Artículo de revisión

Ascariasis. Review of the literature

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Resumen

La ascariasis es la helmintiasis más común en el humano; se calcula que afecta cerca de 1,500 millones de personas en el mundo. Ocurren cerca de 20,000 muertes al año por complicaciones intestinales de la ascariasis. En el presente documento se revisan los principales cuadros clínicos, las complicaciones y el manejo de esta entidad. Se hace énfasis en las medidas de tratamiento de cada una de las entidades clínicas y de las medidas de control ambiental y sanitario necesarias para su adecuado control.

Palabras clave: Ascariasis, helmintiasis, obstrucción intestinal, perforación intestinal, desnutrición, control ambiental y sanitario.

Abstract

Ascariasis is the most common helminthiasis in humans; it affects 1,500 million people around the world. Approximately 20,000 deaths every year are caused by intestinal complications associated with ascariasis. A review of the main clinical features, the complications and the treatment of this parasitic infection are analyzed. We emphazise the relevance of the treatment of each one of the clinical pictures and the environment and sanitary measures to its adequate control.

Key words: Ascariasis, helminthiasis, intestinal obstruction, intestinal perforation, undernutrition, environment and sanitary control.

Definition

Ascariasis is a parasitic infection caused by *Ascaris lumbricoides*, a helmint whose natural habitat in the adult stage is man wherein it can remain without causing any symptoms. When these worms are numerous they interfere with nutrition and give rise to various complications such as intestinal obstruction, appendicitis or perforation of the intestine. In their larval stage they are able to migrate from the intestine to the lung and back to the intestine through different organs; on the other hand they may migrate erratically and give rise to different pathologic conditions such as allergies, pneumonia, nephritis, pancreatitis, cholangitis and several less common problems.

Epidemiology

A. lumbricoides is the most common intestinal worm affecting humans. It has been found in warm climates, in moderately warm climates between latitudes 40° north and 40° south. Ascariasis is endemic in countries with warm humid climates or moderately warm and humid climates where environmental conditions favor the development of worm eggs until they reach the infectious stage. Owing to their great resistance these eggs remain viable in this stage for months or years [1-4].

It is estimated that *A. lumbricoides* affects about 1,500 million people in the world; in other words, one out of every four persons is infected [3-6]. The prevalence of this problem is greater in undernourished individuals in African, Asiatic and Latinamerican countries, where 80 to 93% of the children, mostly preschool and school children are affected [7-12]. Fortunately in most of the cases the infection is asymptomatic and it may go unnoticed, especially in the adult population. It becomes a problem in individuals with a high concentration of parasites; such is the case for 1.2 to 2 million cases a year. Approximately 20,000 deaths a year are caused by intestinal complications of this infection, i.e., intestinal obstruction, volvulus, perforation or intususception. Intestinal obstruction is seen in two of every thousand infected individuals; fatalities following intestinal obstruction occur in 6 of every 100,000 infected persons.

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Intestinal ascariasis is considered one of the main factors involved in children's undernutrition in countries where the disease is endemic. It is estimated that a high concentration of intestinal parasites in between 13 and 40 adults causes a daily loss of 4 grams of proteins out of a diet providing 15% of proteins. This large number of parasites is also responsible for a poor intestinal absorption of liposoluble class A and E vitamins thus leading to a deficiency of these elements in infected individuals [13-15].

The incidence of ascariasis in Mexico varies according to the different geographic and climatic conditions in the country. It is lower in the northern states: Baja California, Chihuahua, Coahuila, Sonora, Nuevo León and in some of the central plateau states such as Querétaro, Puebla and Tlaxcala with areas of arid climate and sandy soil where it is difficult for the parasite eggs to go through the process of embryogenesis. Conversely, in southeastern states and in the costs of the Pacific and the Gulf of Mexico such as Veracruz, Tabasco, Nayarit, Michoacán, Hidalgo, Guerrero, Chiapas, Colima, Quintana Roo, Sinaloa, Yucatán and Oaxaca where a tropical and humid climate owing to abundant rain, and a clayey soil, favor the embryogenesis of the eggs thus giving the highest incidence of infections in the pediatric population from one to four years of age [1].

