

Splenomegaly and splenectomy in sarcoidosis

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SUMMARY The natural history of 30 patients with sarcoidosis who showed histological evidence of granulomatous involvement of the spleen has been studied; 24 patients had splenomegaly, 16 of whom had splenectomy. The main indication for splenectomy was splenomegaly and resultant discomfort. Corticosteroids reduced spleen size but reduction or withdrawal of the relatively high dosage required resulted in rebound splenomegaly within a period of three months to three years. Haematological abnormalities were controlled by splenectomy in all patients so affected, but the natural history of their sarcoidosis remained unaltered.

In a recent worldwide review of sarcoidosis, splenomegaly was noted in 233 (6%) of 3676 patients (James *et al.*, 1976). The reported frequency of splenomegaly has varied with ethnic group and known duration of disease; in the UK this has ranged from 11 to 31% of all patients (James *et al.*, 1976; Selroos, 1976; Smellie and Hoyle, 1960).

The opportunity was therefore taken to investigate the natural history and outcome of illness in a highly selected group of patients with sarcoidosis and with histological evidence of granulomatous involvement of the spleen, with or without splenomegaly. In all, 30 patients were studied; 24 had splenomegaly and in 16 splenectomy was undertaken.

Patients and methods

The 30 patients seen between 1956 and 1977 were divided clinically into three groups:

Group 1 12 patients with gross splenomegaly, of whom 10 underwent splenectomy

Group 2 12 patients with palpable spleen, of whom six underwent splenectomy

Group 3 6 patients who had a non-palpable granulomatous spleen which was removed at necropsy.

The natural history and outcome of illness, the haematological effects of hypersplenism, the effect of corticosteroids, and the indications for splenectomy

were studied in all patients. Splenic function studies were undertaken in three patients.

Results

The age, sex, and clinical group of patients on diagnosis are given in Table 1.

Table 1 Age, sex, and clinical group of patients on diagnosis

| Group | Age (years) | | | | | | Total |
|---------------|-------------|-------|-------|-------|-------|------|-------|
| | 0-9 | 10-15 | 16-20 | 21-40 | 41-60 | > 60 | |
| <i>Male</i> | | | | | | | |
| 1 | 0 | 0 | 0 | 1 | 0 | 1 | 2 |
| 2 | 1 | 0 | 0 | 3 | 3 | 2 | 9 |
| 3 | 0 | 0 | 1 | 2 | 2 | 0 | 5 |
| <i>Female</i> | | | | | | | |
| 1 | 0 | 2 | 0 | 6 | 0 | 2 | 10 |
| 2 | 0 | 0 | 0 | 2 | 1 | 0 | 3 |
| 3 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| Total | 1 | 2 | 1 | 15 | 6 | 5 | 30 |

Group 1 Gross splenomegaly

Group 2 Palpable spleen

Group 3 Granulomatous non-palpable spleen

Of the total of 30 patients, 17 were male and 13 female. On diagnosis 16 patients were aged between 21 and 40 years, but it is noteworthy that two (group 1) were girls aged 11 and 13 years and one (group 2) a boy aged 7 years.

The clinical and histological evidence of sarcoidosis in all 30 patients is given in Table 2. In 21 with clinical evidence of pulmonary involvement,

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Table 2 Clinical and histological evidence (excluding spleen) of sarcoidosis in 30 patients

| Organ/tissue/site | Group | | |
|-------------------|-------------|-------------|------------|
| | 1 n = 12 | 2 n = 12 | 3 n = 6 |
| Lung | 10 | 8 | 3 |
| Liver | 2 (2)† | 2 (2)† | 0 |
| Lymph node | 3 (2)† | 1 (1)† | 1 (1)† |
| Heart | 0 (1)* | 1 | 0 (1)* |
| Muscle | 0 | 1 (1)† | 0 |
| Skin | 3 (2)† | 0 | 0 |
| Pleura | 1 (1)* | 0 | 0 |
| Bone marrow | 0 (2)* | 0 | 0 |
| Kidney | 1 (1)† | 0 | 0 |
| CNS | 0 | 0 | 1 |
| Ocular | 1 | 1 | 0 |

Figures in parentheses indicate number of patients with histological evidence compatible with sarcoidosis: †during life; *at necropsy.

histological evidence in support of a diagnosis of sarcoidosis was not sought. Three patients (one from each group) showed clinical or histological evidence of involvement of the heart by sarcoidosis and one (group 1) clinical and histological evidence of sarcoidosis involving the pleura. In addition (not shown in Table 2), eight of 12 patients—four in group 1, two in group 2, and two in group 3—showed positive Kveim reactions after cutaneous tests made with Kveim material prepared from spleen K12.

