SERIAL FEATURE

Algorithms in the Diagnosis and Management of Exotic Diseases.

III. Strongyloidiasis

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Strongyloidiasis is a potentially lethal helminth infection for which effective treatment has only recently become available. Although most helminth parasites do not multiply within man, Strongyloides stercoralis has the capacity to cause an overwhelming infection, which develops via a process called autoinfection. The incidence of this complication appears to be markedly enhanced in immunodepressed individuals.

S. stercoralis, although uncommon in comparison with the other major intestinal nematodes, is widely distributed through the tropics and has a patchy distribution in temperate regions. In the United States, surveys from the southern and border states indicate a prevalence of 0.4%–4%. Occasional autochthonous cases have been found in northern cities. Prevalence in institutions, particularly those for the intellectually retarded, may be high, with 5%–35% of the inmates infected. Imported cases are seen most often in immigrants from Puerto Rico and other areas of the Caribbean and in veterans of wars in Southeast Asia.

Life Cycle

Although man is the principal host of S. stercoralis, the parasite can survive and reproduce in the soil. There are three possible cycles.

1) The free-living cycle. The basic life cycle of the parasite takes place in water-logged topsoil. Larvae passed in the feces from an infected host moult and differentiate into free-living males and females. After fertilization, eggs are released and hatch into rhabditiform (free-living) larvae. These larvae may differentiate after a series of molts into free-living adults and repeat the cycle or metamorphose into the filariform larvae, which are infective to man.

2) The parasitic cycle. Filariform larvae penetrate the skin, usually of the feet, and pass via the bloodstream to the lungs, where they break out into the alveolar spaces. After two additional molts, the adolescent larvae ascend the tracheobronchial tree to the glottis, are swallowed, and reach the upper small intestine, where the fertilized females burrow into the mucosa. The males are not tissue parasites and are voided in the feces. Deposition of eggs begins about 28 days after the initial infection. The thin-shelled eggs hatch rapidly within the intestinal wall or in the lumen, and the first-stage rhabditiform or noninfective larvae are passed in the feces. These larvae are 225 × 16 μm in size and have an elongated esophagus with a pyriform posterior bulb.

3) Autoinfectious cycle. Sometimes development is accelerated; rhabditiform larvae moult and metamorphose into filariform larvae within the intestine. These infective forms, 550 μm in length, may penetrate the intestinal mucosa or the perianal skin and migrate to the small intestine via the lungs. This mechanism enables the infection to persist beyond the life-span of the adult females and may lead to the development of overwhelming infections.

Epidemiology

Transmission of S. stercoralis is facilitated by poor personal and public hygiene. Under optimal conditions of warmth, light, moisture, and oxygen, contamination of the soil with infected feces is followed by development of the free-living generation. When infective filariform larvae are
formed, they may remain alive in the soil for several weeks. On contact with the skin or, rarely, with the buccal mucosa of man, the parasitic cycle is re instituted. Contrary to most other helminth infections, the patient’s worm burden is dependent not only on the intensity of exposure but also on the degree of autoinfection.

Disease Syndromes

Although millions of people throughout the world are infected with *S. stercoralis*, many individuals are asymptomatic or have only vague abdominal symptoms. Studies in institutions have shown that 15%–30% of individuals with proven strongyloidiasis are asymptomatic. Vague symptomatology in the remainder cannot be attributed wholly to strongyloidiasis because of the lack of comparison with uninfected controls.

1) Cutaneous and pulmonary manifestations. These manifestations reflect the migration of the parasite within the host. Penetration of the skin by filiform larvae usually produces little reaction, but repeated infection may result in the development of a pruritic, papular, erythematous rash. The frequency of pulmonary signs and symptoms is uncertain, but they are not strikingly common. Cough, shortness of breath, wheezing, and fever may develop as the larvae pass through the lungs. Transient pulmonary infiltrates have been observed on chest X ray, and peripheral eosinophilia has been found.

2) Intestinal manifestations. These manifestations begin with the invasion of the intestinal mucosa by the fertilized female worms and are the commonest mode of presentation of strongyloidiasis [1]. Abdominal pain occurs; it is often epigastric and burning in nature, is occasionally dull or crampy, and may be exacerbated by food. Diarrhea (with stools usually containing mucus) is common, sometimes alternating with constipation. Some patients complain of nausea and vomiting. These symptoms may be relatively acute in onset or may be chronic, with periodic attacks occurring for many years. Weight loss is common. Urticaria, observed in 5%–22% of cases, is usually generalized, although some patients may have serpiginous wheals beginning perianally and extending to the buttocks, abdomen, and thighs. Patients with chronic strongyloidiasis often present with an eosinophilia that may be the only sign of infection, although a normal eosinophil level in blood does not negate the diagnosis. In more severe infections, a malabsorption syndrome or protein-losing enteropathy may develop [2].

