A Review of Echinococcal Disease

JOSEPH W. LEWIS, JR., M.D., NEAL KOSS, M.D., MORRIS D. KERSTEIN, M.D.

Echinococcal infestation, although still a rare occurrence in most of the United States, is being seen with increasing frequency. Three cases of hepatic echinococcosis are described. A review of the salient features of the disease is presented along with various aspects of diagnosis and therapy.

From the Department of Surgery, Yale University School of Medicine, New Haven, Connecticut

WITH THE ADVENT of more efficient and inexpensive means of transportation, increasing proportions of world populations are meeting and mixing. During the fiscal year ending June, 1973, slightly over 400,000 immigrants registered in the United States alone, approximately 6,500 of whom settled in Connecticut. With this migration, diseases uncommon in a particular region may appear with increasing frequency, thereby confronting the clinician with perplexing diagnostic and therapeutic problems. For example, in the last 3 years individual cases of echinococcosis originating in Greece, Italy and Hungary respectively were seen in the New Haven, Connecticut area. These cases are presented to reacquaint the physician with the salient features of this disease and the current modes of diagnosis and treatment; the major portion of this report will center around hepatic *Echinococcus granulosus* infestations.

Case Reports

(I.P., 816834) A 20-year-old Greek sailor entered the United States in early 1971. He presented with a right lower quadrant mass and vague epigastric pain, present intermittently for three months. He denied change in bowel habits, diarrhea, vomiting, weight loss, chills, fever, or jaundice. His vital signs on admission: blood pressure 108/70; pulse 84; and, rectal temperature 99.4 F. Pertinent physical findings were limited to the abdomen where a 6 cm in diameter mass was palpable to the right of the midline just above the pubis. It was freely movable, slightly tender to palpation with no pulsations or nodules. It was firm and felt to be intraperitoneal in origin. A suggestion of a similar mass was present

under the right costal border. A third tender soft mass was felt anterior to the rectal wall at approximately 7 cm from the anal verge. Chest x-ray was within normal limits. Admission laboratory data included: hematocrit of 48%, WBC 10,100 with 59% segs, 1% bands, 0% eosinophils, bilirubin (total/direct) 0.33/0.11 mg %, SGOT 104 units, and alkaline phosphatase 32 units.

At laparotomy, multiple echinococcal cysts were found in the omentum, the perivesical and rectovesical spaces, the porta hepatis and posterior surface of the right diaphragm (Fig. 1). Most cysts had a stalk and were excised easily. Exposure of the diaphragm cyst was difficult and spillage occurred locally with its excision. The fluid contained many daughter cysts and the typical scolices were seen (Figs. 2 and 3). After removing the surrounding packs, the area was irrigated thoroughly with saline and a sump tube was left in place. There was no obvious primary intraperitoneal source that accounted for the initial seeding of cysts in this patient. His postoperative course was complicated by fever and a right lower lobe pneumonitis, treated with antibiotic therapy and pulmonary toilet. The patient refused further study or treatment after convalescence and returned to Greece on discharge.

(A.R., 100634) An 18-year-old Italian youth immigrated to the United States at the age of 10 years. His childhood was spent in rural Northern Italy where frequent contact with sheep, dogs, and other farm animals occurred. He was well until 5 days prior to admission when crampy, nonradiating right upper quadrant and epigastric pain developed. Two days later the patient had a shaking chill and a temperature of 102 F orally but denied nausea, vomiting, change in bowel habits or jaundice. Several similar painful episodes had occurred within the last year but were self limited and required no treatment.

On admission his blood pressure was 130/86 with a pulse of 70 and a rectal temperature of 99.8 F. There was no scleral icterus, jaundice, or cutaneous malformation. Dull tenderness without guarding or rebound was present in the right upper quadrant and a smooth, nontender liver edge was palpable 3 cm below the right costal border.

Admission laboratory data: hematocrit 48%, WBC of 11,300 with 34% eosinophils (on repeat - 49%), prothrombin time (control/patient) 13/17 seconds, total bilirubin 1.1 mg %, BSP retention 8%, alkaline phosphatase 74 units, SGOT 26 units, SGPT 138 units, and LDH 380 units. The echinococcus indirect hemagglutination titer was 1:35,600 (diagnostic level 1:800) and the bentonite flocculation titer read 1:5,120 (diagnostic 1:800). Multiple fresh stools for ova and parasites were

390

FIG. 1. Hydatid cyst with its stalk removed from the porta hepatis of patient number one.

rigors of World War II. Later, as a teenager, he worked as a shepherd in Hungary where many of his sheep died from an unknown disease. In 1956, he emigrated to the United States and was essentially asymptomatic until postprandial epigastric and right upper quadrant colicky pain developed 16 years later. An oral cholecystogram was within normal limits and an UGI series showed a small hiatal hernia at this time. A bland diet did not relieve the pain which actually worsened over the next three months and became associated with nausea, vomiting, and jaundice. These symptoms cleared spontaneously, but recurred two months later. On admission to the West Haven VA Hospital, the patient was acutely ill with upper abdominal pain. His blood pressure was 120/80, the pulse 68 and the temperature 99.6 F rectally. The sclera and skin were nonicteric and examination of the head, neck, and chest revealed no abnormalities. Marked right upper quadrant tenderness with voluntary guarding was present but no signs of peritoneal irritation could be elicited. No masses or organomegaly were present and brown guaiac negative stool was found in the rectum.

