

HEPATITIS ASSOCIATED WITH UNDULANT FEVER

Report of a Case

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HEPATITIS with jaundice may occur in the course of human *Brucella* infection although the paucity of published accounts of hepatic involvement in brucellosis indicates that it is uncommon. However, as shown by the autopsy material of Hughes¹ and findings in the liver in specimens obtained by needle biopsy in proved cases of brucellosis,² it is evident that pathologic changes in the liver may be a common result of this infection. Jaundice and a positive culture for *Brucella* organisms in the bile may indicate origin in the gallbladder or duct and are possible manifestations of hepatic involvement. Additional verifications of this theory appear in the experimental work of Amoss.³ He infected guinea pigs with *Brucella* organisms and showed that these organisms caused focal lesions in the liver, spleen and lymph nodes. The reactions around these focal areas start as an exudative inflammatory process and lead to the formation of granulomatous nodules which contain a central necrotic mass.

Chaikin and Schwimmer⁴ reported a case of hepatitis associated with undulant fever in which jaundice was the first symptom.

A patient who was recently admitted to the Cleveland Clinic illustrates the usual clinical and laboratory evidence of hepatitis associated with brucellosis proved by a positive culture for *B. abortus* in the blood.

Case Report

A white grocery merchant, age 33, was admitted to the Cleveland Clinic in November, 1947, with the complaint of fever and jaundice. He had become ill in 1943 while on duty at the Great Lakes Naval Training Station. Attacks of chills and fever lasting a few days necessitated hospitalization on four or five occasions and led to his discharge from the service at the end of eight months. The diagnosis was "recurrent catarrhal fever."

Since 1943 he continued to have recurrences of chills and fever, occurring about every one or two months and persisting for a few days. On occasions he received 1 to 2 Gm. of sulfadiazine daily in short courses without apparent relief.

In September, 1947, he suffered pain in the knees, ankles, and finger joints, and approximately a week after the onset developed a high fever and generalized muscular aching. Shortly thereafter he developed gradually increasing jaundice. The urine became dark, but the stools retained a normal color, and there was no pruritus. There was some constipation. At the same time he complained of severe, persistent, aching pains in the right upper quadrant of the abdomen. There was no nausea or vomiting, and his appetite remained good. He had lost approximately 10 pounds. Two days before admission to the Clinic he had perceived some diminution in jaundice, the temperature was lower, and he had become somewhat stronger. This remission of symptoms may possibly be attributed to a daily parenteral dose of streptomycin for four days prior to admission. Several previous short courses of penicillin had failed to alter the course of the disease.

On physical examination the temperature was 98.6 F, pulse 76, and blood pressure 98 systolic, 72 diastolic. The patient appeared chronically ill, and moderate jaundice was present. The only other significant physical manifestation was a tender, smooth liver, palpable two fingers' breadth below the mid right costal margin.

Laboratory examinations revealed hyperbilirubinemia, bilirubinuria, and urobilinogenuria. The icteric index was 32, and the urine showed strongly positive tests for bile and urobilinogen. The stool was normal in appearance. The thymol turbidity was elevated to 7.0 units, and the Hanger test was 2 plus. A diagnosis of undulant fever was made and confirmed by a positive blood culture for *B. abortus* and a positive blood agglutination in a dilution of 1:2560. A skin test showed a positive reaction to *Brucella* organisms.

A roentgenogram of the chest showed increased peribronchial markings in both lung fields with a tendency toward nodulation. A cholecystogram faintly demonstrated the gallbladder after two doses of dye. Calculi were not identified.

The patient was referred to his family physician, who had suspected the presence of undulant fever, for treatment. It was recommended that treatment include streptomycin, 0.5 Gm., and sulfadiazine, 1.0 Gm. every six hours, as well as a high carbohydrate, high protein, high caloric diet, and bedrest.

The patient visited the Clinic for follow-up examination eight weeks later. He had received a total of 28 Gm. of streptomycin and a total of 42 Gm. of sulfadiazine, according to the suggested dosage schedule. His only complaint was some residual tightness of the finger joints but no pain. The fever had disappeared, and the jaundice had subsided a few days after institution of treatment. The liver was no longer palpable or tender.

Laboratory examinations at this time revealed a slight bilirubinuria, and two specimens of urine were negative for urobilinogen. The icteric index was 5. Slight elevation of thymol turbidity (5.3 u.) persisted, as did a mildly positive Hanger test (2 plus). In the absence of jaundice a bromsulfalein excretion test was made and found to be normal. Blood culture was negative. Undulant fever agglutination of the blood was 1:80. Culture and microscopic analysis of bile obtained by duodenal drainage was negative. A cholecystogram revealed a normally functioning gallbladder without calculi.

The patient was advised to continue with the previously suggested diet and a modified rest schedule because of the continued slight elevation of the thymol turbidity and positive Hanger test.

The source of infection in this patient cannot be stated with certainty. He had lived on a farm until the age of 18 years. Unpasteurized milk and its products had been used. He had also worked as a meat cutter during the past four years.

The diagnosis of undulant fever in this case was confirmed both by a positive blood culture and high blood agglutination titer. A diagnosis of hepatitis seems justified in view of the enlarged tender liver, jaundice, bilirubinuria, urobilinogenuria, normal stools, elevated thymol turbidity, positive Hanger test, and subsequent normal cholecystograms. A course of streptomycin and sulfadiazine given simultaneously was followed by the disappearance of the *Brucella* organisms from the blood stream, the lowering of the blood agglutination titer, disappearance of the jaundice, and improvement of the liver function.

References

1. Hughes, M. L.: *Mediterranean, Malta, or Undulant Fever* (London and New York: Macmillan and Co., 1897).
2. Hoffbauer, F. W., and Spink, W. W.: Biopsy of liver in patients with active brucellosis; description of hepatic lesions. *J. Lab. and Clin. Med.* 32:315-316 (March) 1947.
3. Amoss, H. L.: Localization of *Brucella*. *Internat. Clin.* 4:93-98 (Dec.) 1931.
4. Chaikin, N. W., and Schwimmer, D.: Hepatitis in course of *Brucella* infection. *Rev. Gastroenterol.* 10:130-132 (March-April) 1943.