Hepatic abscess complicating ulceroglandular tularemia

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In a patient with the clinical features of classic ulceroglandular tularemia a solitary hepatic abscess was found during an ultrasound examination. Hepatic tularemia has rarely been reported since the advent of specific therapy, which prevents the disease from reaching the disseminated state. This case, however, shows that the liver can be involved early in the course of tularemia. Increased serum levels of hepatic enzymes may be the only sign of such a complication.

Chez un patient qui montrait les caractéristiques cliniques de la tularémie ulcéro-ganglionnaire classique un abcès hépatique solitaire fut découvert à l'échographie. La tularémie hépatique a rarement été signalée depuis l'avènement d'un traitement spécifique, qui empêche la maladie de se disséminer. Ce cas montre, toutefois, que le foie peut être touché tôt dans l'évolution de la tularémie. L'augmentation des taux sériques des enzymes hépatiques peut être la seule manifestation de cette complication.

Since 1928, when Francis[1] proposed a system of classification for tularemia, many reports have described epidemics and sporadic cases involving the five classic forms: glandular, ulceroglandular, typhoidal, oculoglandular and oropharyngeal. In addition to the relatively common pleuropulmonary complications, many unusual presentations have also been described: meningitis,[2] pericarditis,[3] peritonitis,[4] osteomyelitis and rashes.[5] Hepatic tularemia was once seen at the autopsies of patients whose disease had become disseminated because they could not be treated,[1,6,7] but it has rarely been reported since the advent of chemotherapy. We describe a patient with classic ulceroglandular tularemia in whom there was focal necrotizing hepatitis with the formation of a central abscess early in the course of the infection. *Francisella tularensis* was documented by needle aspiration and culture of liver tissue. To our knowledge, identification of the organism from an isolated hepatic abscess along with successful treatment with chemotherapy alone has not previously been reported.

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Case report

In a previously healthy 66-year-old man a spiking fever developed abruptly, with chills, myalgia, progressive weakness and anorexia. Later that week he complained of mild discomfort in the right axilla and a severe, continuous headache with photophobia. A local physician prescribed a 5-day course of ampicillin to be taken orally, but there was no improvement. The patient was then admitted to our hospital, where it was learned that he had been on a hunting trip before the onset of his illness. He remembered having cut his right thumb while cleaning a wild rabbit and some partridges.

The patient showed signs of toxemia only during recurring bouts of fever (temperature up to 40°C measured orally) but otherwise appeared comfortable. An indolent ulcer was noted on the right thumb and a mobile, nontender lymph node 2 × 3 cm in size was palpated in the right axilla. There was no conjunctivitis, pharyngitis or hepatosplenomegaly.

The leukocyte count and hematocrit were normal, but the erythrocyte sedimentation rate (determined by the Westergren technique) was 87 (normally 0 to 6.5) mm/h. The following serum levels were determined: glutamic oxaloacetic transaminase 59 (normally 7 to 27) U/l, glutamic pyruvic transaminase 81 (normally 4 to 36) U/l, γ-glutamyl transpeptidase 169 (normally 11 to 63) U/l, alkaline phosphatase 194 (normally 36 to 92) U/l and bilirubin normal.

The chest x-ray film was normal. An abdominal ultrasound examination showed a hypoechogenic area 2 cm in diameter near the anterior surface of the right lobe of the liver; this could not be visualized on technetium 99m and gallium scintigraphic scans of the same area (Fig. 1). On the 4th day in hospital an aspiration biopsy of the hypoechogenic part of the liver, performed under ultrasound guidance, yielded dense, viscous pus between fragments of macroscopically normal liver tissue. Microscopic examination revealed necrotic foci edged by granulation tissue that contained many polymorphonuclear cells; the surrounding liver parenchyma showed nonspecific reactive inflammation (Fig. 2).

The hepatic specimen was plated directly on glucose–cystine agar (Difco Laboratories, Detroit) and on chocolate agar supplemented with 1% IsoVitalex (Baltimore Biological Laboratories, Cockeysville, Maryland). After 48 hours of incubation colonies of small gram-negative coccobacilli appeared only on the chocolate agar. The Laboratoire de santé publique du Québec identified these as *F. tularensis*. Repeated attempts to isolate the same organism from

blood samples and the skin lesion were unsuccessful.

Following a 10-day course of streptomycin, 500 mg given intramuscularly every 12 hours, the patient recovered uneventfully. An ultrasound scan of the liver was then normal. The titre of agglutinating serum antibodies against *F. tularensis* rose from zero on the 10th day after the onset of his illness to 1:640 on the 26th day. Tests for *Brucella* agglutinins gave negative results.

Discussion

This case clearly illustrates that hepatic involvement can occur early in the evolution of ulceroglandular tularemia rather than only in the terminal stage.[1,6,7] The early detection here reflects the improvement in diagnostic capabilities, including liver biopsy. The abdominal ultrasound examination in our case was done solely because we had found elevated serum levels of hepatic enzymes. Recently Martone and associates[8] reported hepatomegaly in two of three cases of pulmonary tularemia; the results of liver function tests were abnormal in all three. These observations suggest that dissemination to the liver in tularemia may be more frequent than has been recognized.