Admission laboratory data included: hematocrit 44%, WBC 4,900 with 53% segs, 0% bands, and 5% eosinophils, bilirubin (total/direct) 4.5/3.1 mg %, alkaline phosphatase 190 units (normal 30-85), SGOT 165 units (normal 10-50), normal amylase and lipase. Chest x-ray and KUB were normal and an UGI series confirmed a small sliding hiatal hernia. Neither oral nor intravenous cholangiography showed any visualization of the biliary tract.

At laparotomy numerous adhesions were found around the gallbladder and in the porta hepatis. The liver was felt to be normal, but the common bile duct was dilated to a diameter of approximately 2-2.5 cm. A cholecystectomy was performed, but no stones were found. Upon opening the common bile duct, green-white tissue strands were extruded and further material was removed by irrigation. Pathologic examination of this material revealed echinococcal scolices (Fig. 4). A T-tube cholangiogram demonstrated material in the distal duct that was extracted with forceps (Fig. 5). Intrahepatic biliary radicles in the right lobe of the liver were distended but no definite space-accompanying mass could be delineated by operative cholangiography. After copious irrigation of the operative area, the abdomen was closed.

A postoperative liver scan (Fig. 6) showed a defect in the right lobe and an hepatic arteriogram demonstrated a mass lesion deep within the anterior segment of the right lobe (Fig. 7). Multiple samples of T-tube
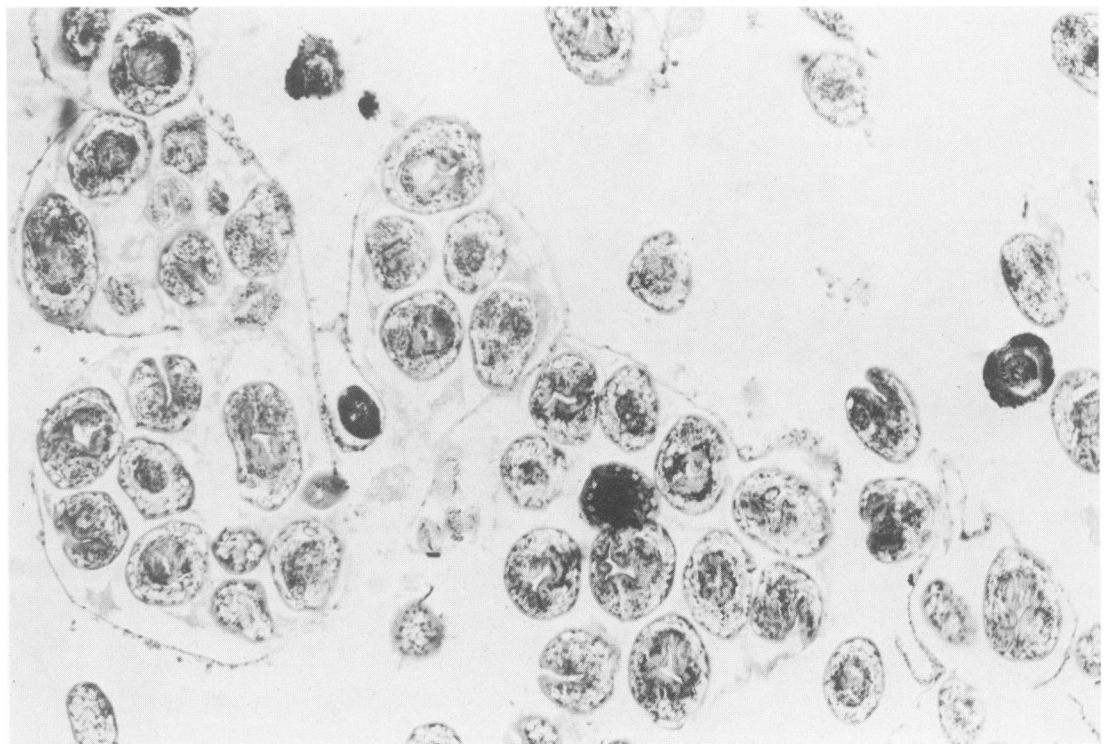
negative. Chest x-ray, UGI series and oral cholecystogram were within normal limits. A liver scan demonstrated a concavity on the inferior border of the liver. The right upper quadrant pain worsened and a temperature spike of 104 F occurred. At laparotomy, multiple, pale-pink fluctuant, 3-4 inch in diameter abscess cavities were found in the left lobe of the liver. Thick, brown purulent material was aspirated from these cavities which were then irrigated with saline and packed with iodoform gauze. Cultures of the abscesses grew alpha *Streptococci*, *Pneumococci* and *Bacteroides* species. Type specific antibiotics were given and the iodoform pack was gradually removed without incident. Pathological examination of the material removed at surgery confirmed echinococcal disease.