Morphology

Ascaris lumbricoides is a clinder-shaped large whitish or pinkish worm. Its anterior end is blunt wherein a triangular mouth exhibits three fleshy lips; its posterior end is pointed. The female worm measures 20 to 40 cm in length; the male is smaller, 14 to 25 cm, and its posterior end is ventrally curved. The female's vulva is located in the anterior third of the ventral part. The reproduction apparatus is located in the two posterior thirds of the worm. The female worm lays approximately 200,000 eggs daily [1-4]. In the absence of a male, the eggs are not fertile. The immature fertile egg is unicellular; it measures 30 to 50 microns in width and 45 to 75 microns in length. Its cover is made of three clearly distinct layers responsible for its shape: a thin internal layer, a thick hyaline layer and an external mamillated layer. One of its poles exhibits a small operculum. Inside the egg there is a developing embryonic and densely granulomatose mass before giving origin to the blastomeres. The ovule is elongated and exhibits and irregular surface; it measures 70 to 80 microns in length [1].

Once the immature fertile eggs are deposited in the soil they develop a first stage rhabditoid larva through an embryogenic process in approximately ten days. In a period of seven to ten more days it undergoes a new process to become a second stage rhabditoid larva before the egg becomes infective, which takes place in approximately four weeks. Because of this larval developmental period on the soil, ascariasis is among the group of helminthiasis transmitted by soil, i.e. geohelminthiasis [1-5].

Transmission mechanism

Infection takes place by the accidental ingestion of infecting larval eggs by direct geophagia or by consumption of contaminated food or beverages with infecting eggs. In children the infection is frequently associated with a history of pica. It has been proposed that ascariasis may be transmitted transplacentally as substantiated by the case of a 40 day old female in whose feces, *A. lumbricoides* was found [1-6,16,17].

Biologic cycle

Once the eggs are ingested they hatch in the duodenum and liberate second stage rhabditoid larvae which invade the intestinal wall, reach the portal circulation, the liver and the right cardiac cavities; when they reach the lung they are trapped in the capillaries of the lung interstitium; at this site they undergo a second change and become third stage filariform larvae. When the larvae go through the pulmonary capillaries they perforate the alveolar membrane and penetrate the pulmonary alveoli; they subsequently ascend and migrate through bronchioles, bronchi and trachea, from there they are swallowed. They reach sexual maturity in the intestine in approximately 60 to 75 days after being ingested. The pregnant female worms start laying eggs which are eliminated with the host's feces. When the eggs reach the soil they begin an embryogenic period of four weeks; a second stage rhabditoid larva develops in them and become infectious, thus completing the cycle [1-3].

Pathogenesis

The specific antigens of the *A. lumbricoides* larvae induce hypersensitivity reactions characterized by local eosinophilia and by an increased level of specific IgE, IgG, IgA and IgM immunoglobulins and also the production of IL-4 and IL-5 cytocines which in turn stimulate the Th_2 subgroup of T cells, helpers CD4+ [6,18-23].

Reinfected patients develop pulmonary hypersensibility reactions due to high rates of IgE leading to severe pneumonitis. Sudden death among children with *A. lumbricoides* infection in endemic countries is caused by an anaphylactic shock syndrome which was seldom diagnosed formerly. Death is attributed to degranulation of mast cells because they have been found in every tissue of the host.

Clinical picture

Uncomplicated ascariasis

Migratory pulmonary stage. Most *A. lumbricoides* infections during pulmonary migration are asymptomatic. The first pulmonary symptoms appear in four to 16 days after the ingestion of infected eggs. Symptoms are more frequent in reinfected patients who have been previously sensitized with parasitic antigens; they result from a hypersensibility response [24,25]. These cases show elevated IgE with the production of vasoactive amines which increase vascular permeability and enhance the deposition of immune complexes in the pulmonary parenchyma.

The clinical manifestations also depend on the number of migrating young parasites, on the immunologic condition of the patient, his age, the nutritional status and the coexistence of other processes capable of exacerbating the respiratory symptoms: severe anemia, anemic heart, hypoproteinemia in cases with severe undernutrition [14,15].

