Enteric Infection 2

INTESTINAL HELMINTHS

Edited by

M. J. G. Farthing MD, FRCP
Department of Gastroenterology,
St Bartholomew's Hospital,
London, UK

G. T. Keusch
Division of Geographic Medicine and Infectious Diseases,
New England Medical Center and
Tufts University School of Medicine,
Boston, USA

and

D. Wakelin
Department of Life Science,
University Park,
Nottingham, UK

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SEVENTEEN

Abdominal angiostrongylosis

P. Morera

Abdominal angiostrongylosis, caused by *Angiostrongylus costaricensis* (Morera and Céspedes, 1971) or *Morerastrongylus costaricensis* (Chabaud, 1972), is a parasitic disease characterized by a granulomatous inflammatory reaction with heavy eosinophilic infiltration of the intestinal wall, especially in the ileocecal region. Ectopic localizations of the nematode cause liver and testicular lesions.

Although the parasite was described in 1971 (Morera and Céspedes, 1971), the disease has been observed in Costa Rican children since 1952. Subsequently, the definitive and intermediate hosts were identified and the life cycle was elucidated (Morera, 1973). Since then, human cases of the disease have been reported from Mexico to Argentina, including some Caribbean Islands. More recently an autochthonous case of the disease has been reported from Africa. In addition, naturally infected cotton rats (*Sigmodon hispidus*) have been found in the USA.

Figure 17.1 Caudal end of a male *Angiostrongylus costaricensis* showing the copulatory bursa and the spicules arising from the bottom of it.

17.1 ETIOLOGY

17.1.1 MORPHOLOGY

A. costaricensis is a filiform nematode that normally lives within the mesenteric arteries of the definitive host. The male is 20 mm long with a copulatory bursa and two spicules approximately 300 mm in length (Figure 17.1). The female is 33 mm long, and the anus and the vulva are located near the caudal end (Figure 17.2).

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Figure 17.2 Caudal end of a female showing the vulva or gonopore (g) and the anus (a) near the tip of the tail.

17.1.2 DEVELOPMENT

In the natural definitive host (often rodents) the adult worms live within the ileocecal branches of the anterior mesenteric artery. Here, the female oviposit and the eggs are carried out by the blood stream into the intestinal wall, where they embryonate (Figure 17.3). The first stage larvae hatch, migrate to the lumen through the intestinal wall, and reach the soil within the rat feces. The molluscan intermediate host, usually veronicellid slugs, become infected by eating the rat feces. Two molts take place in the molluscan fibromuscular tissues, and after 18 days the infective third stage larva matures; these larvae could remain within the mollusc for several months or could be shed with its mucus secretion. The definitive mammalian host becomes infected by eating the infected mollusc. The prepatent period is 24 days.

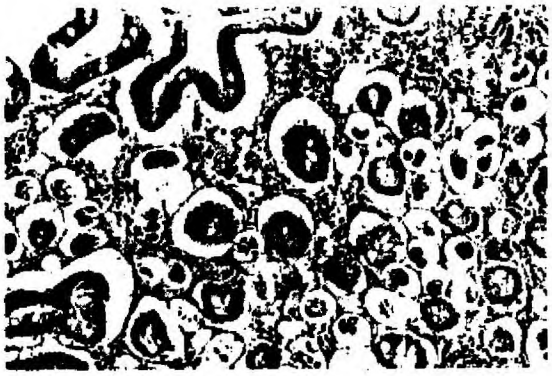

Figure 17.3 Section of the intestinal wall (cecum) of cotton rat showing eggs and embryos scattered in the small vessels of connective tissue.

17.2 EPIDEMIOLOGY

17.2.1 DISTRIBUTION AND PREVALENCE

The disease has been reported from Mexico to Argentina, including some Caribbean Islands. However, it has often been found as a result of routine examination of surgical specimens in pathology departments. In addition, naturally infected cotton rats have been found in the USA (Uberlaker and Hall, 1979). Although human cases have been observed in the Continental USA we do not know whether the cases are autochthonous or not. Recently, the first human African case has been reported (Baird *et al.*, 1987).

In areas where clinical knowledge and the methodology for laboratory diagnosis have been improved, it is becoming clear that this is quite a prevalent parasitic disease. In 1993, more than 650 cases were diagnosed in Costa Rica (population 3 million), to give a probably underestimated, rate of 21.6 cases per 100 000 persons per year. In that country, its distribution is universal, from sea level to an altitude of 2000 m. We think that in areas

where physicians are unaware of the problem, most clinical and subclinical cases probably go unrecognized or misdiagnosed.