(J.K., 041 32 9365) A 35-year old Caucasian man of Hungarian nationality was forced to scavenge food from garbage piles to survive the

FIG. 2. Hydatid fluid from cyst in Fig. 1. Daughter cysts are seen with their surrounding membranes intact (×208).

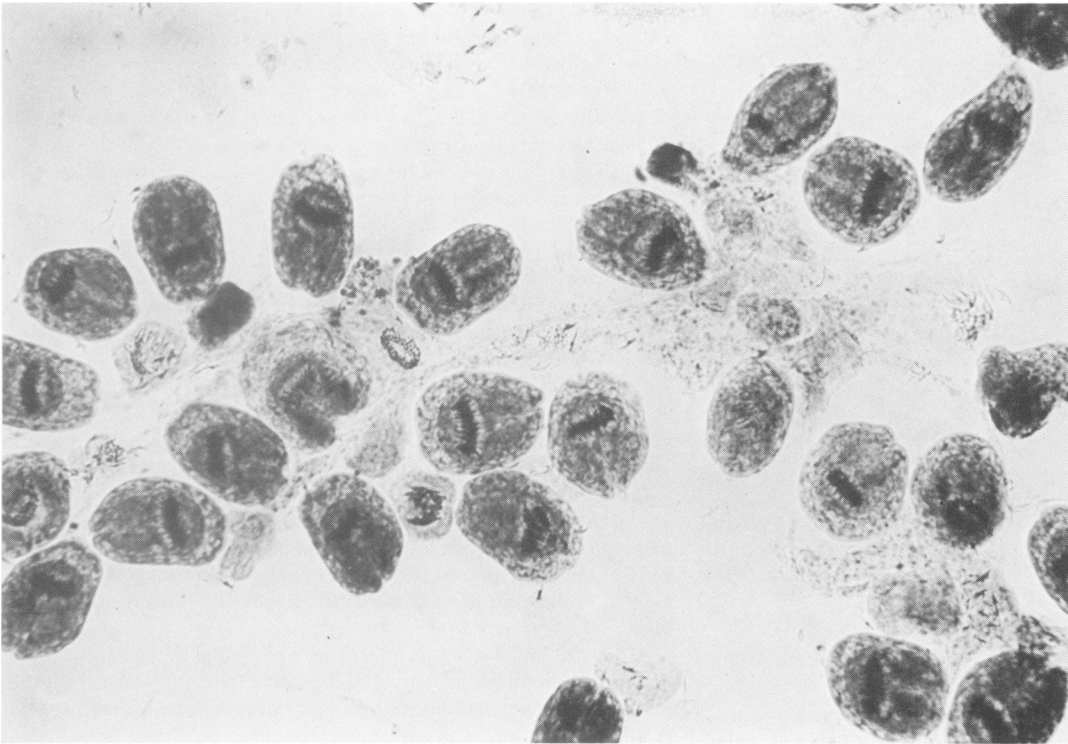FIG. 3. Giemsa staining brings out the scolices in the hydatid fluid (×208).

aspirate showed no scolices or other hydatid material. The indirect hemagglutination titer was 1:1024 (diagnostic level 1:32) and the bentonite flocculation was negative.

One month later, the liver was re-explored; no mass lesion was palpable. After extensive packing of the operative area, a spinal needle was introduced into the anterior segment of the right lobe of the liver and approximately 35 cc of a dark, bile-stained fluid were aspirated. Absolute alcohol (95%) was injected into the cavity while isotonic saline was gently irrigated through the T-tube into the common bile duct to prevent injury to the ductal system. The alcohol was removed after 10 minutes and an incision was made in the right lobe of the liver and the cyst wall was identified and excised. The resultant cavity (estimated volume — 50 cc) was swabbed with absolute alcohol and an omental pedicle was sutured into place to obliterate the dead space and allow absorption of any exudate. An operative cholangiogram showed debris in the common bile duct which was then removed through the original
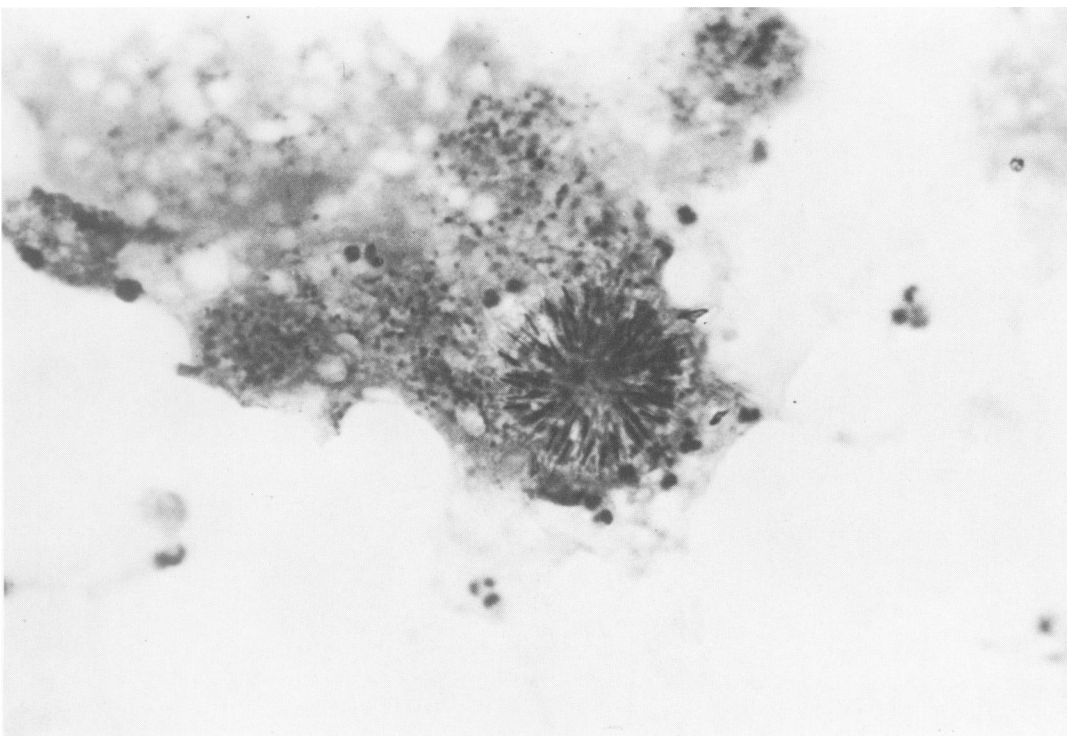

FIG. 4. Microscopic examination (×334) of material from the common bile duct of Patient number three. The typical scolex can be seen under high power.

FIG. 5. Gross appearance of material extracted from distal common bile duct of Patient number three.

choledochotomy. A second cholangiogram following reinsertion of the T-tube showed the site of communication of the cyst with the biliary tree but no further intrabiliary material was seen (Fig. 8). The post-operative course was uncomplicated and a repeat T-tube cholangiogram 2 months later was normal. The T-tube was, therefore, removed. The patient remains symptom free at two years and the indirect hemagglutination test has become negative (Fig. 9).

Occurrence

Echinococcus has a world-wide distribution with heaviest infestations in regions of cattle and sheep husbandry, e.g., Central Europe, South America and eastern Australia. In North America the largest endemic area is

Alaska with an estimated 22% infestation rate in dogs in certain areas.[16] In the Yukon territory alone, up to 40% of the indigenous human population is infested.[3] It is also seen in southwestern Canada and adjacent U.S. states, California,[11] the mid-southern states and Mexico.[23] The first demonstration of the complete cycle of transmission of *Echinococcus granulosus* in the United States occurred in 1969, in the Central Valley of California.[18] In various parts of Italy, 50-90% of slaughtered cattle harbor the disease.[20] In Greece, the annual human morbidity is 7.5 individuals per 100,000[22] and in adjacent Adriatic zones, up to 30% of sheep are infested.[21] Other heavy endemic areas are the western coast of South America, Spain, Portugal, adjacent North African states, mid-eastern Africa, Iraq, southern India, Russia, and eastern Australia.

Parasitology

The word echinococcus originates from the Greek meaning "hedgehog berry," a term descriptive of the gross pathology of the lesion. Another descriptive Greek word applied to this disease is hydatid, "a drop of water." This disease process probably was known to Hippocrates who described, "liver(s) . . . filled with water."[1] The etiologic agent and its characteristics were delineated during the 17th and 18th centuries, but the complete life cycle was not documented until the 19th century.
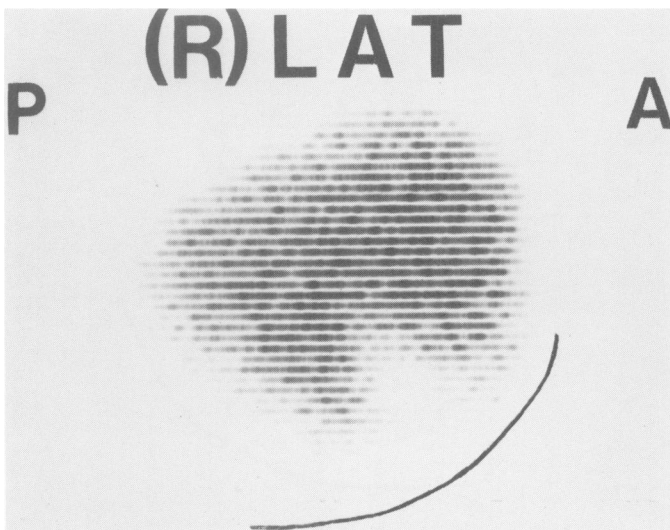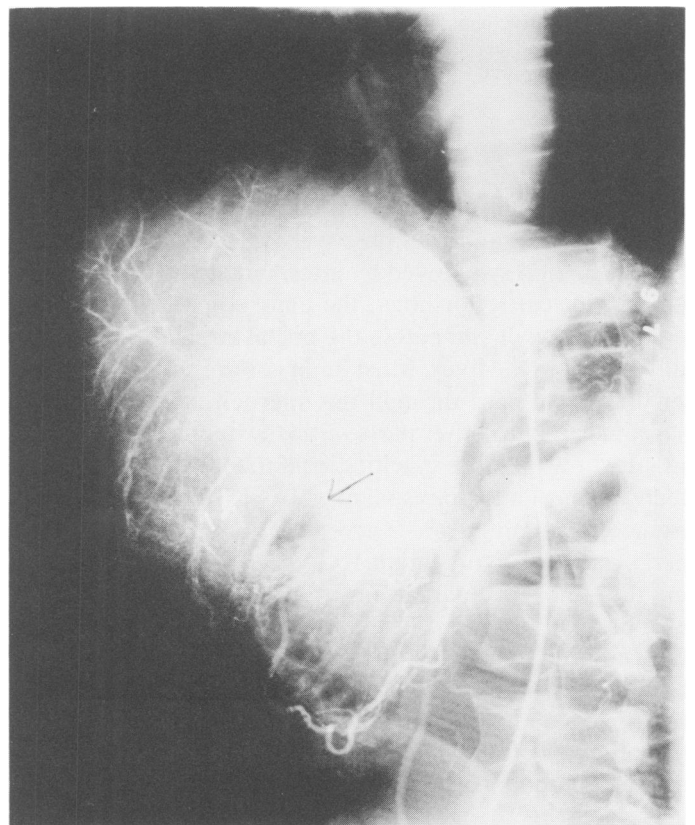

FIG. 6. Right lateral view of liver scan on Patient number three following first operation. This demonstrates a single filling defect in the anterior segment of the right lobe.

FIG. 7. Hepatic anteriogram on Patient number three showing location of cyst in the liver.
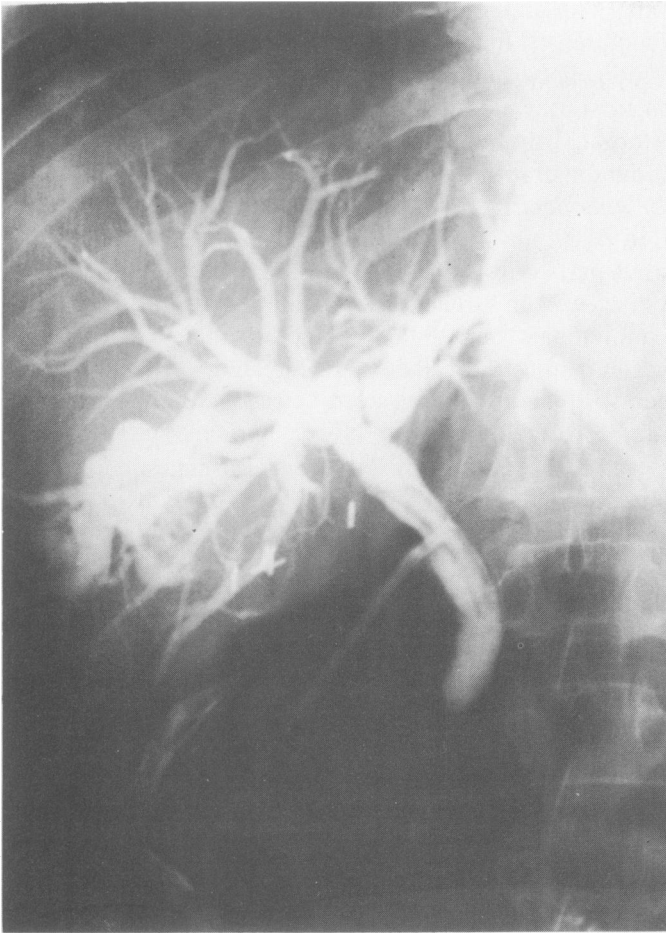
FIG. 8. Intra-operative cholangiogram during second procedure on Patient number three. The cyst fills from the biliary tree, but no material is seen in the biliary tract.

and daughter cysts impacted in the ampulla of Vater producing obstructive jaundice.) The life cycle is completed when the definitive hosts (dogs, wolves, foxes) consume the infested viscera of the intermediate host. A more detailed summary of hydatid morphology and life cycle can be found in standard parasitology textbooks.

Clinical Features

The liver is the most frequently parasitized organ in the human with an infestation rate of approximately 60% followed by the lung with 30% involvement.[17] The remaining fraction is scattered throughout the body with no particular organ system predominating. Since the echinococcal cyst grows slowly, symptoms may not appear for many years until adjacent structures are compressed or deformed producing pain or organ system dysfunction. With hepatic involvement, approximately 75% of cysts are located in the right lobe[17] where they may grow to enormous sizes containing up to 16 liters of hydatid fluid.[5] The patient may accidentally discover an asymptomatic abdominal mass or present with right upper quadrant pain. Many cases are documented following a complication of the initially asymptomatic infestation. Rupture of the cyst into the biliary tract may occur in 5-10% of cases with hepatic involvement.[12,14] This usually presents a clinical picture compatible with choledocholithiasis and cholangitis including colicky right upper quadrant pain, jaundice and fever when secondary infection occurs. The finding of daughter cysts or scolices in the stool or vomitus will confirm the diagnosis. Urticaria and peripheral eosinophilia may be present due to the strongly antigenic nature of the cyst fluid.

The definitive hosts for *Echinococcus granulosus* are dogs, wolves, foxes, and other sylvatic carnivores. This tape worm, usually 4-6 mm in length, lives attached to small bowel villi and the infective ova are shed through the feces. When swallowed by intermediate hosts such as man, sheep, cattle, or hogs, the embryo passes through the intestinal wall and enters the portal circulation, eventually reaching the liver. Most embryos are trapped in the liver, but some pass through the microcirculation to the lungs and rarely to other parts of the systemic circulation (Fig. 10 shows a large calcified echinococcal cyst of the spleen in an elderly physician who was unaware of its presence for many years. There was no evidence of any other systemic involvement.)* Regardless of the location, the embryo enlarges into a tiny cyst which then develops several layers. The germinal epithelium, which produces broad capsules and eventually the scolices, is the active portion of the cyst. A highly antigenic fluid, *eau de roche*, also collects within the cyst cavity and daughter cysts often are found floating therein. (In patient J. K. the echinococcal cyst ruptured into the biliary tree
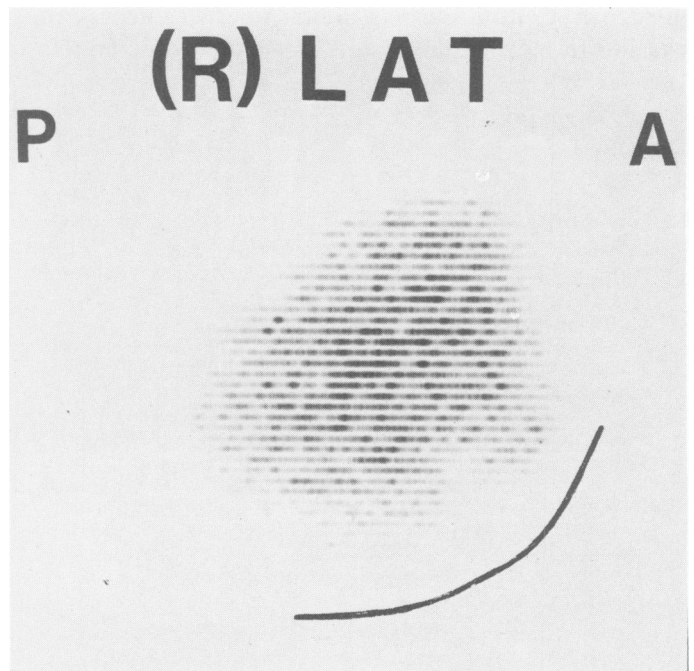

FIG. 9. Right lateral view of liver scan 2 years after first procedure on Patient number three. The defect appears less distinct at this time.

---

*This patient is not included as a case report because we have no other documentation of the disease besides the classic radiologic picture.
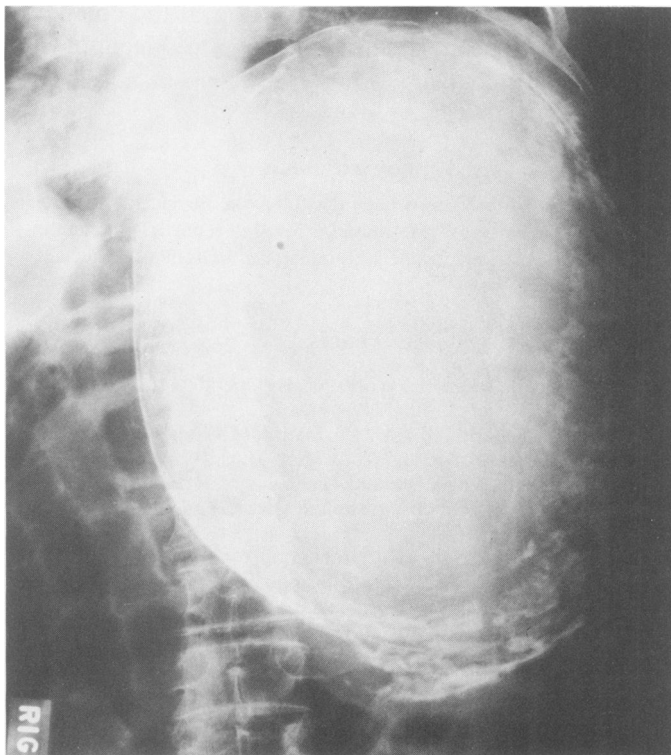
Fig. 10. Abdominal roentgenogram showing huge calcified echinococcal cyst of the spleen.

Secondary pyogenic infection of the cyst may occur without direct communication with the biliary tract. Chills, fever, and right upper quadrant tenderness, with or without a mass will be present. Cysts may rupture into the free peritoneal cavity producing peritonitis and metastatic seeding. In a review of 223 cases of hydatic disease, 30 instances of peritoneal spillage at the time of surgery were documented.[19] Positive evidence of secondary cyst growth was found in only 4 of these 30 patients; 3 out of the 4 were followed greater than 5 years. Rupture through the dome of the liver can produce a subdiaphragmatic abscess which may penetrate into the contiguous pleural space or pulmonary parenchyma.[7] Daughter cysts may be coughed up if erosion into the bronchial tree occurs. Since the hydatid fluid is highly antigenic, spillage beyond the confines of the cyst may result in a severe anaphylactic reaction with circulatory collapse and death. In 5-10% of cases the cyst will die and eventually calcify.[10] This may be caused by rupture into the biliary tree with expulsion of all infective material, hemorrhage into the cyst, or secondary infection of the hydatid cavity.

Laboratory Diagnosis

Since many of the symptoms and signs of echinococcosis are nonspecific and only suggestive, laboratory examinations have been devised to aid the clinician in establishing a diagnosis. The immunologic response of the host to the strongly antigenic nature of the hydatid fluid forms the basis of several determinations. Injection of human and animal hydatid fluid into the dermis of an infested patient is the basis of the Casoni test. An urticarial papule will develop in 59-70% of cases but may also be positive in carcinomatosis, leishmaniasis and teniasis.[2,17] The indirect hemagglutination test for hydatid disease has a much higher specificity and a diagnostic titer virtually confirms the diagnosis. However, negative results may be recorded in up to 35% of patients with pathologically confirmed disease.[2] A complement fixation test, similar to the Wasserman reaction, is available and is positive in up to 80% of patients with the disease.[17] Recently, immunoelectrophoretic tests have been devised that will give up to 93% positive results in proven cases of hydatid disease. The association of at least two tests (the indirect hemagglutination and immunoelectrophoretic assays) will result in laboratory diagnosis of over 94% of all cases.[4]

When the cyst dies or is completely removed surgically, the hemaglutination and complement fixation tests (and occasionally the Casoni reaction) will revert to negative thus affording some prognostic significance. Due to the relatively recent development of specific immunoelectrophoretic determinations for echinococcosis, it is not known whether titers will fall with cyst death.

Eosinophilia, although nonspecific, may be seen in approximately 50% of cases ranging usually between 5-10% of the white cells counted.[2]

Scintillation scans of the liver, spleen, bone, and brain may suggest a space occupying mass that can be further defined by selective angiography. These modalities proved especially helpful in Patient J.K. whose cyst could not be detected by inspection or palpation during the initial laparotomy.

Treatment

Although screening programs for scolicidal drugs exist,[6] to date no effective medical treatment is available and surgery remains the best hope for cure. Effective treatment requires accurate preoperative assessment of the extent of disease and its state of antigenicity. Small calcified cysts of the liver with negative serologic tests need no specific treatment. Suspicion of active disease should be confirmed by serologic examinations and localization accomplished by radioactive scans and selective arteriography. Percutaneous aspiration of cysts in suspected Echinococcosis should not be performed under any circumstance since dissemination or anaphylaxis can occur. Since manipulation or spillage of the highly antigenic cyst fluid at the time of operation also can cause anaphylactic shock, anesthesia personnel should be fully acquainted with this complication with provisions made for specific treatment if a shock state should develop. The intravenous administration of pres-

sors such as epinephrine or aramine to counter the massive peripheral vasodilation coupled with a beta adrenergic agent such as isoproterenol to reverse bronchospasm if present will result in the highest salvage rate.[9] The value of large doses of intravenous steroids is unclear, but probably is beneficial.

If the cyst is large or multicentric within one anatomic unit of the liver, hepatic lobectomy is the procedure of choice.[15] All contiguous structures should be meticulously isolated from the infective material by gauze packs and lobectomy is performed in the standard manner. A different procedure should be employed if a single small cyst in one lobe or several cysts in multiple lobes are found. Again extensive packing of the operative field should be done. If the cyst is not readily visible or palpable, a spinal needle on an aspirating syringe should be introduced into the most likely area demonstrated by preoperative scans and arteriography. Care should be taken with aspiration since the hydatid fluid can be under increased pressure with the chance of dissemination. All fluid should be removed and replaced with an equal volume of a substance toxic to the Echinococcus, such as hypertonic saline (15-20% solution), absolute alcohol, hydrogen peroxide, or certain other solutions.[8] Formalin, which used to be the preferred agent, has been discontinued by most surgeons because of the occasional fatality associated with its use. When the contents of the cyst are bile-stained, one should not use any caustic substances for injection. The material chosen should be left in the cyst cavity for at least 5-10 minutes and all debris and daughter cysts should be removed thereafter. The resultant defect can be managed in several ways. Marsupialization was used extensively in the early treatment of this disease and consisted of suturing contiguous portions of the wound edge to the walls of the cyst cavity. It invariably resulted in a chronically draining wound often with biliary fistulae and should be used only as a last choice when no other alternatives are feasible. *Capitonnage* has been used extensively in countries where echinococcosis is endemic.[17] The superficial portion of the cyst is excised after sterilization and the remaining walls are brought together with a series of purse-string or mattress sutures starting from the bottom and working outward. As an alternative, a portion of omentum with a good blood supply can be sutured into the defect to accomplish the same obliteration of dead space.[13]