Larval migration through the lung causes rupture of capillaries and small focal hemorrhages; the alveolar walls are disrupted and an exudate leading to eosinophilic pneumonitis with tracheobronchitis develops. These symptoms constitute Löffler's syndrome characterized initially by dry cough which turns into productive cough with hemoptysis, fever or febricula, fine basal rales and eventually lung consolidation. Other symptoms and signs include dyspnea, polypnea, distal cyanosis, chest pressure and peripheral eosinophilia. During the migratory stage, bronchial mucus may exhibit Charcot-Leyden crystals and eosinophils [26,27].

As a rule the disease follows a course and remits in approximately one or two weeks. Occasionally asthmatic type symptoms may be present such as bronchial spasm hissing which may be moderate but could become severe in two or three weeks.

Symptoms subside or disappear when the larvae migrate within the bronchi and go out of the lung. In some instances the condition may be fatal. On occasion a skin rash may be present and in severe cases, Quinck angioneurotic edema may occur.

During the migratory stage intestinal and hepatic clinical symptoms are infrequent; it is unusual to observe changes in liver function tests, particularly in the alcaline phosphatase levels [28].

Intestinal ascariasis. A. lumbricoides is responsible for damaging the mucosa and the intestinal wall through a mechanic traumatic process owing to the large size and great mobility of the worms which prevents their elimination by intestinal peristalsis. *A. lumbricoides* also harms the host by consuming part of the daily intake of nutriments such as carbohydrates; in addition it produces antitripsine, an enzyme which interferes with normal digestion and absorption of proteins in the host's diet thus contributing to nutritional impairment [3,14,15].

In cases of uncomplicated intestinal ascariasis with relatively small numbers of parasites patients may be asymptomatic. On the contrary, when parasites are abundant, symptoms such as abdominal distention, meteorism, diffuse abdominal pain and occasionaly nausea, vomit, hyporexia and diarrhea are present.

Complicated intestinal ascariasis

One of the main complications of ascariasis in countries where the disease is endemic and may be fatal, is intestinal obstruction which is usually partial, but may become total. It occurs mainly at the union between the distal portion of the ileum and the ileocecum valve; it is the result of intestinal spasticity caused by neurotoxins produced by *A. lumbricoides* [3,28,29]. However, even a single worm may cause intestinal obstruction.

A recent study indicated that the use of antihelmintics may enhance intestinal obstruction and has a poor prognosis. A large dose of antihelmintic medication paralizes a great number of worms thus facilitating intestinal obstruction as a result of peristalsis at the level of the distal ileum. In a study of several children with ascariasis and a similar number of controls in a pediatric hospital in Mexico, 40.90% of hospitalized patients with intestinal obstruction by *Ascaris* had a history of having been treated with mebendazole or albendazole for one to seven days prior to the complication [30].

Clinical findings of intestinal obstruction include abdominal distension, increased peristalsis, ileum and the presence of a characteristic mass (helmintoma) most often

found in the right upper abdominal quadrant. A complicated obstruction should be suspected in the presence of fever, toxicity and peritonitis, which although unusual is fatal [3].

An exploratory laparotomy in these cases is indicated under the following circumstances: persistency of the abdominal mass for more than 24 hours associated with abdominal pain; a painful abdominal mass, signs of toxicity and increased cardiac rate following the spontaneous disappearance of the mass. Sometimes the migration of larvae facilitates the development of adult parasites in different organs such as the liver, biliary ducts, appendix, retroperiteoneum, lacrimal duct, external ear, pancreas, kidney and bladder [33-36].

Complications of ascariasis following erratic and retrograde migration of the adult parasite. Factors which propitiate the presence of *A. lumbricoides* in ectopic sites include fever, the use of some medications, the ingestion of pepper-seasoned food which may cause retrograde migration of adult parasites and their elimination through the mouth or the nose. In some instances this may lead to suffocation. Erratic migration of the parasite has also occurred through the lacrimal duct, the nose, the kidney, the Eustachian tube; the latter causes suppurative otitis media the etiology of which cannot be explained otherwise [26].

