Behçet's Syndrome with Aortic Aneurysms

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The coexistence of mouth and genital ulceration with hypopyon mentioned by Hippocrates and described by various workers in the early part of this century was first defined as a syndrome by Behçet in 1937. The place of the syndrome as part of a systemic disorder is now clearer, and the underlying pathology appears to be a vasculitis. The disease runs a chronic course, blindness being the greatest disability and central nervous system involvement a cause of death. Thrombophlebitis is fairly frequent, France *et al.* (1951) giving an incidence of 25% and Dowling (1961) 12%; superficial thrombophlebitis migrans and thrombosis of large veins, including venae cavae (Thomas, 1947; Boolukos, 1960) are recorded.

Little attention has been paid to arterial involvement (Schneider, 1965). Mishima *et al.* (1961) described resection of an aortic aneurysm in a 38-year-old man with Behçet's syndrome, and since then have seen a patient with a femoral artery aneurysm (personal communication); Oshima *et al.* (1963) record two aneurysms of smaller arteries; Shikano (1966) mentioned that one of his patients died of a ruptured aortic aneurysm. Mounsey in a clinicopathological conference (*Brit. med. J.*, 1966) described a case of ruptured aortic aneurysm in Behçet's syndrome, treated by aorto-iliac graft: in this case the aortic aneurysm was presumed to be secondary to osteomyelitis of the lumbar spine, though the possible association between aortic aneurysm and Behçet's syndrome was raised.

A further case is reported here, in which arterial aneurysms appeared to form part of this generalized disease.

Case Report

The patient's illness began in 1954, when he was in an Army unit containing men who had been serving in Egypt. He had fever and abdominal pain, appendicectomy was performed, but his symptoms continued for three months. Prolonged pain in the left wrist followed minor trauma, and six months later pains developed in the neck, shoulder, and back, with radiation down the back of the thigh. This was attributed to Scheuermann's disease, and after six months in hospital he was discharged from the Service, wearing a plaster jacket. He began to work in the following year, and was well until 1958. He then had osteomyelitis of the jaw after dental infection. Two weeks later he was admitted to hospital with fever and abdominal pain, followed by fleeting joint pains and a rash resembling erythema nodosum. Intensive investigations did not provide a diagnosis, and he was treated for six weeks with bed rest, aspirin, antibiotics, and corticosteroids, and was discharged well. From this time onwards he had recurrent ulcers of the mouth, penis, and scrotum. In 1960 he had an unexplained venous thrombosis of the left leg, and one year later had a right femoral vein thrombosis. Biopsy of the long saphenous vein showed gross thickening of the vein and infiltration with inflammatory cells, particularly around nutrient vessels (Dr. J. G. Leopold). Because of this, long-term anticoagulant therapy was instituted. In 1962-4 he had episodes of haziness of vision, and in 1964 had bilateral iritis and later a vitreous haemorrhage. He was seen by Mr. Vine Cole, who suggested the diagnosis of Behçet's syndrome, based on the association of aphthous mouth and genital ulceration, panuveitis, and thrombophlebitis. Corticosteroid therapy was begun.

In October 1964 the first recognized pulmonary infarct occurred. Since then he had experienced numerous episodes of febrile pleurisy associated with haemoptysis and transient radiological shadowing. Possibly these are due to thrombosis in pulmonary vessels rather than to embolization. During treatment with steroids and anticoagulants he had a haematemesis and later melaena; anticoagulants were withdrawn. In 1965 right-sided loin pain and haematuria were attributed to renal infarction. In April 1966 he complained of severe continuous pain at the base of the spine and a lesser pain in the shoulders. There was associated severe constipation and rectal bleeding. Barium enema was normal. During five weeks in hospital no cause for the pain was found. After discharge from hospital the pain continued, and in August 1966 became so severe that he was admitted to the Cardiff Royal Infirmary, very ill, Cushingoid in appearance, with a temperature of 37° C., blood pressure 130/80, and dusky, scaling nodules, 0.5-1 cm. in diameter, on both legs. There was some tenderness over the sacroiliac joints but no other arthropathy. He had aphthous ulcers on the lateral border of the tongue and inner surface of the lip. In the right fundus there were many haemorrhages, and central retinal artery thrombosis, and in the left eye less marked vasculitis. Carotid and radial pulses were normal, but the left femoral pulse was weak and the right femoral pulse absent. The abdominal aorta was palpable well to the right of the epigastrium and a bruit could be heard. The abdomen was diffusely tender, and slight movement in bed caused severe lumbar and sacroiliac pain. Psoas spasm was present.