The pathological findings in our case were consistent with hepatic tularemia.[1,6] Although tularemia is usually considered in the differential diagnosis of hepatic granulomas, the most frequent pathological findings in the liver of a patient with tularemia are not granulomas but necrotic foci surrounded by neutrophil infiltration,[9] as in our case. However, typical granulomas may still be observed in tularemia, especially in the lymph nodes early in the course of infection.[10] The good clinical response to chemotherapy alone in our case may have been due to the absence of fibrotic encapsulation and the small size of the abscess. Others have recently reported the efficacy of antimicrobial therapy combined with percutaneous drainage of liver abscesses.[11,12]

The probable, though unproven, mode of dissemination in our case was bacteremic spread from the digital ulcer to the liver. Standard blood cultures yielded no organisms, but special techniques, such as direct spreading of the patient's blood on glucose–cystine agar or supplemented chocolate agar,[13] were not done. We easily recovered the organism from the hepatic specimen by directly plating it on supplemented chocolate agar, but no growth occurred on the classic glucose–cystine agar medium. The use of simpler media, like chocolate agar, has already been suggested.[14] However, our glucose–cystine agar plates were not tested with a nonvirulent control strain of *F. tularensis* before their use. This alone could explain why the isolate did not grow on this medium.

Tularemia is endemic in western and central Canada, and a recent epidemic occurred in Quebec.[15] Physicians should bear in mind the possibility of liver involvement when evaluating a patient suspected of having tularemia. Elevated serum levels of hepatic enzymes may be the only sign of this complication and should prompt an ultrasound examination of the liver. Although nonspecific, this procedure could guide further investigation. In attempts to culture *F. tularensis* we recommend the use of enriched

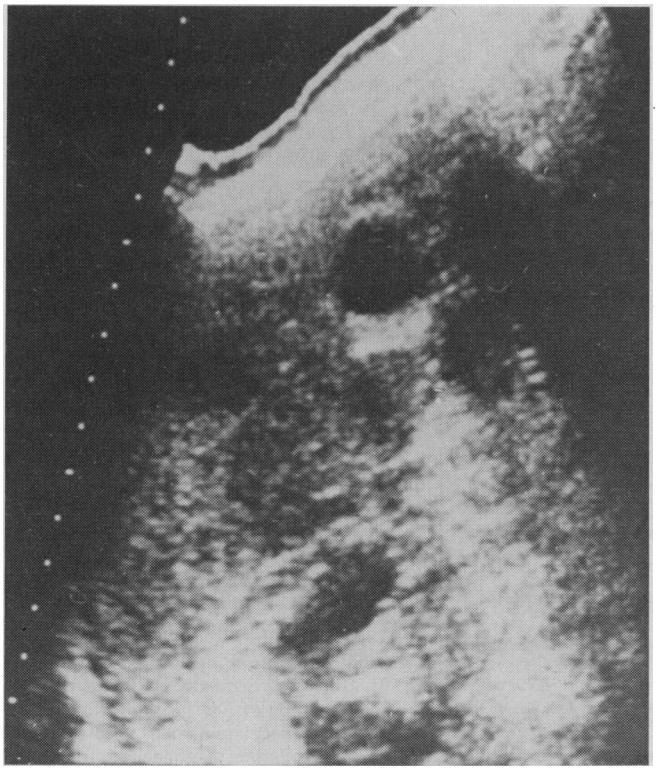

FIG. 1—Transverse ultrasound scan of portion of right lobe of liver. Hypoechogenic mass 2 cm below skin shows fluid characteristics and some cellular elements; it is consistent with an abscess.

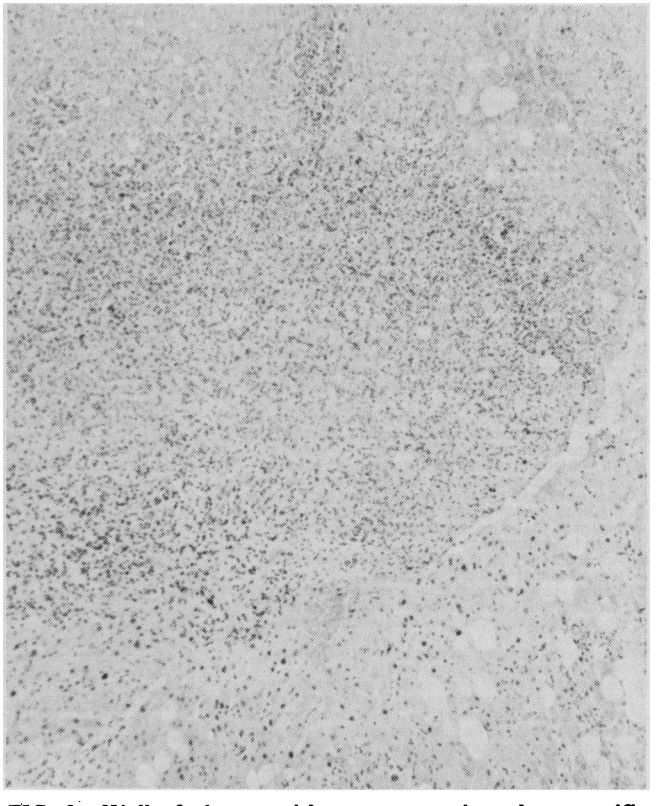

FIG. 2—Wall of abscess with some steatosis and nonspecific reactive inflammation of liver tissue in lower right (hematoxylin–eosin and saffron; ×250).

chocolate agar, as well as the standard glucose–cystine agar.

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