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Clinical symptoms related to patients with hyperinfection syndrome, infected with strongyloides stercoralis: Case series

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Case Report

Abstract

BACKGROUND: Strongyloides stercoralis (S. stercoralis) is endemic in the northern provinces of Iran, and to identify it, in addition to clinical tests, clinical manifestations of the patient are also needed. This study aimed to investigate the clinical manifestations of patients with S. stercoralis infection.

CASE REPORT: Nine patients with S. stercoralis infection were investigated in this study. Out of 9 patients studied, 6 patients lived in the village. Clinical symptoms of patients included cough, cough with sputum, bloody sputum, fever, chills, respiratory disorder, diarrhea and melena, abdominal bloating, weakness, weight loss, blurred vision, double vision, headache, dizziness, severe burning behind the sternum, digestive disorders, heartburn, nausea, vomiting, lethargy, loss of appetite, purulent discharge from the ear, ear disorders, and imbalance. Fever, chills, and cough were common symptoms in almost all patients.

CONCLUSION: Clinical symptoms in patients were different, whereas cough, fever, chills, and respiratory and digestive disorders were reported in almost all of them. Rapid identification and treatment of S. stercoralis is essential, especially in patients with immune system deficiency.

KEYWORDS: Somatic Symptoms; Infections; Strongyloides Stercoralis

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Introduction

Strongyloides stercoralis (S. stercoralis) is a parasite of tropical and subtropical regions that infects about 600 million people annually. Strongyloidiasis affects 613.9 million people annually, with a prevalence of 4% in the United States (US), with most cases reported in immigrants. S. stercoralis is responsible for 30 to 100 million infections per year. It is the most common tubeworm that has infected over 100 million people worldwide.[1,2] The prevalence of S. stercoralis was found at 4.76%,[3] and 0.95% in Northern Iran.[4] Infection with this parasite can cause various symptoms including abdominal pain, diarrhea, weight loss, and anemia. In asymptomatic people, the infection may continue for decades. The parasite can protect itself from the immune system by living in places other than the intestine, such as the bile ducts. In immunocompromised people, it can cause a

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fatal infection. S. stercoralis infects and spreads the larva to multiple organs, including the brain (the most severe complications).[2,4] S. stercoralis is detected by formalin-ether concentration technique (FECT), spontaneous tube sedimentation technique (STST), Baermann concentration technique (BCT), agar plate culture (APC), and real-time polymerase chain reaction (RT-PCR). Albendazole and ivermectin are used for treatment.[1]

A study in Iran showed that the failure to diagnose Strongyloides in a 65-year-old woman with a history of diabetes, who used a high dose of prednisolone to treat her temporal arthritis, led to the spread of S. stercoralis and gram-negative sepsis.[5] Another study in Iran showed infection with S. stercoralis in an 11-year-old male patient. Clinical symptoms included the fever (39 °C) with cramp-like abdominal pain and severe diarrhea along with cervical lymphadenopathy and neck abscess.[6] In a survey conducted in Italy in 2020, the global prevalence of strongyloidiasis was reported as 1.8%, which corresponds to 600 million infected people. Southeast Asia, Africa, and the Western Pacific Region accounted for 76.1% of the global prevalence of strongyloidiasis.[7] Although the stool test is the first and simplest test that is requested to diagnose strongyloidiasis, the test result may be negative despite the presence of a large number of this parasite. Therefore, for an accurate and reliable diagnosis of this disease, doctors should request more complete tests with the help of skilled people. This worm is endemic in the northern provinces of Iran, especially in the rural population; therefore, in this research, the clinical characteristics of patients with S. stercoralis infection have been investigated.