Investigations.—Haemoglobin 12.4 g./100 ml.; white cells 12,200/cu. mm. (polymorphs 55%); platelets 453,000/cu. mm. Plasma fibrinogen 650 mg./100 ml. Total serum proteins 7.5 g./100 ml. (albumin 3.8 g.); electrophoresis showed slight increase in globulin. No L.E. cells present. No evidence of bacterial, mycoplasmal, or viral infection. E.C.G. normal. Chest x-ray film showed heart of normal size; shadowing in the right mid-zone.

FIG. 1.—Thoracic aortogram. Fusiform dilatation of lower portion of aorta.

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The pain became worse and the abdomen more distended. Pressure over the aorta produced severe pain in the back.

Aortograms (Figs. 1 and 2) (Dr. G. de B. Hinde) showed fusiform dilatation of the thoracic aorta, extending to the level of the renal arteries. Below the renal arteries a segment of aorta appeared narrow, and distal to this a large aneurysm involved the superior

FIG. 2.—Upper abdominal aortogram. Fusiform aortic dilatation extending to level of renal arteries.

mesenteric artery, extending to the level of the inferior mesenteric artery.

At laparotomy Mr. Gordon Heard found the aorta and its branches grossly thickened and inflamed, and only $\frac{3}{4}$ in. (2 cm.) at the level of the renal arteries appeared relatively normal, aneurysmal changes extending above and below. Adjacent lymph nodes were somewhat enlarged. No source of infection could be found. Because the aorta was densely adherent to the posterior abdominal wall resection was not attempted, but a bypass graft was inserted from below the renal arteries to the common iliac arteries. An excised lymph node showed nonspecific reactive hyperplasia.

After operation there was some delay before bowel function was satisfactory, but no other problems. He was maintained on prednisolone, 20 mg. daily, with injections of A.C.T.H. 40 units on alternate days. On smaller doses of corticosteroids his vision deteriorated and mouth ulceration was very painful. He had pain between the shoulder-blades which probably differed from that associated with his episodes of pulmonary infarction. A recent penetrated chest radiograph showed less dilatation of the lower thoracic aorta than was seen in the aortogram.

Discussion

Behçet's disease is not very rare in this country; the patients attend ophthalmological, dermatological, or gynaecological departments or do not seek medical advice. Episodes of unexplained fever and arthralgia are soon forgotten and the manifestations of the disease will be separated by such long intervals that several years elapse before their relation as part of a systemic disorder is recognized. If a young patient has arthritis, fever, and an arteritis, a diagnosis of polyarteritis nodosa or systemic lupus erythematosus is usually made. Oral or genital ulceration is not usually mentioned unless specific inquiry is made for these symptoms, and at this stage uveitis may not be present to help the diagnostician.

In young patients aneurysms may not be suspected, particularly now that syphilis and tuberculosis are less common. Had the possibility of aneurysms in Behçet's disease been recognized an earlier diagnosis might have been made in this case. The diagnosis made in April 1966 was of intestinal obstruction, but investigation showed no mechanical cause and

the condition improved. This transient bowel obstruction was probably due to involvement of the inferior mesenteric artery, and in an elderly man the possibility that this event associated with severe back pain was due to aortic aneurysm would not be overlooked. The severe lumbar pain, which is probably due to inflammatory stretching of the arterial wall, may be confused with pain of spinal origin. Arthropathy, possibly spondylitis, is part of the syndrome; many patients are taking corticosteroid therapy, which may cause vertebral collapse. If there are no radiological changes in the spine and pain is persistent, acute inflammatory disease of the aorta should be considered.

It was suspected that the aneurysm was due to acute infection, perhaps associated with corticosteroid therapy, but careful search failed to reveal a source of infection. The macroscopic appearances of the aorta can only be explained by acute inflammatory disease, unlike the granulomatous changes which may be seen in the aorta in Takayasu's disease, associated with distant tuberculosis, or the more chronic destructive lesions seen in tertiary syphilis. Both these latter conditions may be regarded as immune response to infection, in which a delayed sensitivity reaction is found in the aortic wall. In Takayasu's disease antibodies to the aorta are found (Ito, 1966). It is very likely that a search for aortic antibodies in Behçet's disease will give positive results, as antibodies to oral mucosa have been demonstrated (Lehner, 1967), and by immunofluorescent staining of peripheral blood films (Shimizu *et al.*, 1965) less specific cytoplasmic antibodies have been found.