Retrograde migration of the adult *Ascaris* into the stomach causes abdominal epigastric pain, nausea and vomiting of the parasite by mouth. The presence of adult parasites in the appendix may cause appendicitis and intestinal perforation [3,34-36].

When adult *A. lumbricoides* migrate into and occlude Oddi's sphincter it obstructs the common duct which causes nausea, gastrobiliar vomit and sudden severe right upper abdominal quadrant pain, unresponsive to analgesics; occasionally obstructive jaundice may be present. On physical examination pressure on the epigastrium elicitis pain. Fever, leukocytosis, neutrophilia, toxic granulation, bands and a high C reactive protein indicate the presence of an added infection and/or penetration of the parasite into the liver [37].

Obstruction of biliary and/or pancreatic ducts causes biliary colic, cholangitis, ascending cholangitis and pancreatitis. Liver abscesses may develop when migrating larvae introduce bacteriae. These abscesses may lead to pulmonary complications such as right-sided pleural empyema following the transdiaphragmatic rupture of a bacterial abscess caused by *Ascaris* [38].

Egg laying by a pregnant female worm during erratic migration is responsible for the development of granulomas and abscesses, mostly in the liver, the lung and the peritoneum, and a granulomatous peritonitis by the presence of eggs in the biliary duct. Granulomatous cholangitis has been reported [39].

Diagnosis

Uncomplicated ascariasis

Pulmonary larval migration stage. A history of geophagia, prior elimination of oral or rectal *A. lumbricoides* plus a clinical picture of pneumonic involvement suggests Löffler's syndrome [25]. Serial chest X rays for two or three days may then exhibit brief, apical migratory interstitial infiltrates bespeaking of larval migration through the lungs. *A. lumbricoides* larvae are readily seen in direct examination of the sputum, of bronchial aspirate or gastric aspirate during this stage. Suputm smears may show larvae, local eosinophilia and Charcot-Leyden crystals. Blood counts may show transient eosinophilia.

Detection of antibodies by serologic methods such as indirect hemagglutination or ELISA may be useful in cases of pulmonary migration of parasites causing asthma-like symptoms over a period of several weeks [6,37].

Uncomplicated intestinal ascariasis

Most patients with intestinal ascariasis are asymptomatic and because of the non-specific nature of symptoms, the diagnosis must be substantiated identifying the adult parasite or its eggs in the feces. In the event of the elimination of the worms by mouth, nose or anus, the parasite must be identified macroscopically sending the specimen (s) to the laboratory in a jar with saline or 10% formaldehyde.

The method of choice for the diagnosis of intestinal ascariasis is direct coproparasitoscopic examination of a concentrated Faust method to identify the eggs. Ritchie's sedimentation method is also very reliable, even though most laboratories specialized in parasitologic diagnoses do not apply it.

It is most important to ascertain the level of infestation of a patient by serial (three) CPS examinations with the methods of Kato-Miura or Stoll. A massive helminthiasis infestation is when the number of eggs is over 50,000 per gram or per mililiter of feces. This permits an indirect evaluation of potential danger for the patient to develop intestinal complications of ascariasis.

To facilitate the interpretation of screening results it should be kept in mind that there is an adult female worm for each 1,350 eggs in the intestine; therefore, any patient with 50,000 eggs per gram of feces carries of approximately 37 adult parasites.

Patients carrying only male worms of immature *A. lumbricoides* in their intestine will give negative CPS exams tests, in which case the diagnosis of helminthiasis is suspected if there is a history of elimination of the parasite. Under these circumstances the "therapeutic diagnosis", i.e. the administration of an antihelmintic drug induces the elimination of the parasite and confirms the diagnosis.

Conversely, patients carrying only female intestinal worms only elminate *A. lumbricoides* ovules, erroneously designated as non-fertile eggs, often missed in CPS exams and confused by insufficiently trained personnel as detritus or starch granules.

