

CUTANEOUS MANIFESTATION OF GIARDIASIS - CASE REPORT

Aldona Pietrzak¹, Grażyna Chodorowska¹, Janusz Urban¹, Violetta Bogucka², Ewa Dybiec³¹Department of Dermatology of Dermatology, Medical University of Lublin, Lublin, Poland²Department of Educational Psychology and Psychoprevention UMCS, Lublin, Poland³Department of Paediatric Radiology, Medical University of Lublin, Lublin, Poland

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Abstract: *Giardia intestinalis* is a protozoan parasiting the gastrointestinal tract of vertebrate hosts widely distributed throughout the world. Patients with giardiasis are usually asymptomatic but the presence of the parasite may lead to a variety of clinical manifestations, including skin lesions. In this report we present a case of a 31-year-old female patient with skin lesions of granuloma annulare type confirmed by a skin biopsy, who was diagnosed with giardiasis. The clearance of the skin lesions after antiparasite treatment seems to support correlation between dermatological symptoms and infection with *Giardia intestinalis*.

Address for correspondence: Aldona Pietrzak, Department of Dermatology, Medical University of Lublin, ul. Radziwiłłowska 13, 20-080 Lublin, Poland.
E-mail: bpietrzak@pharmanet.com.pl

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INTRODUCTION

Protozoal infections of the gastrointestinal tract are regarded as a significant cause of morbidity and mortality [9]. Among them, *Giardia intestinalis* (syn. *G. duodenalis* or *G. lamblia*) accounts for 2.8 million infections annually [1]. It is the most common intestinal parasite responsible for diarrhoea in humans [13]. Typical symptoms other than diarrhoea include abdominal pain or cramping, foul smelling stools, flatulence, bloating, weight loss, nausea, vomiting, fatigue or chills [15, 22]. Besides, *Giardia intestinalis* interferes with absorption of nutrients in the small intestine, especially fats and fat-soluble vitamins. Epidemiological and clinical studies, however, show that 20-84% of infected individuals are asymptomatic [17]. Although giardiasis is not considered as a severe infection, it may sometimes cause severe complications. For example, Genovese *et al.* [6] reported a case of hypokalemic myopathy induced by *Giardia intestinalis* infection in a patient with primary immunodeficiency.

Giardia intestinalis infestation can usually be spread by direct faecal-oral transmission [1, 13, 18]. Moreover, there are also documented cases of *Giardia intestinalis* transmission through certain types of sexual practices, including oral-genital and oral-anal contacts [17]. Waterborne and food-borne transmissions have also been implicated as a cause of giardiasis in humans [2, 20, 24]. For example, Horman *et al.* [12] have found various enteropathogens (*Campylobacter* spp., *Giardia* spp., *Cryptosporidium* spp. or noroviruses) and fecal indicators (thermotolerant coliforms, *Escherichia coli*, *Clostridium perfringens* or F-RNA bacteriophages) in water samples obtained from the lakes and rivers of Finland.

The role of animals, both domestic and wild, as a source of human infestation or contamination of water supply is also well-documented [7, 11, 17, 18, 20, 24], including beavers, deer and what is more, symptom-free carrier states are common in dogs, cats, cattle or coyotes [24, 31]. Although parasitic infestations are frequently associated with visible skin lesions, a diagnosis is

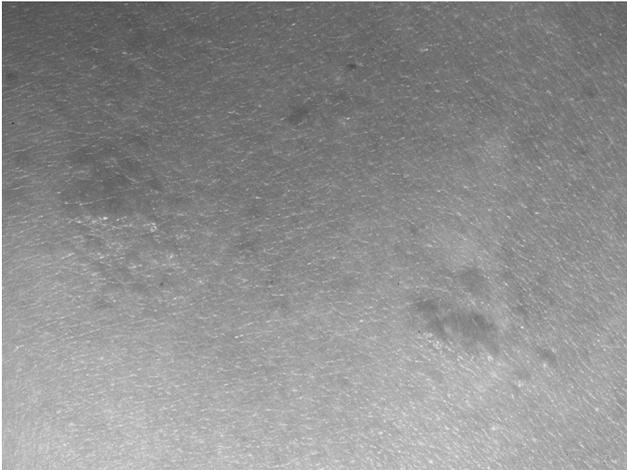


Figure 1. Cutaneous manifestation of giardiasis.

