

Eosinophilic Granuloma of the Ishium

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Eosinophilic granuloma of the bone characterized by marked infiltration of eosinophilic cells was first reported by Finzi in 1929. Since that time nearly 200 papers appeared in literature on this disease by the present time. We have found this disease in the ishium of an asthmatic boy who revealed interesting findings, and are going to present this case.

CASE REPORT

A 15-year-old boy has complained of dull pain in the left hip. Past History: He was hospitalized for 11 months in the Department of Pediatrics, Nagasaki University Hospital, for treatment of asthma bronchiale. After discharge Prednin was administered orally with certain intervals. It is estimated that a total of 3,500 mg of Prednin was given to this boy. He was vaccinated with B. C. G. when he was a third grade school boy, followed by negative as well as pseudo-positive tuberculin reaction in the subsequent years.

Present Illness: He had an accident on his bicycle and struck his left hip in the summer of 1961. The local pain lasted only one day and then disappeared spontaneously without developing any delayed symptom until late April in 1962 when he noticed dull pain in the deep area of the left hip. Medication of anti-neuralgic drugs by his family physician failed to relieve his pain. Roentgenographic examination of his hip revealed a bone lesion in the ishial tuberosity as illustrated in the Fig. 1. His general condition was good at this time. He was admitted to our Department of Surgery on May 19, 1962.

LABORATORY FINDINGS on ADMISSION:

1. Urine: Color is light-yellow. Alkaline. Albumin test is negative. Bence-Jones' albumose test is negative. Glucose is negative. Urobilinogen is normal. Bilirubin is negative. Sediments contain non-crystallin urates

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deposit.

2. Feces: Occult blood test is negative. Parasites are absent. No protozoa is present.

3. Blood: RBC 4.84 million per cu. mm. Hb. 86%. Hematocrit 41%. WBC 7,100 per cu. mm. Basophils 0.5%. Eosinophils 8.5%. Band neutrophils 1.0%. Segmented neutrophils 49%. Lymphocytes 35.5%. Monocytes 4.1%. Platelets 340,000. Bleeding time 3 minutes. Coagulation time 5 min. 30 sec. to 20 minutes.

4. Serological tests for Syphilis: Ogata's test negative. Agglutination test negative. Glass plate method negative.

5. Tuberculin test: 10 x 17 mm.

6. Liver function tests: BSP 2.0%. TTT 0.4. Lugol's test negative. Co-reaction RO (3). Kunkel's test 2.3. Total protein 7.3 g/dl. A/G ratio 1.8. Total cholesterol 184 mg%.

7. Adrenal cortex function:

A. Mineral corticoids: (1) Robinson-Power-Kepler test normal.

(2) Serum sodium 148.8 mEq/l. Serum potassium 5.49 mEq/l.
Serum chloride 103.5 mEq/l.

B. Glucocorticoid: (1) Thorn's test a fall of 78.8%.

(2) 17-hydroxycorticosteroid in urine 4.9 mg/day.

C. Androgenic hormone: 17-keto-steroid 6.0 mg/day.

OPERATIVE FINDINGS: On June 5, 1962, under spinal anesthesia the ischial tuberosity was exposed. There was found a low thumbsize elevation of the bone along the margin of obturator foramen opposite to the tuberosity. When the bone cortex of this tumor was uncovered, a small amount of yellow-brownish pus came out exposing a rather solid but fragile granulomatous mass. This mass was inside of an oval cavity with a wall of smooth surface which was actually the bone cortex of normal strength. The specimen was immediately sent for bacteriological examination and histological examination on frozen sections. Osteomyelitis was diagnosed. Therefore, the cavity was curetted thoroughly before Streptomycin was sprayed and a muscle flap from the major gluteus muscle was packed in the cavity. Fig. 2. shows the specimen stained with hematoxylin and eosin. Marked eosinophilic infiltration is noted in the granulomatous tissues. Peripheries of the tissues are fibromatous, showing infiltration of lymphocytes and plasma cells. There are also giant cells having three to five nuclei. These findings indicate eosinophilic granuloma.