Although the cotton rat (*Sigmodon hispidus*) is considered the most important definitive host, other reports of 11 additional rodent species, one case of coati (*Nasua narica*) in Costa Rica (Monge, Arroyo and Solano, 1978), and of marmosets (*Saguinus mystax*) from Iquitos, Peru (Sly *et al.*, 1982) have found these species to be naturally infected. Studies carried out in Costa Rica showed that the highest infection rate found for *S. hispidus* was 43.2%, similar to that found in Panama (35.0%) for the same species (Tesh *et al.*, 1973).

At least two species of veronicellid slugs in Costa Rica, one in Ecuador and one in Brazil are naturally infected with *A. costaricensis*: 50% of 6025 slugs from 20 Costa Rican localities, from sea level to an altitude of 2000 m, were found to be infected (Morera, 1985). More than 16 000 infective larvae were counted in a single specimen.

Thus, the opportunities for humans to become infected are high.

17.2.2 TRANSMISSION

Although several molluscs are naturally infected, veronicellid slugs are considered the main intermediate hosts. There is no evidence that persons intentionally eat slugs; however, small ones deeply hidden in salad greens could be finely chopped and inadvertently eaten raw. In addition, several cases are known of ingestion of these molluscs by infants. Nevertheless, most human infections are probably caused by ingestion of the infective larvae shed in the secretion of the molluscs. Slugs have been found in ripe fruits that have fallen to the ground. The characteristic mucus trails left by the molluscs can be observed throughout the endemic areas. The propensity for small children to put things in their mouths could explain why they show the highest infection rates.

17.3 PATHOLOGY AND CLINICAL FEATURES

In most cases, the lesions are located in the ileocecal region. They have also been observed in the hepatic flexure, descending colon, regional lymph nodes, liver and testicles.

Two major pathogenetic mechanisms are clearly distinguishable in the infections caused by *A. costaricensis*. The adult worms living within the mesenteric arteries (Figure 17.4) damage the endothelium inducing thrombosis and, consequently, necrosis of the tissues formerly supplied by the vessel. Secondly, eggs, embryos and larvae, as well as excretion/secretion products, produce an inflammatory reaction. Combinations of these phenomena, as well as the patient's susceptibility, and the number and localization of parasites, determine the clinicopathologic differences, ranging from cases in which only the appendix is damaged to those in which major surgery is required.

The gross examination of surgical specimens reveals a rigid and thickened intestinal wall with yellowish foci on the serosal surface and in the mesentery. The intestinal lumen is

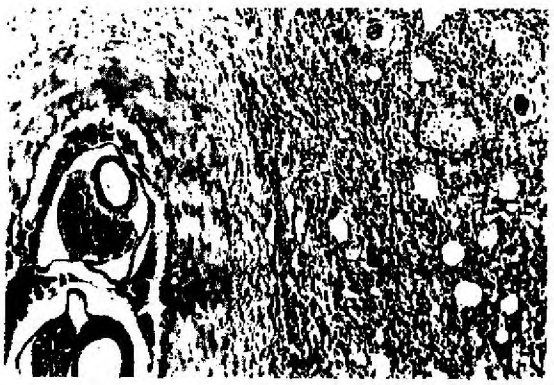

Figure 17.4 Section of human tissue (cecum) showing cross-sections of adult parasites (A) within an artery. Two embryos are also observed (B). The tissue is heavily infiltrated by inflammatory reaction: most cells are eosinophils.

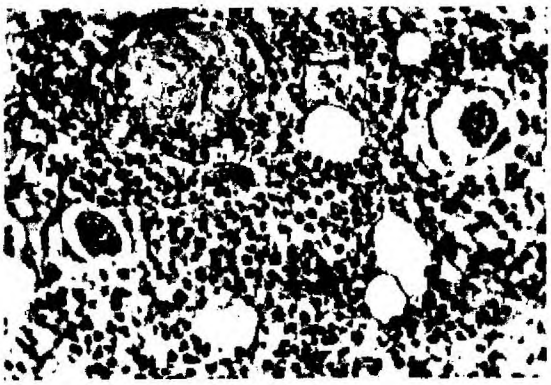

Figure 17.5 The section shows two embryos (arrows) within small vessels of the intestinal wall and heavy eosinophilic infiltration.

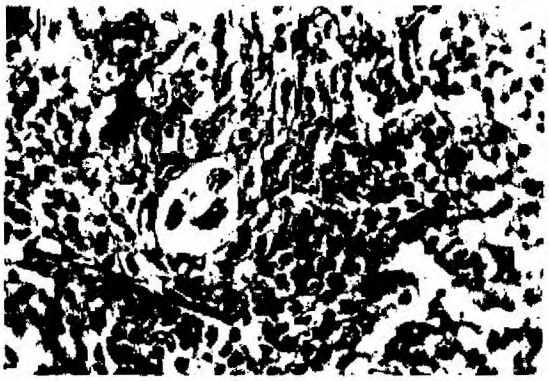

Figure 17.6 Young L1 larva coiled in a small portal vessel; the normal architecture of the liver is masked by the inflammatory reaction.

reduced, sometimes causing partial or complete obstruction. Necrotic areas can perforate. In many cases, even though only an appendicectomy is performed, the surgeon observes lesions of the cecum.

