RUPTURE OF THE HEART AS A RESULT OF *BR. ABORTUS* ENDOCARDITIS

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Undulant fever is not a rare disease in this country; yet endocarditis due to *Brucella* organisms has only twice been recorded here (Rennie and Young, 1936; Hart *et al.*, 1951), and only in the latter case was it confirmed bacteriologically at necropsy. Dalrymple-Champneys (1950), in his series of 983 cases of undulant fever, does not record a single example. In the foreign literature we have found accounts of a further 21 cases confirmed bacteriologically at necropsy; most of these have been reviewed by Hart *et al.*

There seems to have been no previous example of a sudden fatal termination by massive haemorrhage into the pericardium.

Case History

A 51-year-old forestry nurseryman had had no previous severe illness. In July, 1950, he complained of sudden partial loss of vision in the right eye. An ophthalmologist found pale patches below and to the nasal side of the disk, with a complete central scotoma. The blood pressure was 75/50.

When admitted to hospital on September 25 he was a thin ill-looking man with pigmented patches on the forehead. The blood pressure was 95/60; Hb 78% (11.5 g. %), and the white blood cells numbered 4,500 per c.mm. (76% polymorphs). The Wassermann reaction and Kahn test were negative. The urine contained a trace of protein and scanty hyaline casts.

A rigor occurred the day after admission, but following this his temperature showed only an occasional rise to 99° F. (37.2° C.). On October 17 his serum agglutinated a standard suspension of *Br. abortus* in a dilution of 1/3,200. His general condition improved steadily, the sight in the affected eye gradually returned, and his temperature settled. In view of this no specific treatment for the abortus infection was given. He seemed well in himself on discharge on October 26, but his E.S.R. remained high—54 mm. in one hour (Wintrobe).

A month later his ankles began to swell and he became breathless on exertion. During the following week, early in December, he was readmitted with nocturnal dyspnoea and a temperature of 100–101° F. (37.8–38.3° C.). This pyrexia settled after four days, and was assumed to be due to an associated bronchitis.

Examination showed oedema of the ankles and sacral region, and some clubbing of the fingers. The pulse rate was about 100, with frequent extrasystoles, and a systolic murmur could be heard over the whole praecordium. A chest x-ray film showed moderate enlargement of the heart, chiefly left ventricular; the blood pressure was 95/60. The symptoms of congestive failure improved with treatment and the oedema practically disappeared, but a temperature of 99–100° F. (37.2–38.8° C.) recurred during the week before he was allowed to return home on December 23, for Christmas.

When readmitted on January 6, 1951, the signs of congestive failure had returned more severely, the legs were grossly oedematous and the breathing was distressed. The pulse rate was 100 and regular, and the blood pressure 105/75. No cardiac murmur could now be heard. The

only electrocardiographic findings were slurring of the P–R interval with a depressed T wave in all leads except CF 4; both auricular and ventricular extrasystoles were occurring. A blood count showed Hb, 11.1 g. % (75%); white cells, 5,500 per c.mm. (banded polymorph neutrophils 3%, segmented polymorph neutrophils 88%, lymphocytes 5%, monocytes 4%). He remained afebrile and a single blood culture at this time was sterile. Yet he steadily became worse and died suddenly on January 14, eight days after his readmission and six months after his first symptoms.

Thus the clinical course of the illness was that of a mild *Br. abortus* infection with apparent spontaneous recovery, followed by rapid congestive heart failure. He had had comparatively few of the usual signs and symptoms associated with bacterial endocarditis. The original blindness may have been due to an embolus, but none other was observed. The spleen was never palpable and the patient was afebrile during most of his illness.

Necropsy Findings

A post-mortem examination was carried out 50 hours after death. The heart (275 g.) was not enlarged. The

left ventricle was 17 mm. thick, the right ventricle 6 mm. The coronary arteries were healthy. The tricuspid, pulmonary, and mitral valves were normal. The aortic valve was bicuspid, a single large cusp replacing the usual right and non-coronary cusps (see Figs. 1 and 2). This combined cusp was smaller than two normal ones but larger than a single one: it measured 40 mm., while the other (left) cusp measured 33 mm.

FIG. 1.—Diagram of transverse section of heart at level of aortic valve. L.A.=left auricle. R.A.=right auricle. R.V.=right ventricle. I.A.S.=interauricular septum. I.V.S.=interventricular septum. P.A.=posterior aneurysm. A.A.=anterior aneurysm. L.C.=left cusp. C.C.=combined cusp. Black areas show perforations in cusps. O represents coronary orifices.

FIG. 2.—Part of aortic valve, opened out after cutting through the left cusp. The top of this cusp with attached vegetations has been removed to show opening into posterior aneurysm. Lettering as in Fig. 1.

Opposite the centre of the combined cusp a low ridge ran along the wall of the aortic sinus in the long axis of the aorta. It was 3 mm. wide and less than 1 mm. high, with a rounded outer surface and parallel borders—an appearance almost pathognomonic of a congenital lesion (Koletsky, 1941). Microscopical examination of serial longitudinal sections through the ridge confirmed this. They showed a thickening of the elastic-containing media only and no evidence of an inflammatory reaction. If the lesion had been acquired, such a central ridge should have contained fibrous tissue from the annulus fibrosus on the lumen side of the elastic tissue of the aortic media (Lewis and Grant, 1923).

There were large friable vegetations on both cusps, especially posteriorly, where their margins were fused together for a distance of 1.5 cm. Microscopically these vegetations consisted of fibroblasts with a few lymphocytes and histiocytes, covered by blood clot, fibrin, hyaline necrotic material, and masses of 'Gram-negative coccobacilli'. The posterior third of the combined (right) cusp had been almost completely destroyed by ulceration; only a narrow band at the free margin remained attached to the aorta posteriorly; beneath this was a ragged hole about 2 cm. in diameter. There was also a smaller hole in the other (left) cusp near its attachment anteriorly. Both cusps were slightly thickened. Microscopically the larger showed fibrosis (maximum thickness 3 mm.), and at its junction with the aorta some small deposits of calcium were identified by von Kossa's method. Such changes are common in congenital bicuspid valves in the absence of infection (Lewis and Grant, 1923).

The myocardium, although its cut surface appeared normal to the naked eye, was under the microscope diffusely inflamed, especially just beneath the endocardium. Numerous small foci of necrosis scantily infiltrated with mononuclear and occasional polymorph cells were seen, and also collections of similar cells unassociated with muscle necrosis and having a very occasional central foreign body giant cell. Near the aortic valve there was an occasional acute abscess full of polymorph leucocytes. No fibrosis of muscle was seen apart from a patchy area in the interauricular septum. Since none of these lesions resembled an Aschoff nodule, and since the mitral valve and the endocardium of the left auricle appeared healthy, old rheumatic infection seemed unlikely.

The aortic sinuses opposite the two holes in the cusps were greatly dilated to form localized smooth-walled aneurysms. The smaller (anterior) aneurysm had a narrow orifice opposite the perforation in the left cusp—that is, in the extreme anterior part of the sinus; it extended for about 1.5 cm. to the left beneath the undilated part of the sinus. The larger (posterior) aneurysm involved an area about 1.5 cm. in diameter, and was situated in the most posterior quarter of the sinus; it extended posteriorly, upwards, and to right and left for about 1 cm. Externally its bulging upper dome could be seen between the aorta and the left auricle. The smooth walls of these aneurysms and the presence of the congenital bicuspid valve suggested at first that they might be congenital in origin. There is, however, no recorded case of a congenital aneurysm of the left aortic sinus, presumably because its formation is not affected by the aorto-pulmonary septum. Furthermore, when the posterior aneurysm was investigated microscopically by studying serial horizontal sections at 1-mm. intervals, it was found to have a smooth uninflamed fibrous wall 2 to 3 mm. thick, containing peripherally numerous histiocytes filled with iron pigment. It was continuous below with the fibrous tissue of the annulus fibrosus; at the sides and above the elastic tissue of the aortic media was bent outwards before abruptly giving place to the fibrous tissue of the aneurysm wall. If the aneurysms were congenital, one would expect at least the upper part to be lined by elastic-containing media, even if the lower part were lined by fibrous tissue from the annulus fibrosus.

The blood reaching the pericardial cavity had burst through a small hole in the left wall of the posterior aneurysm and emerged between the left auricular appendage and the aorta, tracking for about 0.5 cm. beneath the visceral pericardium. Microscopically this hole was an acute inflammatory sinus, but serial sections taken above and below it showed a closed cavity filled with pus cells in the wall of the aneurysm (see Fig. 3). This suggests that

FIG. 3.—Transverse section through posterior wall of aorta and upper part of posterior aneurysm at level of top of aortic valve. ($\times 2\frac{1}{2}$. Verhoeff's elastica.)

the perforation was not due to inflammation of the inner surface of the aneurysm but to an abscess in the wall, which may have been embolic in origin or, more probably, arose by direct spread from the vegetations near the attachment of the left cusp.

Other Organs.—The lungs were oedematous (right 800 g., left 550 g.), and there were bilateral pleural effusions, each about 200 ml. The spleen (500 g.), liver (1,800 g.) and lymph nodes were all congested. Microscopically they contained scattered collections of inflammatory cells and small granulomata consisting of epithelioid cells with a varying amount of collagen and an occasional foreign body giant cell but no central caseation. The kidneys, normal in size, had microscopically a non-specific interstitial inflammatory reaction. The remaining organs showed no unusual features.

Bacteriological Findings.—*Br. abortus* was isolated from the patient's bone marrow, and also by guinea-pig inoculation from part of an aortic-valve vegetation which had been washed repeatedly in sterile saline and 70% alcohol and ground before injection into the animal. (The guinea-pig's serum agglutinin titre to *Br. abortus* rose to 1 in 320 in five weeks.) The cultures of *Br. abortus* were identified by their nutritional requirements, and by biochemical tests, dye-inhibition tests, and serology. This confirmed the diagnosis of *Br. abortus* carditis and septicaemia.

Comment

Of the 22 cases of *Brucella* endocarditis confirmed at necropsy, 14 were due to *Br. abortus*, the organism causing undulant fever in Great Britain. In addition to the case described by Hart *et al.* in this country, 10 cases have been recorded in America (Scott and Saphir, 1928; Spink and Nelson, 1939; Smith and Curtis, 1939; Spink *et al.*, 1942, 1948; Wechsler and Gustafson, 1942; Call *et al.*, 1944; Quintin and Stalker, 1946; Voth, 1949), and three in Central Europe (Matzdorff, 1933; Steyrer, 1934; Rothman, 1935). All were males, reflecting the curiously high incidence of brucellosis in men (Stableforth, 1952), and all died after an illness lasting 3 to 11 months. One case of recovery has been described (Spink *et al.*, 1948).

Although in at least two cases (Rothman, 1935; Spink and Nelson, 1939) the heart valves attacked were apparently normal, the infection resembles *Streptococcus viridans*

endocarditis in usually seeking out valves which have been previously damaged by rheumatism or which are congenitally deformed. In nearly all the recorded cases, including the two previously described in England, old rheumatic valvulitis has been found. Our case is the fourth example of infection superimposed upon a congenital bicuspid aortic valve (Wechsler and Gustafson, 1942; Voth, 1949; Spink *et al.*, 1948).

Cases of bacterial endocarditis due to *Brucella* organisms have certain distinctive characteristics. These are well illustrated by our case, and may be summarized as follows:

1. The aortic valve is usually attacked. Occasionally the mitral valve is also involved, but in only two cases was the disease confined to it (Rennie and Young, 1936; Spink *et al.*, 1942).

2. There is a great tendency to produce ulceration. The valve cusps become perforated and there are often haematomata in the myocardium or in the auricular or ventricular septa. In the first case described by Call *et al.* (1944) the inflammatory process had ulcerated through the root of the aorta as far as the epicardium, but, unlike our case, rupture into the pericardium had evidently not occurred.

3. Aneurysmal dilatation of the aortic sinuses is common. Probably (see Jones and Langley, 1949) inflammation of the sinus wall causes separation of the annulus fibrosus from the aortic media, so that blood passes through the wall of the aorta and stretches the exposed muscle of atrium or septum. It then clots and eventually becomes organized, so giving rise to an aneurysm lined by fibrous tissue. That this is the correct explanation in our case is supported by the presence of the surrounding histiocytes filled with iron pigment.

4. A persistent leucopenia is common, but, unlike uncomplicated brucellosis, there is a relative neutrophilia rather than a lymphocytosis, apart from one exception (Steyrer, 1934).

5. Extremely low blood pressure, which was a prominent feature in this case—the systolic pressure being only once recorded as above 100 mm.—has also been found in other cases. In one of these (Gounelle and Warter, 1935) a pressure of 60/45 was recorded, and five others had pressures of 105 mm. systolic or less at one time or another. Furthermore, evidence of alteration in conduction of the heart muscle has been demonstrated in several cases, although not in ours. Both these factors may well be due to the severe myocarditis commonly present.

6. The accompanying bacteraemia often gives rise to a variety of focal lesions in the viscera, such as the granulomata, suppurative lesions, and focal necroses seen in our case (compare Matzdorff, 1933; Sprunt and McBryde, 1936; Rabson, 1939; Call *et al.*, 1944) as well as embolic lesions.

7. There may be improvement in symptoms and cessation of pyrexia for a period, even when infection remains active (Call *et al.*, 1944; Voth, 1949; Hart *et al.*, 1951), so that a patient with *Brucella* endocarditis may appear deceptively well—an important practical point, well illustrated by our case. There was little evidence of septicaemia, only slight pyrexia, no definite embolic manifestations, and no clinical enlargement of the spleen, at a time when the histological evidence suggests that the endocarditis was progressing.

The possibility of such rare complications reinforces the need for the early diagnosis of all cases of undulant fever and their treatment with full courses of antibiotics.

Summary

A case of *Brucella* endocarditis is reported. It was superimposed on a congenital bicuspid aortic valve and gave rise to aneurysms of the aortic sinuses. Terminal rupture of the heart resulted from a small abscess in the wall of one of these aneurysms.

The characteristics of this type of endocarditis are described in the light of this and previous cases.

The possibility of such a serious latent complication emphasizes the need for early diagnosis and treatment of all cases of brucellosis.

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OBSERVATIONS ON GOLD THERAPY IN RHEUMATOID ARTHRITIS

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Gold salts have been widely used for the treatment of rheumatoid arthritis for about 20 years, and during that time many reports of the results have been published. Although some of these reports have been of small numbers of cases, others have been extensive; for example, Forestier (1935) reported on over 550 treated patients, and Hartfall *et al.* (1937) on 690. The general impression from these reports is that a favourable response may be expected in about 80% of cases. Thus Short *et al.* (1946) analysed the results of gold treatment in cases collected from 35 published reports. Making allowance for the different criteria adopted, they found that it was claimed that 84% of 1,943 cases showed definite improvement of any degree, 59.3% of 2,924 showed noteworthy improvement, and 22.6% of 1,825 were arrested. It is probably true to say that on this basis gold has become the most widely accepted single therapeutic weapon in the treatment of rheumatoid arthritis.

Need for Controlled Trials

Unfortunately, none of the results in the early series were controlled in any way, and even now the number of reports of controlled series is strikingly few. Control of results in rheumatoid arthritis is essential for two reasons. The first is that spontaneous improvement and arrest can occur at any time; it seems to occur more often in patients who have developed the disease at an earlier age and in earlier stages of the disease, and it is notable that it is for such patients that gold is said to give the best results. The exact course and the natural history of untreated rheumatoid arthritis are difficult to assess, as with such a prolonged and disabling condition it is impossible to keep patients entirely without treatment, either from their doctor or from friends. Few figures are available even for the results of simple and non-specific treatment, but Short *et al.* (1946)