Smear tests for microorganism were negative, but culture in agar-agar medium after 24 hours incubation in bouillon succeeded to isolate Gram-positive white staphylococcus.

Postoperative roentgenograms of all bones revealed no other lesions. Leukocytosis and eosinophilia are still in progress, showing the following blood and bone marrow findings:

1. Blood: RBC 4.82 million per cu. mm. Hb. 93%. WBC 10,700 per cu. mm. Basophils 0.5%. Eosinophils 16.0%. Band neutrophils 0.5%. Segmented neutrophils 56.5%. Lymphocytes 18.0%. Monocytes 8.5%.

2. Bone Marrow: Numbers of nuclei cells 201,750.

| | | | |
|----------------|------|---------------------|------|
| Myeloblasts | 1.5% | Monoblasts | 1.0% |
| Neutrophils | | Immature | 1.0 |
| Promyelocytes | 7.0 | Mature | 2.5 |
| Myelocytes | 1.5 | Proerythroblasts | 0.1 |
| Metamyelocytes | 8.0 | Macroblasts | |
| Band | 9.5 | Basophilic | 2.0 |
| Segmented | 22.5 | Polychromatophilic | 0.5 |
| Eosinophils | 3.0 | Normoblasts | |
| Basophils | 0.3 | Basophilic | 1.0 |
| Lymphoblasts | 1.5 | Polychromatophilic | 15.5 |
| Lymphocytes | 21.0 | Orthochromatophilic | 1.0 |
| | | Plasma cells | 1.0 |

DISCUSSION

The first report of eosinophilic granuloma of the bone is attributed to FINZI⁸⁾ who discovered a lesion similar to multiple myeloma but rich in eosinophilic cells in the skull of a 15-year-old boy and reported in 1929. Later, in 1940, LICHTENSTEIN and JAFFE⁹⁾ named this condition as eosinophilic granuloma. Reports on this disease have been accumulated ever since. O'NEIL¹⁰⁾ reviewed 189 cases which were reported by 1955 in the Western literature. In Japan, TERASHIMA collected 16 cases, including the first case in Japan reported by TAKAKI and URAKAWA¹⁴⁾, and published the review in 1957.

Many explanations have been attempted on etiology of this disease. Relation to trauma^{11),12)}, and tuberculosis, have been discussed, and chronic inflammatory stimulation, parasites, granuloma virus and allergy have been blamed, without leading to any acceptable conclusion.

In our case, there are trauma, allergic condition such as asthma bronchiale, positive tuberculin reaction and identified Gram-positive cocci. None of them can not escape suspicion of responsibility. At the present time, however, it is generally approved that this disease belongs to reticuloendotheliosis, which is classified by MUNDT⁹⁾ as shown in the table (Table 1). Three diseases under category B are essentially the same disease manifesting different symptoms according to the differences of severity, location and phase of the lesion.

Onset of this disease is relatively sudden, with initial symptoms of local mild pain, heat and tenderness. Lesion can be both singular and multiple. The age of the patients is under the age of twenty years

Table 1.
Die fuenf Retikuloendotheliosen des Knochenmarks

- A. Familiaere primaere Lipoideinlagerung:
1. Gaucher 'sche Krankheit
jedes Alter, Cerebrosids Kerasin.
 2. Niemann-Pick 'sche Krankheit
Kinder (meist weiblich), Phosphatids Sphingomyelin.
- B. Nicht hereditaere sekundaere Lipoideinlagerung:
3. Letterer-Siwe 'sche Krankheit
bis 2 Jahre, Cholesterin.
 4. Hand-Schueller-Christian 'sche Krankheit
Kinder ueber 2 Jahre, Cholesterin.
 5. Eosinophiles Granulom
im jugendlichen Alter, Cholesterin.
Befunde; lokaler Knochenschmerz, Leukocytose, Eosinophinophilie.
Verlauf; gutartig.
Knochen; kortikale Lokalisation, pathologische Frakturen,
(RÖ : scharf begrenzte rundliche Aufhellung der flachen Knochen)

in the majority but elderly patient is not rare, as shown in the Table 2. Male outnumbers female in the ratio of five to one according to GARSCHÉ'S⁴⁾ study of 159 cases. Familiar locations of lesions are shown in the Table 3. The skull predominates over others, followed by the rib, femur, and pelvis.