Histopathology demonstrates granulomatous inflammatory reaction with heavy eosinophilic infiltration, especially in the mucosa and submucosa; the serosa and muscular layers are often involved to a lesser degree. Eggs, embryos and larvae appear in small cavities lined by endothelium (Figure 17.5). Unfertilized eggs usually degenerate and are difficult to recognize. These structures as well as the excretion/secretion antigens are easily identified by immunochemical techniques. Large areas of necrosis are caused by arterial thrombosis. Eggs and embryos are present in the mesenteric lymph nodes, which also show reticuloendothelial hyperplasia and eosinophilic infiltration.

Hepatic lesions caused by *A. costaricensis* are similar to those caused by *Toxocara canis* (Morera *et al.*, 1982). However, the finding of eggs, embryos (Figure 17.6) and even adult worms in the hepatic parenchyma establishes the diagnosis.

In excised necrotic testicles histologically showing extensive parenchymal hemorrhagic necrosis, worms could be observed obstructing the arteries of the spermatic cord (Ruiz and Morera, 1983).

Abdominal angiostrongylosis predominantly affects children. From 116 patients studied in a pediatric hospital, 53% were of school age, 37% were of preschool age and 10% were infants. Of these patients, 64% were male and 34% female (Loría-Cortes and Lobo-Sanahuja, 1980).

When the worms are located in the ileocecal region, most patients complain of pain in the right iliac fossa and the right flank. Palpation in this area often causes pain. Rectal examination is also painful in about one half of the cases, and most patients present with fever ranging from 38 to 38.5°C (100.4°F to 101.3°F), but rarely accompanied by chills. In chronic cases, a mild fever may persist for several weeks. Anorexia, vomiting and constipation are also present in about 50% of patients. A very important finding is a tumor-like mass that, if present, can be palpated in the lower right quadrant and may be confused with a malignancy.

Although a few patients have no hematologic abnormalities, leukocytosis and eosinophilia are usually present. White blood cell counts usually range between 15 000 and

Figure 17.7 X-ray of the cecal region showing filling defects (arrows) of the intestinal lumen.

50 000/mm^3 and eosinophilia from 20% to 50%. The leukocytosis has been as high as 169 000/mm^3 with a 91% eosinophilia.

A barium follow-through or barium enema examination is often helpful in making the diagnosis. Radiological changes are localized in the terminal ileum, cecum appendix and ascending colon. The contrast medium shows incomplete filling (Figure 17.7) and irritability of the involved areas. The lumen is reduced by the thickening of the intestinal wall.

Sometimes the patient complains of pain in the upper right quadrant; in these cases, the liver is almost always enlarged and tender to palpation. At laparoscopy, small yellowish spots are seen on the surface of the liver. Most patients have hepatic involvement along with intestinal angiostrongylosis.

When the testicle is involved, the most remarkable findings are acute pain, accompanied by redness that later changes to purple. Eosinophilia and leukocytosis are also conspicuous. All patients with testicular necrosis have been misdiagnosed as having testicular torsion and the correct diagnosis was only made following surgery.

17.4 DIAGNOSIS

In infected rats, the L1 larvae can be easily identified in the stools; however, this is not true in humans. In man an immunological test should therefore be used to confirm suspected cases. Immunoelectrophoresis and Ouchterlony immunodiffusion tests give good results (Sauerbrey, 1977); however, an inexpensive and rapid latex bead agglutination test also gives high sensitivity and specificity rates.

17.5 TREATMENT

Surgery, when necessary, is the treatment of choice for abdominal angiostrongylosis. However, as knowledge of this often self-limiting disease increases, more non-surgical cases are being followed. Three drugs, diethylcarbamazine, thiabendazole and albendazole, have been used with 'remission' of symptoms reported. However, there was no objective evidence to prove that cure was attributable to the drugs. In fact, *in vitro* and *in vivo* trials in experimentally infected rats demonstrate that the parasites are excited by the drugs instead of killed, causing erratic migrations and worsening of the lesions (Morera and Bontempo, 1985). Thus, chemotherapy is not recommended until experimental studies demonstrate a more efficacious drug. Non-surgical patients should therefore be observed carefully: while some may have remission of symptoms, others could eventually develop an acute syndrome that requires surgery.

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