Table 3 gives the radiological form of sarcoidosis according to the most recent chest radiograph: of nine patients who showed no radiological abnormality at that time, six had presented with hilar lymphadenopathy and/or pulmonary mottling, and the remaining three had extrapulmonary lesions only. Of the 13 patients with pulmonary fibrosis, nine presented with hilar lymphadenopathy and/or pulmonary mottling and four with radiological evidence suggestive of pulmonary fibrosis.

Table 3 Radiological form of sarcoidosis according to most recent chest radiograph

| Chest radiograph | Group | | |
|---|-------|----|---|
| | 1 | 2 | 3 |
| Normal | 4 | 4 | 1 |
| Hilar lymphadenopathy | 1 | 2 | 1 |
| Hilar lymphadenopathy with pulmonary mottling | 2 | 0 | 0 |
| Pulmonary mottling only | 0 | 0 | 0 |
| Pulmonary fibrosis | 4 | 6 | 3 |
| Total | 11 | 12 | 5 |

In one patient (group 3) a diagnosis of sarcoidosis was made at postmortem examination following sudden death; in one patient (group 1) a recent chest radiograph was not available.

Among the 24 patients with splenomegaly (groups 1 and 2), 11 were anaemic, 12 were neutropenic, and 10 thrombocytopenic; three of these were

pancytopenic. Bone marrow was examined in seven patients; of these, six showed an active normoblastic marrow, but in one (who also had coeliac disease) the marrow was megaloblastic. One patient (group 2) had hereditary spherocytosis. Two patients (group 2) who had splenomegaly and thrombocytopenia showed shortened platelet survival, and one patient (group 1), who had a normal red cell life and a normal red cell mass with a normal platelet count, showed an increased plasma volume consistent with splenomegaly.

OTHER DISEASES

Group 1

One patient had ulcerative colitis diagnosed before the onset of sarcoidosis, one developed miliary tuberculosis and tuberculous meningitis, one developed a tuberculous abscess on the arm, and one coeliac disease, during the course of sarcoidosis.

Group 2

One patient showed evidence of involvement of the liver by amyloid disease and one had hereditary spherocytosis.

Group 3

One patient developed carcinoma of the colon and died with hepatic secondaries.

OUTCOME OF SARCOIDOSIS

Corticosteroids

Twelve patients (groups 1 and 2) were treated with prednisolone; of these, two were treated specifically for splenomegaly. Spleen size regressed in six, including the latter two, but increased again in all patients when corticosteroids were tailed off or withdrawn.

Splenectomy

Sixteen patients (10 group 1, 6 group 2) underwent splenectomy for sarcoidosis; of these, five patients (group 1) had elective splenectomy without prior treatment with corticosteroids. The main indications are given in Table 4. The majority had gross enlargement of the spleen with discomfort; subsidiary reasons included probable infarct and suspected rupture of the spleen. Of the total of 16 patients, two in group 1 and two in group 2 remain well without evidence of resurgence in the activity of sarcoidosis. In eight (7 group 1 and 1 group 2) the sarcoidosis remained active and progressive after splenectomy. One patient (group 1) died immediately after splenectomy, and one patient (group 2) underwent splenectomy but died subsequently from

Table 4 *Main indications for splenectomy*

| Indication | Group 1 n = 10 | Group 2 n = 6 |
|------------------------------|-------------------|------------------|
| Gross enlargement/discomfort | 6 | 1 |
| Infarct | 1 | — |
| Rupture | 1 | — |
| Haematological | 2 | 3 |
| Other reasons: | | |
| Suspected lymphoma | — | 1 |
| Hereditary spherocytosis | — | 1 |

amyloidosis. Two patients (1 group 1, 1 group 2) were lost to follow-up.

Deaths

Of the 30 patients, three in group 1, four in group 2, and five in group 3 died from sarcoidosis. Of these, one (group 1) died after splenectomy, five (1 group 1, 1 group 2, 3 group 3) died from respiratory failure, two (1 group 1, 1 group 3) died from involvement of the heart by sarcoid, and three (group 2) died from the respiratory complications of aspergillomata (2 from profuse haemoptyses and 1 from postoperative bleeding into the cavity of a removed aspergilloma). One patient (group 3) with CNS involvement committed suicide. In addition, four patients (3 group 2; 1 group 3), died from other causes.