sometimes difficult to make [3, 8, 10, 19, 22]. The literature data indicate that the most common cutaneous manifestations of giardiasis are urticaria and angioedema [16, 25, 27, 29, 32]. Mouth ulcers, pruritus and atopic dermatitis are also seen in patients [27, 29]. Giacometti *et al.* [20] reported the presence of *Giardia intestinalis* in stools and skin lesions in patients with chronic urticaria, atopic dermatitis, or pruritus of unknown origin. Other authors have also reported chronic intestinal invasion associated with extraintestinal lichen planus-like skin manifestations and mucocutaneous eruption [16, 32]. An occurrence of erythema nodosum has been rarely reported in patients with *Giardia intestinalis* invasion [8, 10, 16, 30]. In this report, we present a patient infested with *Giardia intestinalis* with skin lesions diagnosed as granuloma annulare and confirmed by the histopathological examination.

CASE DESCRIPTION

A 31-year-old female patient, a physician, was referred to the Outpatient Clinic of the Dermatological Department in Lublin with a 2.5 month history of skin lesions. Initially, the patient noted the appearance of 2 painless itching areas which subsequently multiplied whereas itching subsided. Examination revealed nummular lesions (1-4 cm in diameter) with tiny, vesicle-like papules and without any signs of inflammation, located on the skin of shoulders, upper parts of the arms and back. There were no lesions on the chest. No mucosal involvement was present (Fig. 1).

Physical examination revealed the afebrile patient in good condition with enlargement of the submandibular lymph nodes (the size of peas), right axillary lymph nodes (the size of mirabelle plum) and inguinal lymph nodes (1.5 cm in diameter).

An induration of 14 mm in diameter was observed after tuberculin testing, but in X-ray examination of the thorax no organ changes were found.

The peripheral blood examinations revealed elevated erythrocyte sedimentation rate (10/20 mm/h) and total

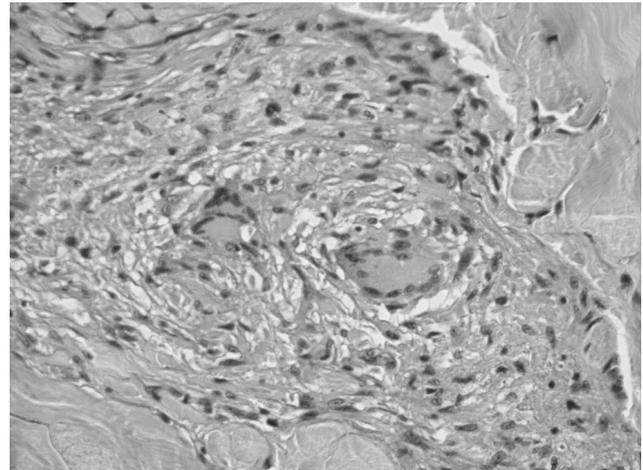


Figure 2. Histological structure of the skin biopsy specimen. H-E, $\times 41$.

WBC of $4700/\text{mm}^3$. Biochemical parameters including serum levels of creatinine, bilirubine, uric acid, diastase and iron were within reference ranges. Laboratory tests revealed a flattened blood sugar curve and an increase in serum level of LDL cholesterol (156.42 mg/dl; upper reference range: 135 mg/dl). Liver function tests were within normal limits. Protein electrophoresis revealed highly elevated levels of $\alpha 1$ - and β -globulins. Estimation of immunoglobulins showed normal serum levels of IgG, IgA and IgM but a marked increase in serum level of IgE (324 ng/dl; upper reference range: 240 ng/dl). Test for the detection of anti-nuclear antibodies was negative (Hep-2).

