BRUCELLA ABORTUS INFECTION OF THE GALL-BLADDER TREATED WITH STREPTOMYCIN

Report of a Case

JAMES S. HEWLETT, M.D., and A. CARLTON ERNSTENE, M.D.
Division of Medicine

Although streptomycin inhibits the growth of Brucella organisms *in vitro*, its use in the treatment of brucellosis in man has given conflicting and, for the most part, disappointing results.[1,2,3,4,5,6,7,8] The antibiotic agent is known to be excreted in the bile in considerable amounts, and it was this fact which suggested that it might be more effective in the treatment of Brucella infections of the gallbladder than in similar infections in other tissues. In the case to be reported here, Brucella abortus was cultured from bile obtained by duodenal drainage, and treatment with streptomycin* resulted not only in control of the patient's symptoms but also in persistently negative subsequent cultures of the bile.

Case Report

A white, single man, an office worker, aged 58, was admitted to the hospital on July 18, 1946, because of lassitude, weakness, and fatigue of two months' duration. His appetite had been poor, and he had lost 8 pounds in weight. There had been no known fever, chills, or night-sweats. The past medical history was negative except for an influenza-like infection five years earlier. The patient denied having had contact with farm animals and the use of unpasteurized dairy products.

Physical examination disclosed a well-developed and well-nourished man who did not appear acutely ill but seemed moderately depressed. The temperature on admission was 100 F., the pulse 84, and the blood pressure 120 systolic and 84 diastolic. The pupils reacted normally, and ophthalmoscopic examination showed no diagnostic changes. The lungs and heart were normal on percussion and auscultation, and abdominal examination revealed no areas of tenderness and no masses or palpable solid organs. Neurologic examination gave normal findings.

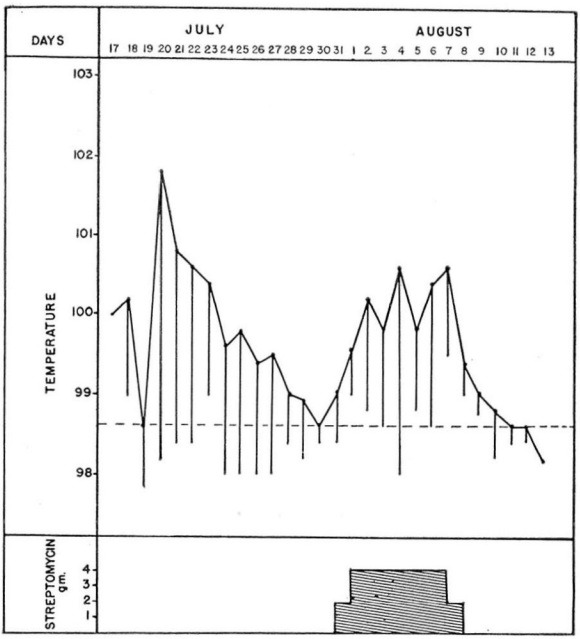
The urine contained no albumin, sugar, or abnormal cellular elements. The red blood cell count was 4,930,000 and the hemoglobin content 13.0 Gm. The leukocyte count was 5600, and differential counts revealed 43 per cent neutrophils, 44 per cent lymphocytes, 10 per cent monocytes, and 3 per cent non-filamented neutrophils. The erythrocyte sedimentation rate was 0.7 mm. per minute (upper limit of normal 0.45 mm.). The Wassermann reaction of the blood was negative.

Roentgenograms of the thorax revealed nothing abnormal, and x-ray studies of the stomach, duodenum, and colon were also negative. The gallbladder visualized well after

* *The streptomycin was supplied by Commercial Solvents Corporation through allocation by the Committee on Chemotherapeutics and Other Agents, of the National Research Council Dr. Chester S. Keefer, Chairman.*

cholecystographic dye and contained a small signet-ring calculus. Intravenous urograms gave normal findings.

During the first four days in the hospital, the maximum daily temperature ranged from 98.6 F. to 101.8 F. (chart). Blood cultures were made on July 22 and 23, and an agglutination test for Brucella was performed. The cultures remained sterile after two weeks of incubation. The Brucella agglutination test, however, was positive in dilutions up to and including 1:512 (table). Because it is known that in certain cases of bru-



Chart

cellosis the organism localizes in the gallbladder, and because it seemed that the presence of gallbladder disease might increase the likelihood of such an occurrence in the present case, a duodenal drainage was done on July 25 and cultures were made of the bile. These yielded a prompt and abundant growth of Brucella abortus*.

* *The method employed for culturing and identifying the organisms was as follows: Approximately 20 cc. of bile obtained by duodenal drainage was diluted to 50 cc. with sterile distilled water. Gentian violet, to give a concentration of 1:100,000, and penicillin, to give a concentration of 10 units per cc., were added to discourage the growth of other organisms. The mixture was centrifuged, the supernatant fluid discarded, and the sediment streaked on blood agar plates containing 2 per cent tryptose and 1 per cent glucose. Incubation was carried out in an atmosphere containing approximately 10 per cent carbon dioxide. At the end of seventy-two hours, suspected colonies were subcultured to obtain a pure growth for subsequent studies. Identification of the organism was accomplished by agglutination with anti-Brucella sera and by further subculture on a series of blood agar slants containing thionin, basic fuchsin, and methyl violet, respectively.*

Streptomycin was administered by intramuscular injection in doses of 0.5 Gm. every three hours day and night from 12:00 m., July 31, until 9 a.m., August 7 (chart). The total amount given was 28 Gm. There had been a gradual decline in the fever before beginning streptomycin therapy, and for three days before the first dose was administered the maximum elevation had not exceeded 99 F. On the day after beginning treatment, however, the temperature rose to 99.6 F., and throughout the remainder of the period of treatment there was a daily elevation to as high as 100.6 F. On the first two days after completion of the course of streptomycin the maximum temperature was 99.4 F. and 99 F., respectively. The temperature then remained normal.

