POLYCYSTIC HYDATID DISEASE IN BRAZIL: REPORT OF FIVE NEW HUMAN CASES AND A SHORT REVIEW OF OTHER PUBLISHED OBSERVATIONS

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This paper describes five additional Brazilian human cases of polycystic hydatid disease due to Echinococcus vogeli, reviews the previous cases reported in Brazil, including one report of E. oligarthrus (20 in total), and some epidemiological aspects of this disease which is no longer a curiosity but rather a problem that is not medically easy to handle. Its presence should be expected in any rural area of the New World where humans have not eliminated wild felids/canids, bush dogs, pacas, agoutis and other wild rodents.

Key-words: Polycystic hydatid disease. Echinococcus vogeli. Brazil.

Echinococcus granulosus is known to be endemic in humans, ungulates and domestic dogs in Uruguay, Argentina, Chile, the Andean zone of Peru and Rio Grande do Sul, Brazil. However, the parasite probably is present in every country in the continental Americas, but sporadic human cases are rare or seen in immigrants from endemic areas of the same or another country. The reason for this is not clear, but it may be due to epidemiological circumstances that prevent transmission, or to the behavior of the strain of the parasite present in non-endemic areas.

In addition, hydatids showing a polycystic morphology, rather than unilocular, had been observed in humans and animals and were cataloged as alveolar, multicystic or multilocular hydatids and interpreted as due to E. granulosus, E. multilocularis (cycle canid-small rodent, in the arctic zones) or more recently to E. oligarthrus (wild cat-agouti cycle, mostly in tropical areas). However, these diagnoses were not substantiated by experimental infections in carnivores to obtain the adult worms which are easy to differentiate.

Fortunately, while working in Colombia, we were able to infect dogs and cats with polycystic hydatid metacestodes of human and animal origin and demonstrated the presence in the country of the two neotropical Echinococcus species E. oligarthrus and E. vogeli (Ev). We described the larval characteristics of Ev, also polycystic, in the only important known host, the paca (Cuniculus paca). The adult parasite had been described by Rausch and Bernstein26 in a bush dog (Speothos venaticus) from Ecuador and, as they had predicted due to the food habits of the bush dog, the intermediate host was found to be the paca.

As mentioned above, experimental infections demonstrated that the metacestodes of the two neotropical species were both polycystic. The differential morphological characteristics were studied and described. It was found that the shape, the relative proportion of handle and guard/blade and the size of the hooklets of the proteroscolices were of particular importance7 8 28 29.

Since the original description of polycystic hydatid disease (PHD) in 1979 involving 13 cases in 4 countries, no less than 63 human cases due to Ev (and also E. oligarthrus) have been found in 10 countries, including Brazil.

This paper describes the information available (mostly pathological) on 5 additional Brazilian human cases of polycystic hydatid disease (PHD) and discusses the other cases reported in Brazil (Table 1), and some epidemiological aspects of this interesting disease which is no longer a curiosity but rather a problem not medically easy to handle.

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<th>Table 1.</th>
<th>Braziliana human cases of polycystic hydatid disease</th>
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<td>Number</td>
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*PTHD: Pre-operative therapy, done with albendazole in 2 cases.

220
Polycystic hydatid infections in Brazilian animals. Brumpt and Joyeux found in the liver and spleen of 1 of 4 agoutis (Dasyprocta agouti = D. leporina) collected in Alburquerque, Lins, State of Sao Paulo, a polycystic hydatid that they described as the metacestode of a new species of Echinococcus: E. cruzi rather than E. oligarthrus. Based on a careful study of the differential characteristics of the 2 neotropical species, Ev and E. oligarthrus, from different origins and the original slides of E. cruzi, it was arrived to the conclusion that the rostellar hooklets from protoscolices of E. oligarthrus and E. cruzi corresponded in form, although those from the latter were slightly greater in length. The difference was considered of no taxonomic significance and therefore they placed E. cruzi in synonymy with E. oligarthrus.

The occurrence of the larval stage of Echinococcus spp in the Americas by species of host and country were summarized. In Brazil, other metacestodes collected in agoutis near Belem were also found to be E. oligarthrus but the report of E. granulosus in a Brazilian agouti by Lutz lacks sufficient information to allow a definitive taxonomic opinion. In addition to these observations, E. oligarthrus has been reported in various countries and in a few species of mammals; Proechimys spp. (spiny rat), and once in Cuniculus paca, and in Didelphis marsupialis (opossum). More recently Ev was found in Sylvilagus floridanus (wild rabbit) from Venezuela and in pacas from Para State (Moraes, this report); in Acre State, in Bolivia and in Ecuador.