Case Report

The interview was conducted in the Clinical Research Development Unit of Ayatollah Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran, in March 2024. Given that the study was conducted as a case series, all cases [age range: 35 to 70 years, mean ± standard deviation (SD): 53.30 ± 10.50 years] diagnosed between 2012 and 2019 were considered (Ethics code: IR.MUBABOL.HRI.REC.1403.081). Moreover, only important data from the patient's medical and treatment history were mentioned. Mebendazole (100 and 500 mg) usually was prescribed twice a day, morning and evening, for 3 days. Albendazole (400 mg) was prescribed as chewable tablets in a single dose, with or without food. Ivermectin (3 mg) was usually taken as a single dose. In all cases, patients were discharged in good condition (Table 1).

Identification method of S. stercoralis: A small amount of fresh stool was requested from the patients. Then the sample was mixed well to ensure the uniform distribution of parasites throughout the stool. In the next step, a small amount of the prepared sample was transferred to the microscope slide using a wooden applicator or a pipette. The slide was examined under the microscope using low magnification of 10X and 40X to detect the presence of S. stercoralis larvae. Larvae are identified by their characteristic size and shape, body length, body width, esophageal length, abdominal cavity length, tail shape, and transverse size at the tip of the tail, which includes a larva with an elongated body and a pointed tail (the diagnostic method was the same for all patients) (Figures 1 and 2).[8]

Figure 1. Microscopic appearance of Strongyloides stercoralis (S. stercoralis)

Table 1. General characteristics of the patients infected with Strongyloides stercoralis (S. stercoralis)

Number	Gender	Age (year)	Living place	Hospital visit date	Common symptoms	Treatment
One	Man	50	Village	2012	Cough, fever, chills, coarse crackles in the lung	Mebendazole (500 mg)
Two	Man	60	Village	2014	Night sweats, weight loss, cough, nausea, hemoptysis, bronchitis	Mebendazole (500 mg)
Three	Woman	53	City	2015	Diarrhea, melena, weight loss, blurred vision, double vision, headache, dizziness, vomiting, bloating	Mebendazole (100 mg)
Four	Woman	55	City	2015	Rectorrhagia, abdominal colic, nausea, vomiting, hemoptysis, diarrhea, lethargy, fever, chills, weight loss	Mebendazole (100 mg)
Five	Man	70	Village	2015	Weakness, lethargy, fever, cough, nausea, vomiting, loss of appetite, abdominal swelling	Albendazole (400 mg)
Six	Woman	55	Village	2015	Dizziness, vomiting, hemoptysis, duodenitis	Albendazole (400 mg)
Seven	Man	35	Village	2016	Cough, weight loss, purulent discharge from the ear, weakness, lethargy, diarrhea, fever and chills, bronchiectasis	Mebendazole (100 mg), ivermectin (3 mg)
Eight	Woman	61	Village	2018	Imbalance, ataxia, blurred vision, breathing disorder, cough, anorexia	Mebendazole (100 mg)
Nine	Man	41	City	2019	Fever, cough, chills, heartburn	Mebendazole (100 mg)

Figure 2. Lugol's iodine staining of Strongyloides stercoralis (S. stercoralis)

Patient one: The patient was a 50-year-old man living in the village who had come to the Ayatollah Rouhani Hospital in Babol City with a cough and fever on October 22, 2012. The patient had a history of cough and fever for two to three years, but two weeks ago, the cough and fever became severe. Fever and chills were repeated periodically and lasted for minutes; the patient experienced at least three periods of fever and chills during the day. Condensation was observed in the bases of the lungs (the base of the lungs is located on the diaphragm and the apex of the lungs is adjacent to the first rib). Computed tomography (CT) showed that there were coarse crackles in the lung bases. The patient was treated with mebendazole (500 mg). It was prescribed twice a day, morning and evening, for 3 days.