On the day following the last injection of streptomycin, the Brucella agglutination test was still positive in a dilution of 1:512, but cultures of bile obtained by repeating the duodenal drainage remained sterile (table). The patient was discharged on August 12. His appetite was greatly improved, the lassitude and mental depression had cleared to a considerable degree, and he reported that he felt much better. The temperature was recorded four times daily for the next three months and did not rise above normal.

TABLE

Summary of Brucella Agglutination Tests, Bile Cultures, and Blood Cultures

Date	Brucella Agglutination	Bile Culture	Blood Culture
1946			
7–22			0
7–23	1:512		0
7–25		+	
8–8	1:512		
9–3		0	
9–11	1:128		
1947			
4–1	1:16	0	

Further duodenal drainages were done on September 3, 1946, and April 1, 1947, and on both occasions cultures of the bile for Brucella remained sterile (table). The Brucella agglutination test was positive in a titre of 1:128 on September 11 and in a titre of 1:06 on April 1. The patient has continued to feel well and has been working regularly.

Discussion

Although it is known that Brucella may invade and localize in any tissue or organ of the body, only a few cases have been reported in which localization in the gallbladder has been demonstrated. Infection of the gallbladder in all probability occurs more frequently than the literature

indicates, but there is as yet no way in which its true incidence can be estimated. The recorded observations demonstrate that the infection may or may not give rise to localizing symptoms.

White[9] reported a case in which a woman who had previously suffered from an undiagnosed febrile illness developed pain, tenderness, and an indefinite mass in the right upper quadrant. Cholecystectomy was performed, and Brucella abortus was cultured from pus aspirated from the gallbladder. Four months after operation the patient was well and had gained 20 pounds. Leavell and Amoss[10] recovered Brucella by duodenal drainage in a patient with chronic brucellosis. Cholecystectomy was performed, and the patient was entirely well three months later. Amoss[11] also recorded an unusual case of brucellosis in which removal of a cystic ovary, the fluid of which yielded a pure culture of Brucella, resulted in only temporary improvement of the patient. Brucella organisms were cultured from bile obtained by duodenal drainage, and a cholecystectomy was carried out. There had been no earlier symptoms referable to the gallbladder. Mettier and Kerr[12] reported a case of acute brucellosis in which symptoms of acute cholecystitis developed six months after the patient was first seen. Cholecystectomy was performed, and cultures from the gallbladder wall and the bile were positive for Brucella melitensis. There was no recurrence of symptoms during the following two years. Kennedy[13] recovered Brucella melitensis from the bile in 2 of 8 cases of brucellosis.

It has been established that streptomycin is excreted in the bile in considerable amounts. Heilman[14] and his associates made observations on a patient who was given the antibiotic agent in doses of 100,000 units every three hours by intramuscular injection. Two hours after the first injection the concentration of streptomycin in the blood was 6 units per cc. and the concentration in the bile 12.5 units per cc. During the second and third days of administration the concentration in the bile ranged from 3 to 6 units per cc. Adcock and Hettig[15] gave 500,000 units of streptomycin by intramuscular injection to each of 2 patients who had a T-tube in the common duct. In the first patient the concentration in the blood reached a maximum of 30.5 units per cc. at the end of one hour and then declined gradually until only a trace remained at the end of twelve hours. The maximum concentration in the bile amounted to 7 units per cc. and was attained at the end of three hours. In the second patient the concentration in the blood reached a maximum of 34 units per cc. at the end of thirty minutes, while the maximum concentration in the bile amounted to 10 units per cc. and was attained at the end of the fourth hour. A trace was still detectable in the bile at the end of twelve hours.

In the case reported here the positive agglutination test for Brucella and the presence of Brucella abortus in the original culture of bile leave no doubt that the patient was suffering from active brucellosis. The clinical improvement and the disappearance of the organisms from the bile after the course of treatment with streptomycin suggests, furthermore, that the infection was limited principally, or possibly entirely, to the gallbladder. Judging from published reports, brucellosis affecting other organs of the body seldom responds to streptomycin as favorably as did the infection in the present case. The difference in response between this and other types of Brucella infection may be due to the fact that the organisms in the gallbladder are subjected to a higher concentration of the antibiotic agent than occurs in other tissues.

The fever which was present during the first ten days of the period of observation and subsided spontaneously before treatment with streptomycin was started must have been due to the Brucella infection. It would have been of interest to have postponed the use of streptomycin in order to determine the duration of the afebrile period, but this was not feasible because of the demand for hospital beds. The recurrence of fever upon the institution of streptomycin therapy and the prompt return of the temperature to normal after completion of treatment indicate that this particular febrile episode probably was directly attributable to the antibiotic itself. Fever is a common toxic effect of streptomycin.[2,8,14] No other manifestations of toxic action were observed in this patient.

In view of the present experience, further use of streptomycin in cases of brucellosis in which the presence of the organisms in the gallbladder can be demonstrated appears to be advisable.

Summary

A case of active brucellosis has been reported in which Brucella abortus was cultured from bile obtained by duodenal drainage. Treatment with streptomycin resulted not only in control of the patient's symptoms but also in persistently negative subsequent cultures of the bile. The favorable result probably can be attributed to the fact that Brucella organisms in the gallbladder are subjected to higher concentrations of streptomycin than occur in other tissues.

In view of the present experience the further use of streptomycin in cases of brucellosis in which the presence of the organism in the gallbladder can be demonstrated appears to be advisable.

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