Strongyloides stercoralis infection: neglected parasitic infection among cancer patients

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Abstract

Introduction:
Cancer patients are susceptible to severe parasitic infections particularly Strongyloides stercoralis (S.s) infection. Accordingly, this study aimed to determine the prevalence of parasitic infections with highlighting Strongyloides stercoralis infections in 139 cancer patients admitted to oncology ward of Imam Khomeini hospital of Sari during 2009.

Material and Methods:
In this descriptive and cross-sectional study, fecal samples (n=139) were collected from different cancer patients. After completing the questionnaires, the samples were examined by direct smear and formalin ether sedimentation methods.

Results:
In this study, of 139 patients with different types of cancer 53.9 % (n=75) and 46.1% (n=64) were male and female, respectively. In the stool exam, two cases (1.4%) infected with Rhabditiform larvae of S.s were detected while both of them were affected with Multiple Myeloma cancer.

Conclusion:
This study showed that in endemic areas, three times stool examination by formalin-ether technique for detecting Strongyloides stercoralis must be requested before chemotherapy in cancer patients.

Keywords: Strongyloides stercoralis, Cancer, Infection, Multiple Myeloma

Introduction
Strongyloidiasis is a parasitic disease created by a nematode called Strongyloides stercoralis (S.s). This parasite has a complex life cycle in 3 stages: skin, respiratory, and digestive. In its life cycle, the parasite larvae are transformed into free-living rhabditiform, or in certain cases, into filariform larva (infective stage) in the digestive system.

The larvae either penetrate the skin to infect humans, or transform into free-living adult nematodes and continue their lives in the soil (1). Ordinarily, filariform larvae move through the body in the blood stream to the lungs (pulmonary migration), then migrate toward the trachea, passing through esophagus and stomach, and eventually mature in the small intestine. In the third stage of their life cycle,
rhabditiform larvae are transformed into filariform, and before entering stool, infect the host again through intestinal mucosa or pre-anal skin, which is called autoinfection. The onset of autoinfection is when rhabditiform larvae are transformed into filariform in the digestive system, and enter the blood stream by penetrating the intestine wall. In this condition, infection can persist indirectly in an infected host. Some circumstances in the host can lead to a condition known as hyperinfection syndrome. In these circumstances, a large number of larvae spread into organs outside the intestine including the lungs, mesenteric lymph nodes, gallbladder, liver, diaphragm, heart, pancreas, skeletal muscles, kidneys, ovary, brain, and to a less extent, skin. In this condition, mortality rate in various countries is estimated at 87% (2). The hyperinfection syndrome is created and developed in case of cellular immune system deficiency due to underlying malignancy, malnutrition, alcoholism, transplantation of blood stem cells, or receiving corticosteroids or cytotoxic medications (3). With a dramatic increase in parasites, autoinfection can lead to hyperinfection. Widespread dissemination of filariform larvae to the lung, liver, heart, central nervous system and endocrine glands can cause inflammation, and most probably marked impairment in the function of these organs, and even septic shock. Classic signs of strongyloidiasis are indigestion (digestive symptoms), Loeffler syndrome (respiratory symptoms), and peripheral eosinophilia. Sometimes gastrointestinal symptoms may be mistaken for stomach ulcers. Bloating is the most common gastrointestinal symptom, and other symptoms like nausea, vomiting, and diarrhea are also observed. Secondary bacterial infections and meningitis may also occur (1, 2).

Due to reduced level of immune system, cancer patients are susceptible to severe parasitic infections, especially the strongyloides stercoralis nematode infection (3). Excessive infection in these patients causes improper functioning of gastrointestinal tract and migration of larvae to other organs like the lungs and brain. This widespread infection, also known as disseminated infection may lead to pneumonia, meningitis, septicemia, and intestinal inflammation (2). Annually, this parasite infects an estimated 30-100 million people worldwide (1, 2). They are predominantly scattered in warm and humid climates around the world, including Mazandaran and Gillan provinces in the north of Iran, where conditions are conducive to transfer and growth of these parasites (4, 5). The use of immunosuppressive drugs such as corticosteroids, having immune deficiency syndrome, and use of chemotherapy in malignancies through changing normal presentation of infection can cause lack of early diagnosis of the disease. Since these patients are more vulnerable to various infections than healthy people, they have to tolerate more complications and harms due to infections (3-4, 6-7).