Patient two: The patient was a 60-year-old man living in the village who had come to the Ayatollah Rouhani Hospital in Babol City with a cough and fever on October 28, 2014. The patient had night sweats, weight loss, cough, and nausea. He had visited the doctor several times and had taken medicine to treat and diagnose the cause of the cough. A positive response to the drugs prescribed to treat coughs was observed within two to three days. However, the patient's cough started again after stopping the medicine. During two weeks, the cough became severe, so that the patient could not sleep at night due to the

severity of the cough. The cough was accompanied by sputum. The color of the sputum was white and the patient's cough became severe in the early morning. Hemoptysis (bloody sputum) was not observed. Coughs were repeated at intervals of 20 seconds. The patient took several bronchodilator sprays; after taking the bronchodilator sprays, the patient's fever improved, but severe coughing continued. The patient had relative and appropriate sleep and rest. No respiratory distress was observed in the patient. Mebendazole (500 mg), intravenous immunoglobulin (IVIG), nasal irrigation with daily normal saline, and a low-salt and low-fat diet were prescribed for the patient.

Patient three: The patient was a 53-year-old woman living in the city. About 15 years ago, she was suffering from gastroesophageal reflux disease (GERD) and inflammatory bowel disease (IBD) and was under medical treatment. Last year, the patient's symptoms worsened (diarrhea and melena) and the medication continued. The patient visited on January 4, 2015 with a complaint of abdominal bloating, weakness, weight loss, blurred vision, double vision, headache, dizziness, severe burning behind the sternum, sour feeling, bitterness, entering substances and acid into the mouth, black, yellow, or green vomiting, bloating, and swelling in the stomach and intestines. In the last four days, she got constant melena, loss of appetite, and three bowel movements per day. But the stool volume was small and frequent, sometimes hard and sometimes loose. About 4-5 months ago, the patient's condition had worsened. Mebendazole (100 mg) was prescribed for the patient.

Patient four: The patient was a 55-year-old woman, living in the city, with blood group A+, who had been referred with the complaint of rectorrhagia, lower gastrointestinal bleeding (LGIB), on February 4, 2015. The mentioned patient was suffering from fatty liver and IBD; IBD has been chronically present in the patient for 15 years. During the previous two weeks, the patient had bleeding from the anus (clear blood discharge). The patient had abdominal colic pain in the perianal or rectal region since the previous day. Nausea, vomiting, hemoptysis, diarrhea, weakness, lethargy, fever, chills, loss of appetite, and weight loss were observed in the patient. The patient was hospitalized for 4 days and treated with mebendazole (100 mg) and prednisolone (5 mg).

Patient five: The patient was a 70-year-old man living in the village who had dizziness, general weakness, weakness of lower limbs, imbalance in walking, and blurred vision two days before the visit on April 20, 2015. Weakness, lethargy, fever, and recurring coughs had intensified in the last three weeks. There were no ear problems, nausea, vomiting, loss of appetite, and abdominal swelling in the patient. The patient was suffering from hemolytic anemia, thrombocytopenia, and chronic lymphocytic leukemia (CLL) and had received 7 rounds of chemotherapy. On the 16th day of hospitalization, the patient had bloody stools, urinary incontinence, diuresis, lack of consciousness, speech impairment, and cognitive impairment. He had not eaten and was vomiting for about three days. The important clinical findings included the following: erythrocyte sedimentation rate (ESR): 100 mm/hour, C-reactive protein (CRP): 50 mg/dl, and gamma-glutamyl transpeptidase (GGT): 324 U/l (normal: 7-69 U/l). The patient was treated with albendazole (400 mg).

Patient six: The patient was a 55-year-old woman living in the village who visited on August 27, 2015. The patient suffered from dizziness, imbalance, frequent vomiting, hemoptysis, and duodenal infection. Albendazole (400 mg) was used for patient treatment.

