laboratory findings, such as hyperglobulinemia, hypercalcemia, and eosinophilia were likewise obtained only after the roentgenogram suggested the probability of sarcoidosis.

References