The carnivores reported naturally infected with E. oligarthrus are the following wild cats: Felis yagouaroundi, F. concolor, F. onca, F. pardalis, F. Geoffroyi and F. colocolo; several of these cats have extensive geographic ranges. The widest is that of the cougar, Felis concolor, which occurs in northern British Columbia, Canada, and southward to Tierra del Fuego. Some, such as the ocelot and the jaguar, which formerly were present in SW the US seem to have disappeared from this country. On the contrary, the bush dog, Speothos venaticus (Figure 1), distributed from Panama to northern Argentina, and the domestic dog, are the only animals that have been reported naturally infected with Ev and the paca is the only important intermediate hosts (Figure 2).

It should be mentioned that PHD transmission has been reported in zoos where bush dogs served as a source of infection for nutrias, Myocastor coypus, and a group of primates: gorillas, orangutans and chimpanzees. This information should be useful to alert zoo veterinarians to detect infections in captive bush dogs, using antiparasitic drugs to recover the adult worms and in primates, using ultrasound procedures to detect the metacestodes.

Diagnosis. It seems pertinent in this short review to mention how the diagnosis of PHD is carried out in humans.

1. Demonstration of polycystic masses by physical examination or by using imaging
procedures: x-ray, showing polycystic tumors, usually with some calcifications 2-3 cm or more in diameter with irregular borders, but they may have diverse forms and configurations. Ultrasound, CT and MRI are more sophisticated and expensive procedures but useful for diagnosis. The metacestode is usually present simultaneously in various organs of the upper and lower abdomen, the chest, and the orbit (D’Alessandro, unpublished).

2. The patient lives or has lived in rural areas with abundant wild life, and usually is familiar with pacas.

3. Serological tests. IHA and Immunoblot usually are positive in cases diagnosed by other means. Very recently, Gottstein et al. 1995 have obtained a purified Ev antigen, Ev2, allowing discrimination of non-Echinococcus infections and E. granulosus infections from Ev. Only some alveolar hydatid cases could not be discriminated. However, the distribution of E. multilocularis is holartic rather than neotropical so its distribution does not overlap in these regions.

4. Parasitological characteristics of PHD obtained by biopsy, pathological specimens or necropsy: a) the shape, proportions of the parts of the protoscolecos hooklets (better seen in squash preparations) and b) the morphology of the body or walls of the hydatid in tissue sections stained with H & E and PAS.

Case Reports

Case 1. (MVS (A93-87)). A 31-year-old Brazilian female agricultural worker, born in Goias State but living in Mato Grosso at the time of presentation, was admitted to the teaching hospital of Brasilia in October 1987 complaining of an enlarged abdomen, diarrhea, increasing jaundice, and generalized itching since a few months. She had been diagnosed as having viral hepatitis one month earlier in another hospital. At admission she was found to be in poor general health, with a history of a 12 kg weight loss during the previous weeks. She was markedly jaundiced, and the physical exam revealed palmar erythema and signs of generalized skin lesions due to scratching. The abdomen was distended and the liver was hard and palpable 20 cm below the right costal margin. No ascites or abdominal collateral circulation were detected. Main laboratory findings on admission included: total bilirubin, 33 mg/dl with the direct fraction of 21 mg/dl; alkaline phosphatase, 57 U; AST 36 U; ALT 40 U; total protein 6.8 g/dl, albumin 3.2 g/dl; creatinine 0.7/ dl. The WBC count was normal but 11% eosinophils was reported. The abdomen ultrasound showed enlarged liver and spleen with a cavernous mass in the porta hepatis, dilated intrahepatic bile ducts, signs of portal thrombosis, and a calcified nodule in the liver (2 cm x 2 cm). With the diagnosis of obstructive jaundice and portal hypertension, an exploratory laparotomy was carried out one month after admission. Examination of the porta hepatis showed enlarged, recanalized umbilical veins. The gallbladder appeared shriveled and without calculi. When the common bile duct was opened, multiple small vesicles were seen (Figure 3). An intraoperative cholangiogram revealed the left hepatic bile duct to be obstructed. The right

Figure 3 - Echinococcus vogelli cyst obtained from the liver and the biliary drain of case 1. Note the diversity of size and the presence of brood capsules, free and within the cysts. Bar = 1 cm.
hepatic bile duct was impermeable and the cystic duct was fibrotic. A cholecystectomy was performed and external drainage of the biliary system was established. Two days following surgery an episode of bleeding from the surgical excision and the externalized drain was observed, and fluid from the drain contained parasitic cysts. Two weeks after surgery the patient experienced massive hematemesis, hypovolemic shock, and died the following day. At autopsy numerous vesicles were observed on the surface and in sections of the parenchyma and the porta hepatis of the liver (Figure 4). The parasite was alive in some areas and dead in others. The laminated membrane was thick and the germinal thin, showing few calcareous corpuscles. Brood capsules and protoscolices with typical Ev hooklets were frequently seen. Between the host fibrous tissue reaction and the parasite, an accumulation of granular material representing dead eosinophils was frequently seen. In several areas proliferation of the laminated membrane was evident, at times having a cerebroid appearance. In some protoescolices several abnormal looking hooklets were seen (Figure 7).