The cytoplasmic antibody was similar to those occurring in polyarteritis nodosa, rheumatoid arthritis, and dermatomyositis, in contrast to the antinuclear factor found in systemic lupus erythematosus. These immunological findings support the clinical impression that Behçet's syndrome is related to the collagen diseases. Aneurysms of the aorta are described in polyarteritis nodosa (Wolff, 1936) and with giant-cell arteritis (Gilmour, 1941; McMillan, 1950); it must be remembered that division of these syndromes is often artificial, and firm rules may not be stated that only large or small arteries are involved in certain diseases. The evidence for viral infection in Behçet's disease (Sezer, 1956; Evans *et al.*, 1957) has not been conclusive, but the histological appearances could be due to such infection.

Until the cause of the disease is known treatment is empirical. The immediate treatment of the aneurysms must be surgical. Corticosteroids appear to suppress troublesome general symptoms of the disease in some patients, but there is no evidence that they halt the basic underlying disease process. Indeed, it is possible that this therapy may have played some part in the pathogenesis of the aneurysms. The other possible measure is immunosuppression with a drug such as azathioprine, but this will rest on less sure ground than its use in systemic lupus erythematosus. Such therapy is still experimental in this condition, in glomerulonephritis, and in rheumatoid arthritis, but might be tried in patients who have Behçet's disease with life-threatening complications.

The possible association of aortic aneurysms with Behçet's syndrome is suggested by an increasing number of reports, mostly of isolated cases, in the world literature. This complication should therefore be borne in mind in the management of Behçet's syndrome.

Summary

A case is described of aortic aneurysms occurring in a patient with a 12-year history of Behçet's disease. Their relation to the disease is discussed. It is suggested that specific symptoms of the syndrome should be sought in young persons with aneurysms. Aneurysm formation, a possibly fatal complication,

should be considered as a possible cause of pain in Behçet's disease. Treatment is discussed.

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Medical Memoranda

Murmur over Liver in Cases of Severe Anaemia

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A murmur may be audible over the heart and blood vessels in cases of anaemia. A systolic murmur was heard over the liver in three cases of severe anaemia. To our knowledge no reference to such a murmur has been made previously.

CASE REPORTS

The patients were female aged 38, 40, and 12 years suffering from nutritional macrocytic anaemia with ankylostomiasis, nutritional macrocytic anaemia, and thalassaemia. The chief complaints were weakness, pallor, palpitation, exertional dyspnoea, and dependent oedema. Their haemoglobin levels varied from 1.45 to 2.9 g./100 ml. The pulse was of water-hammer type and the rate varied

Phonocardiographic record of murmur over the liver.

between 120 and 130 a minute. The respiratory rate was 20 to 26 a minute. Their blood pressures were 60/0, 115/45, and 110/40 mm. Hg. The neck veins were very distended. The sites of apical impulse were the fifth intercostal space 1 cm. outside the mid-clavicular line, left sixth space 2.5 cm. outside the midclavicular line, and left fifth space on the midclavicular line. One patient had a diastolic gallop. There was no murmur in peripheral vessels. In two patients a soft systolic murmur was heard over the pulmonary area. Their electrocardiograms did not reveal any significant abnormality. The liver was non-pulsatile, tender, and enlarged to 3–4

fingerbreadths below the right costal arch. It was soft in two cases and firm in one. There was a systolic high-pitched murmur over the liver, best heard about 2.5 cm. below the costal arch in the continuation of the right midclavicular line. Application of pressure over the area by the chest-piece of the stethoscope made the murmur a little louder. A phonocardiogram taken in one of the cases recorded the systolic murmur (see Fig.).

In the first case transfusion of 300 ml. of whole blood precipitated pulmonary oedema. Partial exchange transfusion of 400 ml. of concentrated red cells with simultaneous withdrawal of 500 ml. of blood saved her. The other two patients had a very slow transfusion of 200 ml. of concentrated red cells. With transfusion of blood the patients became less dyspnoeic, their pulse rates came down, blood pressures improved, the size of the livers diminished, and the murmurs disappeared within a few hours.

COMMENT

The murmur was probably produced in the hepatic artery owing to accelerated circulation of blood through it as a manifestation of hyperkinetic circulatory state. After appropriate blood transfusion along with improvement of the circulatory state, the size of the liver was reduced and the murmur disappeared.

The murmur was best heard over the liver about 2.5 cm. below the costal arch in the continuation of the right mid-clavicular line. This site suggests that the origin of the murmur was in the hepatic artery. The murmur was not a transmitted one from the heart or the abdominal aorta, as in none of these cases was there a murmur in the abdominal aorta and that heard over the pulmonary area was never very pronounced.

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