Patient seven: The patient was a 35-year-old man living in the village who had visited the Ayatollah Rouhani Hospital in Babol City on

February 4, 2016. The patient had a fever, chills, and cough since 2 years ago. Eleven months ago, he developed a severe cough that severely disturbed the patient's sleep. Five months before the visit, the patient had been hospitalized four times (two times each about 20 days) in Amol Hospital, Amol City, Iran, and Baqiyatullah Hospital in Tehran City, Iran. The patient stated: "cough becomes more intense after eating and at night while sleeping". He had lost 25 kg of weight and had purulent discharge from the left ear, weakness, lethargy, diarrhea, and severe fever and chills 5 weeks ago. Bronchiectasis was also diagnosed in the patient. A colonoscopy showed gastritis, enteritis, and rectal polyps in the right colon. The cause of diarrhea was diagnosed as Strongyloides infection. Diarrhea took two weeks to cure. The patient's fever continued and was accompanied by profuse sweating (so that the patient's clothes became wet) in the evening. The important findings of the patient included the following: ESR: 61 mm/hour (normal: 1-13 mm/hour), CRP: 85 mg/dl (normal: < 1 mg/dl), immunoglobulin A (IgA): 6 g/l (normal: 0.8-3.0 g/l), hemoglobin (Hb): 7.3 g/dl (normal: 12.4-14.9 g/dl). Mebendazole (100 mg), ivermectin (3 mg), IVIG (injected to reduce allergic symptoms in acute cases), blood transfusion, and hydrocortisone were prescribed to the patient. The reduction of IgA was observed and the general condition improved after receiving IVIG.

Patient eight: The patient was a 61-year-old woman living in the village who was referred due to imbalance, ataxia, inability to walk, blurred vision, breathing disorder, cough, and anorexia on November 6, 2018. The patient's problem started in 2014 and got worse. During the day, the patient had vomited several times, which contained food. The patient had a history of gastrointestinal (GI) cancer, but magnetic resonance imaging (MRI) of the brain did not show any disorder or lesion. Hydrocortisone was one of the drugs prescribed to the patient. Chest pain, palpitation, hemoptysis, heartburn, diarrhea, nausea, and vomiting were stopped during hospitalization and after treatment. The patient was treated with mebendazole (100 mg) and IVIG.

Patient nine: The patient was a 41-year-old man living in the city and a driver who visited the hospital on August 6, 2019, due to a recurring fever and cough that had worsened over the past three weeks. Severe and frequent coughs made the patient unable to perform daily tasks. The patient has had this problem for about four years and it has appeared occasionally. He complained of periodic fever and chills (twice a week that started four months ago) and heartburn. Additionally, the patient was taking immunosuppressive drugs for four years due to immune system deficiency. Finally, mebendazole (100 mg) was prescribed for the patient and the patient was discharged with a satisfactory general condition.

Discussion

Various clinical symptoms in patients infected with S. stercoralis were investigated. The most common symptom of this type of contamination is abdominal bloating, which causes bowel obstruction by stopping the movements of smoke and edema. Symptoms are seen in the form of diarrhea, anorexia, malabsorption, and nausea.[8-10] In the study conducted by Moradali et al. in Iran, out of 214 patients examined, 1.9% of chemotherapy patients and 1.4% of hemodialysis patients were positive for anti-Strongyloides immunoglobulin G (IgG) antibodies.[9] Infected people often do not have specific clinical symptoms, but in patients with a weak immune system, if not treated, it leads to more than 80% death. In our study, there were patients with GI cancer, GERD, IBD, hemolytic anemia, thrombocytopenia, and CLL who were under medical treatment. Therefore, accurate

and timely diagnosis of this infection can prevent the death of the patient. Strongyloidiasis is a life-threatening risk factor in people undergoing chemotherapy and hemodialysis; therefore, these patients should be screened for strongyloidiasis before prescribing immunosuppressive drugs, dialysis, and kidney transplants.