Case 2. (OAF, Brasilia University, BU-29023) Year 1976. A 45 year-old female from Curralinho, rural area of Para State, with no clinical history available. A liver biopsy contained a polycystic hydatid with a laminated membrane showing a cerebroid appearance (Figure 8). The parasite was mostly dead and surrounded by histiocytes arranged in a palisade fashion. Protoscolices and hooklets conformed to those of Ev.

Case 3. (DMB, BU-28000). Year 1976. A 67 year-old male from Macapa, Amapa State. Tumors of the liver and of colon were excised after 7 years of illness. The metacestode was dead but it showed Ev hooklets and proliferating, cerebroid laminated membrane.

Case 4. (MSS, BU-13539). Year 1971. A 51 year-old female from Moju, Para State, underwent surgery 4 times, 3 of which antedated 1971. During the first surgery,

Figure 7 - Unstained squash preparation of fixed protoscolices of case 1, showing normal and abnormal booklets (arrows) of E. vogeli. Bar = 20µm.

Figure 8 - Tissue section (H & E). Convoluted laminated membrane within the lumen of a cyst (case 3) given the appearance of a cerebroid formation. Bar = 20µm.

Polycystic lesions from the liver and omentum were removed. This is the only information that was obtained.

Case 5. (BSR, studied by Mario Moraes in 1987). A 56 year-old agricultural worker from Paragominas, Para State. In 1980 he had been told that he was infected with hydatid disease. The patient died in 1987 and an autopsy could not be performed. However, specimens available from previous biopsies showed he was infected with polycystic hydatids with a laminated membrane showing a cerebroid appearance. Protoscolices and Ev hooklets were seen. This patient had brought with him an Ev-infected paca to demonstrate the parasitic lesions of the animal.

In summary, five new cases of PHD are reported. In 4 the characteristics of the metacestode and, in particular, the protoscolices' hooklets indicate that the infection was due to Ev. The first patient died of complications after surgery carried out to allow the bile to drain. Little clinical information was available from the other 4 cases except that the illness that originated the surgery to make a diagnosis demonstrated that it was a PHD and that the parasite involved in at least 3 cases was Ev due to the morphology of the hooklets. Whether the cerebroid appearance of the laminated membrane of the 4th case is sufficient to indicate that it is due to Ev is a point that should be confirmed by the study of more E. oligarthrus in humans.

A summary of the data of the new and previously reported human cases in Brazil is presented in Table 1.

DISCUSSION

As stated earlier, it is understandable that PHD was not diagnosed until recently. Ev was described in 1972 in the bush dog, but the metacestode was not recognized until the observations made with Colombian material. With the differential criteria established, it became possible to recognize that Eo was the origin of an Echinococcus heart infection found outside the endemic area of E. granulosus in Brazil. Also that cases 2 and 3 in the present report, recognized in 1976 as polycystic and therefore not due to E. granulosus, were not published by Moraes up until now, in the present report. They were both Ev. Reports of all Brazilian cases, including those presented in congresses (as new, overlooked, or previously unreported), are summarized in Table 1.

So far, in Brazil, there have been 20 PHD cases reported, 9 males and 11 females; the mean age was 41 with a range of 12 to 76 years. Only 7 were younger than 30. Three cases were asymptomatic individuals; 2 with groups of rounded calcifications in the liver and lung (considered probably dead and calcified metacestodes of PHD) and the patient with E. oligarthrus in the heart, who died of tetanus and at autopsy showed this parasite as an accidental finding.
The location of the parasites was: liver alone (9 cases), liver and lung (5 cases), base of the mesentery (1 case) and cysts in the liver and other organs in the last 4. Five of these 20 cases died as a consequence of the PHD which had caused liver cirrhosis, obstructive jaundice, portal hypertension and or esophageal varices.

Of the 20 cases, 11 were definitely due to Ev and one to E. oligarthrus because the typical characteristics of the hooklets; in 7, however, hooklets were not seen and in 2 there were no pathological specimens available for microscopic examination (only radiological). Although the typical characteristics of the E. oligarthrus metacestode is well established, only one case of a dead E. oligarthrus in a man's heart has been described showing not only hooklets but its cystic appearance, not different from that shown in animals.