Discussion

The salient clinical findings, treatment, and outcome of illness in 24 patients with sarcoidosis and splenomegaly are presented and compared with those of a further six patients with sarcoidosis in whom a clinically non-palpable, but granulomatous spleen was removed at necropsy. There have been several previous reports of spleen involvement, splenomegaly, and splenectomy in sarcoidosis, but these have dealt mainly with isolated cases (Young and Mooney, 1968) or necropsy findings (Branson and Park, 1954). All have perforce taken little account of the treatment and control of splenomegaly or of the effects of splenectomy on the clinical outcome. Although the present cases are highly selected, they provide the opportunity to assess the clinical presentation, management, and results of treatment, including splenectomy, which was undertaken in 16 patients.

All 24 patients with splenomegaly had longstanding sarcoidosis, and 12 were treated with corticosteroids which had an unpredictable effect on splenomegaly. A marked increase in size of the spleen was subsequently noted in no fewer than seven patients after an interval of three months to three years and following the tailing off or withdrawal of corticosteroids which all seven had received

for more than one year previously. In four patients this rebound increase in spleen size was associated with a general resurgence in the activity of the sarcoidosis, but in three an increase in spleen size only was noted. In either event, these seven patients were again subject to abdominal discomfort, to the possibility of haematological disturbances resulting from hypersplenism, and to other complications of gross splenomegaly. Thus, although the spleen will usually involute after treatment with corticosteroids, the findings in the present study suggest that the resultant decrease in its size is likely to be dose-dependent, and withdrawal of corticosteroids may not infrequently be followed by rebound splenomegaly. Accordingly, if the spleen is very large, or if haematological features associated with hypersplenism are already present, splenectomy is most likely to be the treatment of choice. Moreover, there is some evidence to suggest that corticosteroids may occasionally exert a deleterious effect on hepatic sarcoidosis, a not uncommon concomitant of splenomegaly (Nelson and Schwabe, 1966).

The haematological picture in the 24 patients with splenomegaly is in keeping with earlier reports (Bruschi and Howe, 1950); two patients in group 2 had palpable spleens and low platelet counts with clinical purpura and easy bruising, and these features conformed to those of hypersplenism with an overactive marrow. Ten patients showed thrombocytopenia; studies of spleen function were undertaken in three patients, of whom two showed thrombocytopenia. The results suggested that thrombocytopenia may have resulted from an autoimmune reaction with platelet destruction similar to that seen in idiopathic thrombocytopenic purpura. Studies in the third patient (who had anaemia but a normal platelet count) showed a normal red cell mass with an increased plasma cell volume. The latter finding is in keeping with those reported by Hess *et al.* (1971).

Previous reports have shown an increased mortality and morbidity among patients with splenomegaly and thrombocytopenia (Bruschi and Howe, 1950; Edwards *et al.*, 1952). All patients in the present series who underwent splenectomy achieved complete resolution of their haematological problems, and splenectomy is clearly the treatment of choice if the haematological changes are severe and the spleen is grossly enlarged. However, the benefits that accrued from splenectomy were limited to the removal of haematological effects of hypersplenism and did not otherwise appear to influence the outcome of the sarcoidosis or of hepatic problems associated with this. Thus, biopsy of the liver in one patient some three years after splenectomy showed the presence of fresh granulomas. A second patient subsequently developed glaucoma resultant upon

long-standing uveitis and also had recurrent jaundice. Both patients continued to have problems consequent upon portal hypertension; clearly, this was not due simply to increased portal flow associated with hypersplenism but may have been attributable to pre-sinusoidal obstruction by granulomas around the porta hepatis or to periportal fibrosis as in simple cirrhosis (Vilinskas *et al.*, 1970).

The spleens of six patients (group 3) were not enlarged clinically, but all showed histological evidence of granulomatous involvement at necropsy. These findings are in keeping with our recognition of the spleen as a common site of involvement in patients with sarcoidosis. Thus, Branson and Park (1954) found splenic involvement in 49.5% of cases at necropsy, and Selroos (1976) demonstrated splenic involvement by fine needle aspiration in 50% of patients presenting with bilateral hilar lymphadenopathy as the only clinical manifestation of sarcoidosis. All 30 patients in the present series were highly selected. Although five patients in group 3 died as a direct result of their sarcoidosis, the causes (3 respiratory failure, 1 involvement of the heart), with the exception of one patient with CNS involvement who committed suicide, were in no way different from those encountered among the seven patients who died as a direct result of their sarcoidosis in groups 1 and 2. Moreover, apart from the presence and treatment of splenomegaly in the 24 patients in groups 1 and 2 (and complications arising directly therefrom) the presentation, course, management, and outcome of the sarcoidosis itself were closely similar in all 30 patients in the present series.

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