There may be moderate –6 to 10%– peripheral eosinophilia. Abdominal X rays in uncomplicated intestinal ascariasis are usually non-contributory. However, ascaris may be seen in 1.5% of the patients. Under favorable conditions, the presence of intestinal gas may on occasion permit the delineation of the parasites. Another clue may be the aspect of bread crumb which is far from being conclusive evidence of ascariasis.

Complicated intestinal ascariasis

In patients with intestinal obstruction by *Ascaris*, X ray examination shows distention in 74.2% of the patients; gas and fluid images in 56.1%; absence of distal gas in 50%; linear *A. lumbricoides* contours in 39.4%; edema of the intestinal wall in 12.1% and findings compatible with an immobile intestinal loop in 7.6% [30].

Abdominal ultrasound may show dilated intestinal loops with a thickened wall and a mass of worms causing obstruction. The presence of the so-called "helmintomas" is seen as a complex echogenic mass made of intestinal gas, worms and fecal matter reminiscent of a "medusa head" in the longitudinal axis view and as a rosetta in a transaxial section. The parasites are shown as echogenic structures with an anechoic canal which corresponds to the celomic cavity of the worms. There is antiperistaltic mobility (if peristalsis is present) and an irregular mobility in the absence of peristalsis [3,40-42].

Serologic tests are most valuable in cases of erratic migrations, also in the presence of granuloma, of liver abscess, of cholecistitis, of empyema and of pancreatitis. Indirect hemaglutination of ELISA tests may be valuable [6,43].

Erratic and retrograde migration

The diagnosis of biliary or pancreatic ascariasis may be done by cholangiography or by retrograde endoscopic cholangiopancreatography. In the presence of a right pleural empyema following the passage of larvae from a liver abscess, eggs may be found in the aspirate obtained by thoracocentesis. The centrifuged sediment of the aspirate should be cleared with potassium chloride. If there are associated pathologic conditions, a biopsy may be indicated. A histopathologic study permits the identification of eggs, larvae or adult parasites. If erratic migration of the parasite is suspected, ultrasound, computed tomograms or magnetic resonance may prove very valuable to establish the diagnosis [40-42].

Treatment and prevention

Uncomplicated intestinal ascariasis

In human populations with a high rate of reinfection and a large number of patients with or suspected of having massive ascariasis the treatment of choice is piperazine, 75 to 100 mg/kg/day in one or two doses for two days per os. This drug blocks the neuromuscular plate of the parasite making it unresponsive to acetylcholine: hyperpolarization of the membrane ensues causing flaccid paralysis. This medication acts only in adult nematodes which are then eliminated by intestinal peristalsis. Piperazine should not be used simultaneously with pirantel pamoate as these two drugs are antagonic.

If massive ascariasis is not suspected, pirantel pamoate can be given at the single dose of 10 mg/kd/day per os. This drug inhibits cholinesterase which depolarizes the neuromuscular plate and its nicotinic activation thus causing spastic paralysis of the parasite. Its activity is antagonized by piperazine.

A single dose of 400 mg p.o. of albendazole is also an excellent medication. This antihelmintic drug acts on both larvae and adult parasites; it inhibits tubuline when it unites to its beta subunity; it reduces the energetic levels and causes the death of the parasite. Albendazole also interferes with the uptake and transport of glucose; it inhibits fumarate reductase of mitochondria and reduces the production of ATP which leads to an accelerated glucogen consumption by the nematode who become immobile and gradually die.

Excellent results are obtained with mebendazole at the dose of 100 mg twice a day for three days p.o. This drug inhibits the formation of microtubules; it unites with the beta tubuline of the parasites. In addition it depletes glucogen and reduces glucose transport. This medication may cause retrograde migration of the parasites which are then eliminated by mouth or through the nose.

Nitazoxanide is a recent effective antihelmintic at the dose of 15 mg/kg/day for three days p.o. The drug disrupts the secretion of cholinesterase; the reduction of its nitro group alters the helicoidal structure of ADN inhibiting its synthesis and interfering with the glucose metabolism; it increases glucogen catabolism and causes lactic acidosis which kills the parasite.

Serial control tests to verify the absence of parasites should include three laboratory examinations at 14 and three at 21 days after treatment.