The mycological examination with potassium hydroxide (direct KOH test) was negative. Antigens of *Giardia intestinalis* were detected in the faeces using immunoenzymatic test (Elisa Giardia Lamblia Antigen).

HISTOLOGICAL EXAMINATION

The histological examination of the skin biopsy specimen showed a normal epidermis and foci of incomplete collagen degeneration surrounded by mononuclear and multinucleated histiocytes in dermis. Morphological features revealed by microscopy suggested that the biopsy specimen had been obtained from the edge of skin lesion of the granuloma annulare type. The histological features of the biopsy specimen were markedly inconsistent with the clinical appearance of the patient's skin lesions (Fig. 2).

RADIOLOGICAL EXAMINATIONS

In performed barium enema, hyperperistaltic dolichosigmoid was visualised, periodically contracting. Within splenic flexure of the colon thickening of colonic mucosa was visible. Due to suspected liver cancer precise ultrasonographic (USG) and computer tomography (CT) examinations of the liver were performed. USG examination showed the unenlarged liver and the unwidened bile duct. Several hypodense, blurred-edged areas located peripherally in the right lobe of the liver,

could not be clearly seen. Three-phase computed tomography scanning was performed, slice thickness 2.5 mm with contrast medium in bolus, and revealed focal lesion in VI segment of the liver. Results of radiological examinations suggested that the lesion within the liver was of adenoma type. During the patient observation period some symptoms of psychological anxiety, including trichotillomania, were noticed. However, the personality profile test showed normal levels of neuroticism, psychoticism and extraversion.

TREATMENT

Liquid nitrogen therapy along with topical application of snow paste was initiated due to the clinical symptoms resembled granuloma annulare lesions. The patient was given antihistaminics and A+E vitamins orally. After 1 month of regular treatment the pseuleucodermic lesions developed on all frozen areas. Two months later, β -carotene and UVB therapy were applied. The patient continued topical treatment with ichthyol ointment, tormentil paste and the cryotherapy was reinitiated. Despite administered local therapy, the skin lesions increased in number.

Once antigens of *Giardia intestinalis* had been detected in stool specimens, the patient started oral treatment with metronidazole: 250 mg, 3 times a day, for 10 days; after a 1-week break, the patient continued treatment with metronidazole: 250 mg, 3 times a day, for 3 days; and next took 1 dose of tinidazole (2 g). The administered 50 days-lasting antiparasite treatment produced the complete clearance of skin lesions. During 3 years of the clinical observation no recurrence of the skin disease was observed.

DISCUSSION

Giardia intestinalis is one of the most prevalent enteroparasites found worldwide, being the second most common enteric infection after amebiasis [1, 2, 17, 18, 20, 21, 23]. Majewska *et al.* [18] reported that in Poland the number of giardiasis cases in humans do not exceed 5%. The prevalence study of Ramisz *et al.* [24] including 46,584 inhabitants of Szczecin found that *Giardia intestinalis* infestation had affected 0.75% of the analysed population. Skorochodzki *et al.*, examining the duodenal fluid, showed that 67.75% of hospitalised children were infected with *Giardia intestinalis* [28].

The risk factors of the *Giardia intestinalis* transmission include young age, poor personal hygiene, risky social behaviour, malnutrition, hypochlorhydria and acquired or congenital immunological deficiencies [14, 17, 18]. Moreover, the high invasiveness of the parasite together with the weak potential for inducing host defence mechanisms contribute to the high prevalence of *Giardia intestinalis* infestation [17, 18]. Other risk factors include swimming at least once a week in recreational waters (pools, lakes, rivers), using or drinking water that might be contaminated, and travelling domestically [11].

None of the risk factors mentioned above was observed in the presented case. The patient did not practice any water sports or swimming. She led a very regular and monotonous life, ate at home and did not to travel. Poor personal hygiene as a cause of infection was also improbable. As the most common ways of *Giardia intestinalis* acquisition are person-to-person and waterborne transmissions, the examination of the patient's family members living together was performed. The household members were asymptomatic and their faeces tested negative. Therefore, water as a source of *Giardia* cysts could have been excluded.