3) Manifestations of hyperinfection. Autoinfection may lead to massive systemic strongyloidiasis, with severe, generalized abdominal pain, distension, and shock [3]. A high fever frequently develops, and gram-negative septicemia, which may lead to pneumonia or meningitis, is often found. Massive larval invasion of the lungs may result in cough, wheezing, and dyspnea; neurological signs may suggest cerebral involvement. Polymorphonuclear leukocytosis is common, but eosinophilia frequently does not develop.

The hyperinfection syndrome is being recognized increasingly in patients who are immunosuppressed either as a result of disease (lymphomas, leukemias, carcinomatosis, lepromatous leprosy, and kwashiorkor) or of therapy, particularly with corticosteroids [4, 5]. The syndrome may occur, however, in patients without an obvious predisposing cause.

Diagnosis

The process involved in the diagnosis and management of strongyloidiasis is illustrated in figure 1. Of crucial importance is the physician’s suspicion of the presence of this helminth infection. The patient may present with abdominal pain, diarrhea, or eosinophilia; the sudden deterioration of an immunosuppressed patient should suggest the possibility of infection with *S. stercoralis*.

Once strongyloidiasis is suspected, a geographic history should be obtained. Although the distribution of this helminth infection is widespread, the diagnosis is more likely if the patient has been to the tropics or has lived in an area of known endemicity. A negative geographic history by no means rules out the diagnosis but renders it less likely.

Definitive diagnosis can be made only if larvae of *S. stercoralis* are found in the feces or duodenal fluid. The feces should be examined
first. Larvae may sometimes be seen in simple smears, but it is better to employ a concentration technique. The zinc sulfate concentration method is the simplest.

A suspension is prepared by mixing 1 g or 1 ml of stool with 10 ml of warm tap water. The suspension is poured through a layer of damp gauze in a small funnel into a centrifuge tube, which is spun for 2 min at 1,000 g. The supernatant is decanted, and water (3 ml) is added. The sediment is resuspended by shaking, and the tube is filled with water and centrifuged as described above. This process is repeated until the supernatant becomes clear. The supernatant is then poured off, and a zinc sulfate solution (3 ml; 33 g/100 ml) is added. The sediment is resuspended, and more zinc sulfate solution is added until the tube is filled to about 1.5 cm from the top. The tube is then centrifuged at 2,000 g for 2 min. The surface film is transferred via a loop or pipette to a clean microscope slide, two drops of iodine solution (1% potassium iodide saturated with iodine) are mixed in, and the slide is examined at a magnification of ×100.

Examination of several stool samples may be necessary. Positive stools are found in about 70%-80% of eventually diagnosed cases.

Negative stool findings necessitate sampling of duodenal contents either by intubation and aspiration or by the use of the recently described Enterotest (Hedeco, Palo Alto, Calif.) [5]. This device consists of a gelatin capsule inside which is packed 140 cm of white nylon line. The capsule is swallowed by the patient, and the free end of the line is secured to the face and left in position for 4 hr. In more than 95% of cases, the line extends to its full length and is carried into the duodenum by peristalsis. At this point the gelatin capsule has dissolved, and the line is removed by gentle traction. The distal portion of the nylon line, which is saturated with bile-stained mucus, is drawn through gloved fingers, and a few drops of duodenal contents are thereby expressed onto glass slides. The slides are examined at a mag-
nification of $\times 100$. In one study, strongyloides larvae were found by this means in 51 of 56 persons thought to be infected [6]. If repeated fecal examinations and a satisfactory duodenal sample yield negative results, the patient is probably not infected. No effective immunological method is available for the diagnosis of strongyloidiasis.

Management

Since Strongyloides can multiply within the host, all infected patients should be treated, and the worms should be eradicated. Thiabendazole (Mintezol, Merck Sharpe and Dohme, West Point, Pa.) is given in a dose of 25 mg/kg twice daily for two days. Some patients may experience side effects such as anorexia, nausea, vomiting, dizziness, diarrhea, weariness, pruritis, and headache.

In the hyperinfection syndrome, it is essential that the diagnosis be made as rapidly as possible and that treatment be instituted early. Delay frequently results in death in spite of vigorous treatment. Patients with a past history of possible exposure to Strongyloides who are about to undergo immunosuppressive therapy should be examined for the parasite prior to the onset of treatment and followed carefully during therapy.

References