Obviously, to understand the problems caused by parasitic infections and offer appropriate strategies for early and rapid diagnosis, and to control the infection in patients with a variety of malignancies, first, it is necessary to determine the frequency of parasites in these patients (6-8). Given the limited studies conducted in Iran, and also, the underestimated frequency of this parasite in the world due to inefficiency and low sensitivity of current diagnostic tools, and also the shortage of specialized laboratory personnel, and lack of symptoms mostly in people with healthy immune systems, conducting this study, in order to determine frequency of this parasitic infection in patients with malignancies seemed necessary (5, 8-9). Presently, strongyloidiasis is the most forgotten tropical disease in the world (9), and the hyperinfection syndrome is an emerging infectious disease in some parts of the world (10). The definitive diagnosis of strongyloidiasis is often possible by
observing rhabditiform larvae (first stage lava) in stool, or in sputum samples in disseminated infection cases, or in bronchial and alveolar lavage from the lungs, or in urine. Given the varying and sometimes very low number of larvae excreted in feces at different times, in order to diagnose strongyloidiasis disease, several samples must be examined on different occasions with concentrated method and preferably parasite specific culture media (11, 12). The present study was conducted with the aim to determine the prevalence of parasitic infection, especially strongyloides stercoralis infection in cancer patients in Imam Khomaini Hospital in Sari.

Materials and Methods
This was a cross-sectional descriptive study conducted on 139 patients with various cancers hospitalized in the oncology ward of Imam Khomaini Hospital in Sari in 2010. After obtaining patients’ information including age, gender, place of residence (urban/rural) and type of cancer, patients were trained on how feces samples were collected, and one to three samples, depending on duration of hospitalization were collected from each patient and immediately were sent to the parasitology laboratory at school of medicine in Sari. The collected samples were studied with direct and formalin-ether sedimentation technique (13). To prepare direct smear, using spatula, approximately 2 mg of feces sample was mixed with one or two drops of saline on a slide, and then a lamella was placed on top of that, and examined under the microscope. In the formalin-ether technique, parasite test kit (kar-va-Teb Company-Iran) was used as follows: First, 2-3 grams of feces sample was dissolved in 3.5 ml of the solution preparation in the kit (containing formalin 10% in saline and ethyl-acetate) followed by vigorous shaking. This was centrifuged at 2000 rpm for 2 minutes and the sediment obtained was examined under the microscope (13).

Results
Of the 139 patients in the study, 75 (53.9%) were male and the rest female. The feces test revealed that two patients (1.43%) had strongyloides stercoralis rhabditiform larvae, these two were with multiple myeloma cancer and under treatment with chemotherapy medication. The prevalence of strongyloides stercoralis infection in men was one case (1.6%), and in women, one case (0.75%). One case of the disease was observed in age group 60-75 and another in 45-60 years. Also, in examining feces samples, one case of infection with dicrocoelium dendriticum eggs was observed in a patient with thrombocytopenic purpura. After further investigation of patient’s history and a re-test, it was found that infection was false and due to consumption of infected lamb liver. Also, a case of infection with entamoeba histolytica parasite was observed in a patient with colon cancer. In another patient with multiple myeloma syndromes, concurrent infections of strongyloides stercoralis and tinea sajynata cestodes were observed.

In this study, the most common malignancies were related to stomach cancer (10.8%), and also, mortality rates of patients with cancer during the study were 3 cases (2.15%). Multiple myeloma cancer is the second most common blood cancer in the world. In this study, two cases of strongyloides stercoralis infections in patients with multiple myeloma cancer were observed.