Lack of giardiasis symptoms in the patient's family encourages the search for another source of possible infestation. Zoonotic transmission was unlikely since no pet had been living in the patient's house before the onset of the disease, and she had not come into contact with animals outdoor.

It is possible that the patient may have been infested with *Giardia intestinalis* at work. It has been found that she had not used latex gloves during her professional activities and touched her patient's skin with bare hands. There were no other risk factors for *Giardia intestinalis* invasion in our patient.

Giardia intestinalis lives in the upper small intestine and attaches to the mucosa of the host. The suggestion that specific surface molecules and their receptors are involved in the process of attachment comes from the Weiland and co-workers' study [33]. The authors observed binding of recombinant α -1 giardin to the thin sections of human small intestine. Moreover, it was showed that this binding could be inhibited by adding increasing concentrations of sulphated sugars. Alpha-1 giardin is the *Giardia*-specific surface protein which simultaneously is one of the major antigens eliciting the immune response to infestation [33]. Another surface molecule critical for attachment is taglin, i.e. trypsin-activated lectin present on trophozoite membrane. Thus, both giardins and taglin are of great relevance to the mechanism of attachment [33].

The inflammatory and immune response induced by the *Giardia* infestation seems to be of special interest. It has been found that this parasite rarely invades the intestinal wall and induces little or no inflammation. Therefore, the host defense mechanisms against *Giardia* spp. must act in the lumen of gastrointestinal tract in the absence of classical inflammatory mediators. A detailed analysis of *Giardia*-specific immune response shows that secretory IgA antibodies play a key role in elimination of the parasite [4]. Humoral immunity is probably the most important factor in resolution of *Giardia* spp. infestation. Some authors observed that selective IgA deficiency in patients with giardiasis can be often associated with nodular lymphoid hyperplasia, and such pathological changes are usually irreversible [4, 13]. It is believed that some cutaneous manifestations of *Giardia* invasion, such as urticaria, are probably associated with inflammation and induction of type 2 immune response [7, 13, 26].

Some authors have studied the involvement of the delayed-type immune reaction in the parasite infestation. In the Polish population, Ratka and co-workers have found the nummular eczema as the most frequent skin manifestations of giardiasis [25]. What is specially interesting is that Flisiak and co-workers confirmed the disturbances of the cell-mediated immune response in their patients with giardiasis [5]. Some rare manifestations of *Giardia* infestations have been described, including eosinophilic cellulitis (Well's syndrome) which, it has been suggested, is connected with a hypersensitivity response to different stimuli [3]. The pathogenesis of cutaneous manifestation in the presented case is unclear. Skin lesions were at first asymptomatic and accidentally discovered. At the beginning, they were itching but with the progress of the disease the itching subsided gradually. Both the clinical appearance as well as results of laboratory tests (especially increase in serum level of IgE and disturbances in protein electrophoresis) suggested underlying allergic mechanism.

At admission and during the initial phase of treatment the patient did not present any gastrointestinal symptoms. Later, she reported rare episodes of diarrhoea of unknown origin. These gastrointestinal symptoms did not affect the patient's weight or general condition. The diagnosis of colon irritable was excluded. Furthermore, the presence of liver cancer was eliminated by precise USG and CT examinations. The patient did not consent to radiological examination of duodenum and jejunum. However, it should be stressed that, considering the life cycle of *Giardia intestinalis*, the expected radiological changes associated with giardiasis are observed mostly in the proximal part of small intestine. In immune competent patients the small intestine is normal or develops an inflammatory bowel disease [7], whereas in cases of hypogammaglobulinemia or dysgammaglobulinemia it may show a sprue pattern [6, 9].

CONCLUSION

The pathogenesis of cutaneous manifestation in the described case is unclear. The resolving of the skin lesions after antiparasite treatment seems to support the possible correlation between dermatological symptoms and infection with *Giardia intestinalis*. Moreover, it should be stressed that the histological pattern of the biopsy specimen was unspecific and markedly inconsistent with the clinical features of the skin lesions.

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