Salmonella Aortitis in a Patient with a Hufnagel Valve

By Louis Weinstein, M.D., and Kenneth Kaplan, M.D.

The development of practical technics for the implantation of valve prostheses in the heart and blood vessels has introduced a new factor in the pathogenesis of cardiovascular infections. The purpose of this paper is to describe a patient with rheumatic heart disease and aortic regurgitation, who, 4 years after the insertion of a Hufnagel valve, developed Salmonella aortitis and died following rupture of the aorta.

Case Presentation

J. N. (NECH 130-430), a 44-year-old white man was admitted to the hospital because of fever. Twenty-three years earlier he had had rheumatic fever and was told that he had heart murmurs. Symptoms of congestive heart failure first appeared 10 years later and progressed for the next 9 years. Four years before the present admission to the hospital mitral valvuloplasty was carried out and a Hufnagel valve was placed in the descending thoracic aorta. These procedures produced amelioration of the manifestations of cardiac failure. On three occasions (12, 24, and 40 months after operation) the patient noted that the "clicking" sound of the prosthesis became muffled for 1 to 2 days after which the sound returned to its usual intensity. On the first two occasions, he had experienced sharp pain and coolness of the thighs and calves, which persisted for a short period. He was treated with coumadin anticoagulation after the second episode and experienced no further difficulty.

Two weeks before hospitalization, the patient had cramps and diarrhea for 3 days, followed 3 days later by an elevation of temperature to 104 F. and aching pain in the back and legs. Two blood cultures yielded a Salmonella strain which was identified as Sal. schwarzengrund. He was treated with 2 Gm. of chloramphenicol orally per day for 4 days. Because this appeared to be without effect on the fever, he was referred to the New England Center Hospital for further evaluation and therapy.

The patient had been engaged for 15 years in the manufacture of costume jewelry. Personnel from the factory in which he worked visited various areas in Europe frequently. No history of contact with friends, family, or fellow-workers who were ill was elicited.

When he was admitted to the hospital, the patient's temperature was 101 F. (rectally) and his pulse rate was 64 per minute. He was perspiring profusely. The left border of cardiac dullness was 3 cm. to the left of the midclavicular line. Auscultation of the heart revealed a palpable systolic thrill at the base, a grade-III/VI basilar systolic murmur, and a soft diastolic murmur along the lower left sternal border. A loud clicking noise was heard over the chest and abdomen without a stethoscope. The spleen tip was palpable but not tender. Femoral arterial pulses were decreased in intensity; popliteal, dorsalis pedis, and posterior tibial pulsations were absent.

Treatment with 1 Gm. of chloramphenicol given intramuscularly every 6 hours was initiated on the day of admission, after stool and blood cultures were obtained. The temperature remained under 100 F. rectally for the first 4 days but then rose to 105. Multiple cultures of the blood, feces, and urine were sterile or contained no Salmonella. On the ninth day, the dose of drug was increased to 6 Gm. per day; defervescence occurred gradually over the following 6 days and the temperature remained within normal limits for the next 2 weeks. Treatment was stopped after 28 days because of anemia and bone marrow evidence of arrest of erythropoiesis, and because the patient appeared to be "cured."

Two days after therapy was discontinued, the temperature rose abruptly to 107 F. Successive use of parenteral tetracycline, kanamycin, and streptomycin combined with tetracycline resulted in gradual lowering of the temperature to 101 F. Eleven blood cultures made in the interval between the cessation of chloramphenicol administration and 2 days after initiation of tetracycline yielded Sal. schwarzengrund. Four blood cultures after this were sterile.

During the last 14 days of his life, the patient complained of severe "aching" pain in the chest

From the Department of Medicine, Tufts University School of Medicine, and the Infectious Disease Service of the Pratt Clinic-New England Center Hospital, Boston, Massachusetts.

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and upper back. The episodes of pain started abruptly and lasted 2 to 4 minutes; initially, occurring every few days, they then increased in frequency so that they recurred two to four times a day. Aortography, performed on the forty-second hospital day because of the suspicion of dissecting aneurysm of the aorta did not reveal such a lesion. Repeated electrocardiographic studies showed no abnormalities. Three days later the patient was found dead in bed within a few minutes after complaining of pain in the chest for which he was examined but no findings of note were observed.

Postmortem examination revealed a massive dissecting aortic aneurysm that had ruptured just below the site at which the Hufnagel valve was attached. The vessel had ruptured into the posterior mediastinum with continuous dissection into the left, and to a lesser extent, the right pleural cavities, and into the retroperitoneal space. Blood clots appeared to vary in age from 3 to 4 days to very recent. Histologic examination of the aorta near the Hufnagel valve attachment showed discontinuity of the intima at the site of an atherosclerotic plaque with an acute suppurrative inflammatory reaction, which had destroyed the aortic wall to form an abscess (fig. 1). There was an area of infarction and abscess formation measuring 9 by 7 by 7 cm. in the spleen; Sal. schwarzengrund was cultured from this site.

There was old healed rheumatic endocarditis with distortion of the aortic valve consisting of fusion of the commissures of two cusps and marked thickening of the edges of the third cusp. The mitral valve was widened. The left ventricle was hypertrophied, and there were dense adhesions from old pericarditis. The lower aorta showed changes of arteriosclerosis and thrombotic or embolic occlusion. Ischemic necrosis of the proximal convoluted tubules was noted in the kidneys.

**Discussion**

About 3 per cent of arteriosclerotic aneurysms become infected; gram-positive cocci are the most frequently associated bacteria. However, Salmonella are probably the most common of the gram-negative bacilli involved in suppurrative arteritis or aortitis. Although more than 30 cases of Salmonella arteritis have been recorded, we have been unable to discover any reports in English of infection of the aorta by this species of organism when a prosthesis has been present. A case similar to the one described in the present paper but in which the offending organism was *Staphylococcus aureus* has been described by Kleinman. In this instance, there appeared to be a response to antibiotic therapy followed by sudden death due to aortic rupture at the site of infection. These two experiences suggest that the prognosis for patients in whom prosthetic devices have been inserted in blood vessels and who develop bacteraemia must always be guarded because, despite what seems to be effective antimicrobial therapy, there is a constant risk of infection of the vessel that may lead to dissection and death.

There are possibly three factors that condition the risk of infection at the site of a Hufnagel valve. First, because the device is a foreign body, it may provide a nidus for infection that cannot be adequately reached by antibiotics or host defenses. Second, since there is a tendency for severe obliterative arterial disease to appear distal to the valve and since the aorta or large elastic arteries serve as sites for bacterial infection only when they are diseased, a Hufnagel valve may impose the likelihood of endarteritic bacterial implantation by increasing the severity and extent of an aortic intimal injury. Factors that may contribute to the obliterative arterial process are (a) the presence of an increased diastolic pressure in the segment of aorta distal to the prosthesis, and (b) the valve may be a

**Figure 1**

A suppurrative inflammatory reaction extends through the aortic intima. This intima which is demonstrable on either side of the abscess, contains an atherosclerotic plaque at the site of the perforation. Hematoxylin and eosin stain; × 32.

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source for thromboembolism from a surface defect, or the entire prosthesis may serve as a nidus for thrombosis, possibly because movement of the ball might initiate coagulation. Third, Rodbard has outlined hemodynamic factors which suggest that endocarditis or endarteritis tends to occur in the vascular walls adjacent to the point of abnormal maximal blood velocity. The reasons for this are twofold: (1) the nozzle effect of flow through a damaged valve, abnormal arteriovenous communication, or valve prosthesis, by directing the blood streamline to a convergence point while flow velocity simultaneously increases, reduces the lateral pressure of the blood, and hence diminishes the force applying the blood stream constituents (including defensive and nutritive factors) to the vessel wall at the infected area; (2) the relative negative pressure adjacent to the converging flow draws blood from the adjacent vasa vasorum to the areas of infection. This blood, partially depleted of nutrient material and laden with metabolic wastes, may possess less effective antimicrobial activity than fresh blood flowing directly from the large artery through the vascular lining.

The site of aortic wall infection in the present case was clearly just distal to the Hufnagel valve and was engrafted upon a large arteriosclerotic plaque. Since the site of infection was not in the area at which the prosthesis was attached, the findings are not entirely analogous to those described by Kleinman. Whether the major contributing abnormality to the infection was the increased and nearly obliteratoric aortic arteriosclerosis or whether it was the hemodynamic alterations induced by changes in local flow through the valve cannot be determined. It appears highly likely, however, that the changes observed in the lower aorta were causally related to the Hufnagel valve and that these played an etiologic role in producing and perpetuating a Salmonella aortitis despite vigorous and prolonged “effective” antibiotic therapy.

This case raises the problem of interpretation and treatment of bacteremia in a patient who has had a prosthetic device placed in the circulation. Because local anatomic or hemodynamic factors may diminish the efficacy of chemotherapy, it is important to achieve blood levels of drug many-fold greater than the minimum necessary to inhibit bacterial growth; despite this, the mechanical problems present may make such therapy relatively ineffective in eradicating infection of the vascular wall.

Although patients with this type of disease may develop symptoms highly suggestive of dissecting aneurysm of the aorta during antibiotic therapy (as did both Kleinman’s patient and our patient), aortography may show no dilatation of the aorta. The possibility that an intramural abscess has developed must be considered; the only cure for this may be surgical excision of the area about the prosthesis.

Summary

A patient is described in whom Salmonella schwarzengrund bacteremia was associated with infection of the aorta in the area at which a Hufnagel valve had been implanted 4 years earlier. Despite prolonged and repeated therapy with antimicrobial agents to which the organism was sensitive, an abscess developed in the aortic wall and led to a dissecting aneurysm and death.

The role of the Hufnagel valve in altering the anatomy and hemodynamics in the lower aorta and predisposing to local and persistent infection is discussed. It is suggested, on the basis of the course of this patient’s illness, that the appearance of bacteremia is especially ominous when such a prosthesis is present, and that antimicrobial therapy should be initiated as early as possible, that the doses used be large, and that the treatment be prolonged, without interruption. If manifestations consistent with aortic tear appear, despite apparent control of the infection, the presence of an abscess in the aortic wall must be suspected and the possibility of removal of the prosthesis and excision of the infected area be given serious consideration.

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The Learning Process

The child grows, but is still an experimenter: he grasps at the moon, and his failure teaches him to respect distance. At length his little fingers acquire sufficient mechanical tact to lay hold of a spoon. He thrusts the instrument into his mouth, hurts his gums and thus learns the impenetrability of matter. He lets the spoon fall, and jumps with delight to hear it rattle against the table. The experiment made by accident is repeated with intention, and thus the young student receives his first lessons upon sound and gravitation. There are pains and penalties, however, in the path of the enquirer: he is sure to go wrong, and Nature is just as sure to inform him of the fact. He falls downstairs, burns his fingers, cuts his hand, scalds his tongue, and in this way learns the conditions of his physical well being. This is Nature’s way of proceeding, and it is wonderful what progress her pupil makes.—John Tyndall, Fragments of Science, vol. 1, p. 253.
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LOUIS WEINSTEIN and KENNETH KAPLAN

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