Discussion
In this study, 139 patients with various malignancies were studied. The prevalence of strongyloides stercoralis infection was 1.4% (2 cases). According to a study conducted in Egypt on cancer patients receiving chemotherapy, the prevalence of strongyloides stercoralis parasite was estimated 6.3% (6). In a study by Togeh et
al. in 2000 on cancer patients undergoing chemotherapy, with 1.1%, strongyloides stercoralis was the most prevalent intestinal nematode (4). In a study by Athari et al. in 1998 on patients receiving immunosuppressive medications (cancer patients receiving kidney transplants), 4 cases (1%) of strongyloides stercoralis infection were reported (8). Given the importance of this parasite in causing disseminated strongyloidiasis in this group of patients, which can also lead to deaths, careful assessment of parasitic infections prior to any treatment with immunosuppressive medications is necessary.

According to the Arfae textbook in Farsi (latest edition) (5), most infections with strongyloidiasis in Iran are seen in the northern regions, among residents on the coast of the Caspian Sea, where climate is sufficiently warm and humid. Although in previous studies in most areas in Iran, infection with this parasite was not more than 4%, in an investigation by Sajadi et al. in 1990 on the northern coasts of Iran, 6.1% of locals had strongyloides (5). In Rangbar-Bahadori et al. study, the prevalence of this nematode was reported 1.4% (14).

The annual mortality rate due to this parasite infection in people with impaired or suppressed immune system is estimated more than 87% (1-3). According to studies conducted in a population in China in 2007, use of combined diagnostic and repeat-tests methods led to identification of unexpectedly high prevalence of 11.7% of people with strongyloidiasis disease (15). A similar approach used in northern Ghana revealed strongyloides stercoralis as a parasite with 10.6% prevalence (16). As one of the most important causes of immune system weakness, a relationship was found between malabsorption and the severe form of strongyloidiasis (17). The prevalence of strongyloides, due to low sensitivity of diagnostic tools and lack of qualified personnel is estimated much less than its actual amount. Hence, this disease is rarely identified in most regions that have no information about spread of strongyloides (9). As a result, in these areas, this parasite may only be detected in patients with disseminated strongyloidiasis. It must also be noted that one of the limitations in the present study was lack of availability of patients for three times sampling. Also, in some cases of strongyloidiasis infections, some of the larvae may be detected in stool, sputum, urine, and lung secretions through biopsy (11).

A case of hyperinfection of strongyloidiasis in the respiratory system of a patient with pemphigus vulgaris in Mazandaran province (12), and another in the digestive system of a patient with Behjet’s Disease in Fars province were reported by the authors (18). Of the factors that cause strongyloidiasis disease to be less important and disregarded in Mazandaran province is performing direct feces test, which is of little value in detecting the disease. On such occasions, it is better to use a more sensitive method like agar plates. Another factor in forgetting this disease is lack of specialists’ prescription for formalin-ether test, or even a direct feces test for screening high-risk patients, and also lack of comprehensive epidemiological data on the disease in this province. Therefore, improving doctors’ awareness through training workshops creates a communication bridge between research centers and hospitals, and setting up accurate and sensitive diagnostic tests could provide suitable strategies for controlling this disease and preventing its undesirable complications.

**Conclusion**

Since, on the one hand climate in Mazandaran province is favorable for establishment of parasite life cycle, and agricultural jobs, particularly rice cultivation increase the chance of contact with contaminated soil in this province, and on the other hand, this province is...
considered as one of the endemic regions in the country, and given that lack of treatment of stercoralis infection leads to hyperinfection and eventually death of the patient, it is recommended to oncology specialists in this province and in other similar regions in the country that before conducting any chemotherapy, three feces tests be ordered for, especially with formalin-ether method to detect mild and asymptomatic infections.

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References: