Detection of the *Echinococcus granulosus* Diagnostic Arc 5 in Sera from Patients with Surgically-Confirmed *E. multilocularis* Infection

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Summary. The *Echinococcus granulosus* diagnostic arc 5 was revealed by sera from an Alaskan and a Swiss patient with surgically confirmed *E. multilocularis* infections. The possibility of each patient harboring a concurrent infection with both parasites may be disregarded on the basis of radiologic, scintillographic and surgical data. This conclusion is compatible with ecologic and epidemiologic considerations. These observations suggest that the immunoelectrophoresis test based on arc 5 positivity is not *E. granulosus*-specific as originally described.

Introduction

The only immunodiagnostic technique for human *Echinococcus granulosus* infection with which false positive results have not been obtained to date is the immunoelectrophoresis (IEP) test based on the arc 5 positivity criterion (Capron et al., 1967, 1970b; Quilici et al., 1971; Yarzabal et al., 1974, 1975; Varela-Díaz et al., 1975a, b). Evidence accumulated so far is thus in agreement with the original description of arc 5 as being specific to this metacestode. This conclusion was reached by Capron et al. (1967) on the basis of their findings on the comparative antigenic structure of parasites and the testing of human sera.

Antigen sharing between *E. granulosus* cyst fluid and cyst extracts of *E. multilocularis* has been reported (Capron et al., 1968, 1970; Kagan, 1968) and both antigens have been employed in immunological tests for the diagnosis of infections with the heterologous parasite (Bout et al., 1975; Capron et al., 1968, 1968; Hess et al., 1974; Kagan et al., 1968). Although serologic cross reactions between sera from persons harboring either metacestode have been demonstrated using each of these antigenic preparations, testing of sera from *E. multilocularis* patients has not resulted in the detection of the *E. granulosus* arc 5 (Bout et al., 1975; Capron et al., 1968, 1970).

The present study was conducted to clarify the potential value of the arc 5 IEP test-positivity criterion in the differential immunodiagnosis of *E. granulosus* infections in areas where these species are sympatric.

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Materials and Methods

The IEP test of Capron et al. (1967) was conducted as modified by Guisantes et al. (1975). The lyophilized sheep hydatid cyst fluid (HCF) antigen employed was processed and characterized by IEP with a sheep antiserum to ovine HCF as described previously (Varela-Diaz et al., 1974). The latter antiserum was also employed as a reference reagent in IEP tests of patient's sera to determine reactions of antigenic identity (Varela-Diaz and Coltorti, 1974).

Indirect hemagglutination and indirect fluorescent antibody tests for hydatidosis were performed as described by Hess et al. (1974). Maximal titers observed in non-hydadit sera in IHA and IFA tests were 1:540 and 1:40, respectively. In sera from E. granulosus patients, maximal IHA and IFA titers of 1:393,660 and 1:640, respectively, were recorded under the technical conditions employed.

The latex agglutination test (Williams and Prezioso, 1970) was conducted using lyophilized HCF antigen as described earlier (Varela-Diaz and Coltorti, 1974; Varela-Diaz et al., 1975a). Agglutination at a 1:5 dilution of the serum was considered as a positive test result.

Sera from six persons with parasitologically-confirmed E. multilocularis infection were examined by the IEP test for hydatid disease. Details on each patient's history which were considered pertinent to the present study are as follows:

**Patient A.** Eskimo male born in 1932, resident of Kotzebue, Alaska. First admitted to a hospital at the age of 34 with a history of aching pain over the liver area, the patient had noted a mass in the right upper quadrant and reported to the hospital in Kotzebue. He gave a history of keeping a dog team while at Nontak and on at least one occasion cleaning the dog kennels which were very dusty. He was admitted to the Alaska Native Medical Center, at Anchorage, in 1967. Hepatic scintillography showed multiple defects in both lobes of the liver. On physical exam the liver margin was down well below the costal margin and felt nodular. He was considered non-resectable but was explored at that time to rule out resectability. The liver was found extensively involved with multiple large hard whitish tumor masses in all lobes and probably in all segments of the liver. E. multilocularis infection was diagnosed by histological biopsy at the time. The patient was followed conservatively for a number of years and was able to maintain work as a heavy laborer. There has been a gradual increase in the hepatic mass and on occasions he has developed mild jaundice. In July 1974, X-rays revealed a substernal mass. This was biopsied by mediastinoscopy and proved to be a metastatic E. multilocularis lesion. The serum sample included in the present study was obtained in the same year.

It should also be noted that the patient's mother (ca. 65 years old) was also found to be infected and the lesion was successfully removed by surgery.

**Patient B.** Swiss female born in 1932; resident of Zürich (CH). She was first admitted to a hospital in 1970 with a diagnosis of cholelithiasis. The patient was again hospitalized in September 1972 showing respiratory difficulties, chest pains and 40°C fever. On physical exam hepatomegaly, mainly of the left lobe, was observed and X-rays revealed irregular shadows in the liver due to calcifications. The serum sample was collected at this time.

Laparotomy was performed and a partial liver resection carried out. E. multilocularis infection of the left liver lobe was diagnosed by histological biopsy.

**Patient C.** Swiss male born in 1941; resident of the Schaffhausen area (CH). Hospitalized in 1972 with intrahepatic cholestasis which followed chlorpromazin treatment. He was again hospitalized in 1973 in poor general condition which included emaciation, icterus and hepatomegaly. Scintillographic studies revealed alterations in the left and right hepatic lobes; angiographic studies detected “spotted” areas of pathological processes particularly in the right lobe. Severe cholestasis was diagnosed by laparoscopy and E. multilocularis infection was confirmed by histological biopsy. The distribution of the lesions did not render surgical treatment feasible. The serum sample was collected in August 1973.

**Patient D.** Swiss male born in 1941; resident of Wald (CH). Hospitalized in 1975 with retentive icterus. Hepatic scintillography revealed a large dorso-lateral pathological process in the right liver lobe. An enlarged left hepatic lobe and a large “tumor” of the right liver lobe, with a whitish and localized hard “membrane” were detected by laparotomy. Resection of the right liver lobe was carried out and E. multilocularis infection was diagnosed by histological biopsy. Some of the small vesicles were found to contain protoscolices. The serum sample was collected at this time.

**Patient E.** Swiss male born in 1934; resident of Trin (CH). History of alcoholic abuse; hospitalized in 1970 and 1973 with icterus and fatty liver. General condition deteriorated in 1974 with anorexia, marked loss in body weight, hepatomegaly and increased icterus. Laparoscopy in 1975 revealed hepato-megaly with massive cholestasis, knotty tumour-like masses in left liver lobe and parts of pancreas; hepatogenous splenomegaly. The serum sample was collected at this time. E. multilocularis infection was diagnosed by histological liver biopsy. Surgery was not performed.

**Patient F.** Swiss male born in 1918, resident of Sulz-Rickenbach (CH). First complained of abdominal pain in February 1975 at which time a subfebrile non-icteric state was evident. Hospitalized in May