If the cyst is infected at the time of surgery, large drains should be placed into its depths and brought out through stab wounds. A drainage catheter can also be placed to allow irrigation of the cyst in the postoperative period. Omentum, if available can be used to help wall-off the infected operative area. If the cyst has ruptured into the biliary system, T-tube drainage of the common bile duct should be considered following treatment of the primary hepatic locus.[14]

References

1. Adams, F.: The Genuine Works of Hippocrates. London, The Sydenham Society, 770, 1849.
2. Apt, W. and Knierim, F.: An Evaluation of Diagnostic Tests for Hydatid Disease. Am. J. Trop. Med. Hyg., 19:943, 1970.
3. Cameron, T. M.: Incidence and Diagnosis of Hydatid Disease in Canada: Echinococcus granulosus var. canadensis. Parassitologia, 2:381, 1960.
4. Castagnari, L. and Sorice, F.: Immunoprecipitation Tests in the Diagnosis of Human Hydatidosis. Folia Allergol., 18:511, 1971.
5. Dungal, N.: Echinococcosis in Iceland, Am. J. Med. Sci., 212:12, 1946.
6. Frayha, G. J., Saheb, S. E. and Djani, R. M.: Systematic Search for a Systemic Hydatid Scolicide. Chemotherapy, 16:371, 1971.
7. Hankins, J. R.: Management of Complicated Hepatic Hydatid Cysts. Ann. Surg., 158:1020, 1963.
8. Heslop, J. H.: An Assessment of the Efficacy of Hydatid Scolicidal Agents Used Locally in Surgery. Austr. N.Z. J. Surg., 37:205, 1967.
9. Jakubowski, M. S.and Barnard, D. E.: Anaphylactic Shock During Operation for Hydatid Disease. Anesthesiology, 34:197, 1971.
10. Jidejian, Y.: Hydatid Disease. Surgery, 34:155, 1953.
11. Leiley, P. D., Carney, W. P. and Woods, C. E.: Studies on Sylvatic Echinococcus. III. Host Occurrence and Geographic Distribution of Echinococcus Multilocularis in the North Central United States. J. Parasitol., 56:1141, 1970.
12. Levy, M.: Recurrent Cholangitis Caused by Echinococcosis of the Biliary Passages. Israel J. Med., 6:388, 1970.
13. Lofti, M. and Hashemian, H.: Hydatid Cyst Disease of the Liver and Its Treatment. Int. Surg., 58:166, 1973.
14. Macris, G. J. and Galanis, N N.: Rupture of Echinococcus Cyst of the Liver into the Biliary Ducts. Am. Surg., 32:36, 1966.
15. Pissiotis, C. A., Wander, J. V. and Condon, R. E.: Surgical Treatment of Hydatid Disease. Arch. Surg., 104:454, 1972.
16. Rausch, R. L.: Recent Studies on Hydatid Disease in Alaska. Parassitologia, 2:391, 1960.
17. Romero-Torres, R. and Campbell, J. R.: An Interpretive Review of the Surgical Treatment of Hydatid Disease. Surg. Gynecol. Obstet., 121:851, 1965.
18. Sawyer, J. C., Schantz, P. M., Schwabe, C. W. and Newbold, M. W.: Identification of Transmission Foci of Hydatid Disease in California. Public Health Rep., 84:531, 1969.
19. Schiller, C. F.: Complications of Echinococcus Cyst Rupture. JAMA, 195:220, 1966.
20. Sera, P.: L'adattamento di una Microtecnica allo Emoagglutinazione Indiretta per L'idalidosi. Boll. Inst. Sieroter. Milan, 46:274, 1967.
21. Tartaglia, P.: Das Problem der Echinokokken en Krankheit in Dalmatien. Z. Tropenmed Parasitol., 15:441, 1964.
22. Voyatzis, N. G., Stergiopoulos, J. C., Korres, G. C., et al.: Hydatid Disease in Childhood. Jordan Med. J., 2:270, 1967.
23. Williams, J. F., Lopez Aderas, H. and Trejas, A.: Current Prevalence and Distribution of Hydatidosis with Special Reference to the Americas. Am. J. Trop. Med. Hyg., 20:224, 1971.