It is clear that Ev is found much more frequently in humans than is E. oligarthrus. The former is transmitted from the domestic dog, which is a good host for Ev but not for E. oligarthrus; so far as has been observed, the latter develops to sexual maturity and produces eggs only in wild cats (Felidae) of various species.8

Fortunately, most of the Brazilian investigators have been aware of the studies of PHD, and have recognized its presence in Brazil. In 1992 it was found an endemic area of human transmission in Acre State22. The patients were thoroughly studied and longitudinal observations made possible the evaluation of beneficial response to albendazole treatment in 4 of 6 patients20. On the other hand, 1 year of mebendazole treatment was inefficient to avoid the death of one patient who had long lasting lesions in the liver with obstruction of the biliary system and portal hypertension11. The same failure was observed in two of the Meneghelli patients treated with albendazole20.

Surgical treatment was effective in removing the metacestode from the base of the mesentery and the patient was reported cured (case 4 of Meneghelli)20. In 5 of the 20 Brazilian PHD cases, their fate was unreported. In our experience and in the study of the results reported by others, surgical treatment should be recommended when the metacestode is small, localized and has not responded to medical treatment. Radical cures may be expected in these cases, but probably not when the PHD involves a large portion of the liver or other organs. However, more observations for prolonged periods of time are necessary to assess the chances of permanent improvement or cure in each case.

When the biliary system is involved, or cirrhosis has developed with splenomegaly and esophageal varices, surgery has accelerated the death of the patient due to complications. However, if the itching due to the jaundice is very troublesome, drainage of the biliary tract is usually required.

Surgery has been used successfully as a palliative mean of diminishing the effects of large numbers of cysts, which interfere with normal physiological activity of the stomach and other organs, by removing as many cysts from the mesenteries or those emerging from organs as possible. In addition, the absence of intraperitoneal masses allows the patient to sleep more comfortably (D'Alessandro, unpublished).

In summary, medical treatment with albendazole has been used with good results although really it is too early to assess long lasting cures. However, albendazole should be used and evaluated on the patient's well being. In general, Ev seems to be less aggressive than E. multilocularis and we know of asymptomatic patients who had the infection for several decades.

The epidemiological information obtained from the Brazilian cases is valuable. The Acre patients not only were familiar with pacas but also had seen parasitic vesicles in their abdomen. As in Colombia, the viscera of the pacas are fed to dogs. The conditions in Acre, at least, seem favorable for studies of transmission of Ev due to the number of infected persons reported and unreported20. In this place it has not been established how the pacas get the infection, but Acre is within the geographical distribution of the bush dog. In 19869 it was reported 13 specific places were the bush dog had been seen in Brasil including the states of Minas Gerais, Mato Grosso, Santa Catalina and São Paulo, and these places were shown in a map (Figure 9). Also unknown is the frequency of infection in pacas, in domestic dogs and in humans (which could be assessed by using the latest available serological tests).
In Colombia, people from the enzootic area could not provide information on the presence of the bush dog until a photo of the animal was presented. Then most people recognized the animal. The local name in the Colombian Oriental plains is "zorro guache" and in Brazil the local name is "cachorro do mato vinagre".

A survey of a limited random sample of adult pacas (weighing more than 10kg) should be sufficient to assess the prevalence of E. vogeli infection, considering that the frequency in Colombia was 30% in adult animals, 16% in subadults and none in the juveniles weighing less than 5.5kg.

Although E. vogeli infects humans and animals more frequently than E. oligarthrus the geographical distribution of wild cats is wider than that of the bush dog9. Therefore, the presence of PHD outside the range of the bush dog may be due to E. oligarthrus. However, it has been postulated that animals other than the bush dog and pacas may be involved in the transmission of E. vogeli.

Actually, both possibilities may play a role. To answer this question the collaboration of zoos is required by the treatment with praziquantel of canids/felids that have been capture in the wild as well as those which has been in captivity, in particular for a short time. Long lasting captivity may have an effect on some parasites which are eliminated spontaneously.

It is important to determine the species involved in a case of PHD because, apparently, E. vogeli is susceptible to medical treatment with albendazole although, as stated earlier, long term observations of reported successes require prolonged periods of observation. A number of reports are encouraging, at least in regard to the improvement of the patient's health.

RESUMO

Este trabalho descreve cinco novos casos humanos brasileiros de doença hidatícia policística, causada por Echinococcus vogeli e faz uma revisão de casos anteriores relatados no Brasil, incluindo um relato sobre E. oligartrhus (num total de 20) e alguns aspectos epidemiológicos desta doença, que já não é mais uma curiosidade mas, sem dúvida,

um problema de difícil manejo do ponto de vista médico. Sua presença pode ocorrer em todas as áreas rurais do Novo Mundo, onde o homem ainda não eliminou os felinos e caninos selvagens, cachorro do mato, paca, cutia e outros roedores selvagens.


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REFERENCES