Shafaghi et al. in Iran showed that Strongyloides is endemic in Guilan Province (northern Iran), especially in the rural population.[5] Our study was also conducted in the north of Iran (Mazandaran Province); out of 9 patients studied, 6 patients lived in villages. Shafaghi et al. reported a case of a 65-year-old woman with a history of diabetes mellitus (DM) who used high-dose prednisolone to treat her temporal arthritis. Failure to recognize this worm led to the spread of Strongyloides and gram-negative sepsis, but prompt diagnosis and timely treatment with anthelmintic drugs led to a positive outcome in this patient.[5] Nilforoushan et al. in Iran showed that due to the increase in the number of patients who were facing immune system defects or were using immunosuppressive drugs, strongyloidiasis, especially cases of its widespread infection, was considered one of the country's health problems. In this study, during the years 2004-2006, out of 200 stool samples that were performed by direct microscopic detection and polymerase chain reaction (PCR), six patients were infected with S. stercoralis, all of whom suffered from increased infection syndrome.[10] In our study, during the years 2014-2019, 9 patients with increased infection syndrome were found.

In the study conducted by Xu et al., a 75-year-old man with severe disseminated infection due to S. stercoralis was reported. The patient had a medical history of seasonal bronchitis and, as a result, had taken prednisolone for years.[11] In our study, the age of the patients was almost high; people were 50, 60, 53, 55, 70, 55, and 61 years old, and also two cases of patients with the age of 35 and 41 years were identified. In older patients, poor control of how to use antibiotics leads to the development of resistance to microorganisms, which is one of the causes of increasing infectious diseases in older people, especially in developing countries. Diagnosis and treatment of infection in the elderly is difficult, because elderly patients often do not have signs and symptoms of infection such as fever and leukocytosis, and in case of infection, unusual symptoms such as loss of appetite, nausea, vomiting, and changes in consciousness are observed. It is also difficult to interpret physical and laboratory findings in these patients because most of them have underlying pulmonary and urinary disorders. Respiratory problems are the most common infectious disease in the elderly, accounting for 20%-25% of infections. The risk factors for pulmonary infection in the elderly are inactivity and accumulation of pulmonary secretions, dementia, or Alzheimer's disease, which causes a decrease in consciousness and aspiration. The symptoms of lung infection in the elderly, unlike the young which are in the form of fever and chills, cough, and shortness of breath, can only be with a decrease in the level of consciousness.[12] In our study, a 70-year-old male patient had dizziness, lethargy, fever and cough, urinary incontinence, diuresis, and lack of consciousness, and a hydrocortisone ampoule was prescribed to him. The clinical manifestations of the disease caused by infection with S. stercoralis are not specific. In our study, different patients had different symptoms, and only common symptoms such as fever, chills, and cough were common to all of them. Therefore, early and accurate diagnosis of the disease is very important.[12]

Cabral et al. identified a clinical case of a 49-year-old man with a history of diarrhea and abdominal pain, cramps, generalized edema,

petechial rash, melanoderma, cough, and shortness of breath.[13] Similar to our investigation, respiratory failure with bilateral lung opacity was identified and the patient was admitted to the intensive care unit (ICU). Abdominal CT scan showed liver and duodenal masses. Duodenal biopsy showed the presence of S. stercoralis and liver biopsy showed the presence of carcinoma. In our examined patients, there were also GI disorders. The patient died 50 days after hospitalization. A high level of endogenous cortisol has been observed, which in this patient, may have facilitated the progression to severe fatal infection.[13] According to the results, S. stercoralis can live without symptoms in the intestines of people suffering from it. This infection is not serious for most people but can be fatal for people with compromised immune systems.[14] People become infected when they come in contact with soil or water contaminated with infectious worms. Chronic infection usually causes skin rashes, vomiting, diarrhea, constipation, and respiratory problems such as pseudo-asthma.[14,15]

In this research, writing all the patient information was not possible due to the large volume of material. It is also suggested that molecular techniques be used to identify this parasite, along with phenotypic and simple methods.

Conclusion

S. stercoralis can be found more abundantly in northern cities of Iran than in other areas, especially in rural areas, due to its humid climate. Cough, fever, chills, and respiratory and digestive disorders were present in all patients. Moreover, in some cases, ear disorders and dizziness were detected. Following tests and clinical evidence and rapid identification and treatment are necessary, especially in patients with immune system deficiency.

Conflict of Interests

Authors have no conflict of interests.

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