Treatment failures

Not uncommonly some patients continue to eliminate parasites several days after receiving special treatment. This may be due to insufficient efficacy of the medication or to the fact that the patient harbors a mixed cycle parasites, i.e., ascariasis in the intestinal stage and ascariasis in the migratory stage. This is seen in patients with protracted geophagia and frequent reinfections in whom the migrating parasites during their tracheobronchial passage are not exposed to the medication; when they reach their final stage they lodge in the intestine. This problem must be approached by a careful history including the previous occurrence of respiratory involvement which may be related to the intestinal pathology. Patients in whom a double cycle is suspected require CPS control examinations one and two months later, at a time when the parasites have reached maturity and their eggs can be identified in the feces.

Complicated intestinal ascariasis

When an obstructive process has been documented recently and the patient's general condition is satisfactory a conservative treatment is preferable to a surgical procedure. The patient should be given a hydroelectrolite intravenous treatment; nasogastric suction for 12 to 24 hours should be performed; antibiotics and antihelmintic medication with piperazine at the dose of 100 to 150 mg/kg in 15 to 30 mL of mineral oil or vasesline should be given repeatedly by nasogastric Miller-Abbott catheter (tube). Prior to this treatment the patient should be given antimicrobial medication and febrifuges because a few hours after the effect of the antihelmintic medication retrograde migrations may occur enhanced by the presence of fever. This may lead to a fatal upper respiratory obstructive suffocation. Aspiration may be interrupted for one or two hours. If obstruction is not relieved, a surgical intervention is indicated as soon as there is clinical and radiological evidence of this complication or else, in the presence of signs of acute abdomen, of intestinal perforation, of volvulus or of intestinal infarction [30].

A laparotomy is definitely indicated under the following circumstances: a) persistence of a stationary mass for more than 24 hours; b) persistent abdominal pain; c) painful mass. Relative indications to operate are: a) Toxemia and b) increased heart rate even when the abdominal mass is no longer palpable.

The current surgical procedure includes manually squeezing and pushing the mass of parasites towards the colon. Should this not be successful, the worms can be extracted through an enterotomy which is subsequently sutured horizontally if the surgical incision was performed vertically in order to avoid future intestinal strictures. In the presence of intestinal necrosis or infarction an intestinal resection is indicated [3,30]. Some authors report better results with intestinal resection and end to end anastomoses [32]. Antihelmintic medication should be given immediately after surgery to eliminate any remaining parasites in the intestine.

Gastrographin at the dose of 15 to 30 mL by nasogastric tube has been used in some cases to treat partial intestinal obstruction. Gastrographin is a hyperosmolar substance which causes an excess fluid environment around the mass of parasites and enhances their separation.

Biliary ascariasis

Recent appearance of this condition in the absence of laboratory data of infection or penetration of tissues and with no indication of poor health of the patient may be treated with intravenous fluids and electrolytes, nasogastric suction, antispasmodics and antihelmintics. Occasionally the parasites have been extracted from the biliary duct by suction during endoscopy [39,40]. When this fails, surgery is indicated especially in the presence of narrow biliary ducts, of several parasites or when these have penetrated the liver parenchyma.

Prevention

Disposal of feces and avoidance of defecating on the soil are mandatory. Children should be taught to wash hands prior to the ingestion of foods. Vegetable patches must never be irrigated with contaminated water nor ever fertilized with human feces.

Large scale antihelmintic treatments are only justified when the infection prevalence is greater than 70% [30,45]. The success of deparasiting programs depends on several factors which include especially: a) the access to helminthiasis maps in affected areas in order to contribute to proper cost-benefit actions; this is important because these programs have to be implemented in poor countries where this type of studies are lacking; b) studies of the mechanism of transmission of helminthiasis in affected areas in order to define periodicity and calendarization for the administration of chemotherapy; c) epidemiology surveys and studies on the attitude of human populations involved in the program and able or willing to outline strategies to optimize the use of resources; d) studies to indicate coverage in space and time.

Deparasitization plans have been effective when they are based on programs of sanitary education and enforcement of control measures such as the building of latrines to dispose of human feces.

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