Eosinophilia of the peripheral blood is a common finding, and its grade is up to 10% according to French. Absence of eosinophilia is not infrequent.

Table 2.
Age Incidence

| 189 cases by O'Neil | | | |
|---------------------|----------|-------------|----------|
| 0-10 ys. | 62 cases | 40-50 ys. | 8 cascs |
| 10-20 ys. | 44 cases | 50-60 ys. | 3 cases |
| 20-30 ys. | 38 cases | over 60 ys. | 17 cases |
| 30-40 ys. | 17 cases | | |

Table 3.
Localisation of eosinophilic granuloma in the bone
189 cases by O'Neil

| | | | |
|-----------|-----|------------|---|
| Skull | 102 | Clavicula | 8 |
| Ribs | 54 | Tibia | 7 |
| Femur | 31 | Radius | 3 |
| Pelvis | 24 | Fibula | 2 |
| Mandibula | 18 | Sternum | 2 |
| Humerus | 16 | Metacarpus | 1 |
| Vertebrae | 14 | Metatarsus | 1 |
| Scapula | 12 | | |

Roentgenograms demonstrate various sizes of round or oval osteolytic opaque mass with blurred contour, originating from the bone marrow and invading into the bone cortex, occasionally with bony proliferation of the periosteum.

On histological examination marked infiltration of eosinophilic cells are seen in the granulatous tissues, accompanied by the presence of neutrophils, plasma cells and lymphocytes. ENGELBRETH and HALM¹⁾ divided the course into four stadia:

1. Proliferative stadium: with marked increase of histiocytes and few eosinophils.
2. Granulomatoid stadium: with marked infiltration of eosinophilic cells and increase of histiocytes and capillaries.
3. Xanthomatoid stadium; with a few xanthoma cells.
4. Fibrous stadium; recovering stage.

It is believed that the first and second stadia correspond to eosinophilic granuloma, the third and fourth stadia to Hand-Schueller-Christian disease.

Bacteriologically all previous reports proved no microorganism except one by YAMAMOTO¹⁵⁾ who successfully isolated *Mycobacterium tuberculosis* from the lesion, and assumed that eosinophilic osteomyelitis can develop either to tuberculous osteomyelitis or eosinophilic granulomatous osteomyelitis. From our lesion we isolated Gram-positive white staphylococci, and are wondering if this could be non-causative bacteria which happened to deposit on the lesion from air. If this possibility can be excluded, this case will be the first case in which any coccus was isolated from eosinophilic granuloma.

Prognosis of this disease is extremely favorable, healing spontaneously in the majority of cases. According to FARBER'S²⁾ explanation, eosinophilic cells decrease and get replaced by monocytes and fibroblasts, and then xanthoma cells change to lipophagens by vacuolation process, finally repaired by connective tissues and bone tissues.

This good prognosis justifies the treatment with curetting and resection. Recently, however, steroid hormones and irradiation⁶⁾ were introduced for the treatment of multiple lesions. Although the healing mechanism is little understood, HOMBO⁵⁾ has treated eosinophilic granuloma of allergic patient, who had suffered from repeated attacks of asthma and urticaria, with irradiation. Allergic symptoms disappeared and tumor diminished its size after one course of roentgen-ray irradiation totaling 2,000 r.

Our case is also receiving roentgen-ray therapy and steroid hormone treatment and will be studied in following examinations.

SUMMARY

1. We discovered eosinophilic granuloma in the left ishium of a 15-year

old boy.

2. The patient is asthmatic and had blunt injury of the ischial region one year ago, adding data on the etiology of this disease.

3. A coccus suggestive of staphylococcus albus was isolated from the specimen. This is the first case in literature in which any coccus was isolated from eosinophilic granuloma. There is a good possibility of bacterial infection as a cause of this disease. We believe that further investigation is necessary before any conclusion can be drawn on this problem.

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Fig. 1. Roentgenogram of the pelvis



Fig. 2. Microscopic film of the granuloma.

