Atopic dermatitis caused by ascariasis and cured with nitazoxanide

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ABSTRACT

Introduction: Ascariasis is mostly studied from the epidemiological, public health and gastrointestinal perspective. In consequence, there are currently hardly any reports that associate ascariasis with atopic diseases and what is more, most of the available studies are either inconclusive or contradictory.

Case study: We report a case of chronic atopic dermatitis caused by Ascaris lumbricoides infestation that was cured with nitazoxanide. The studied patient was a 1.5 year boy that suffered from refractory atopic dermatitis. No improvement was observed during prior to nitazoxanide standard treatment including topic steroids, oral antihistaminics and eliminatory diet. After nitazoxanide treatment, all atopic dermatitis symptoms vanished.

Conclusions: Patients with ascariasis may present atopic dermatitis as the main symptom. The treatment should include antihelmintic medicines. In children < 24 months of age nitazoxanide is considered as a safe and effective drug.

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Słowa kluczowe: ascariasis, ascaris lumbricoides, atopic dermatitis, nitazoxanide

INTRODUCTION

Ascaris lumbricoides is an intestinal parasite (nematode) and it affects nearly 1.2 billion people worldwide [1]. Ascariasis usually causes gastrointestinal symptoms such as abdominal pain, diarrhea, nausea and vomiting but it's extraintestinal symptoms also have been described. Ascaris infections are mostly studied and analyzed from the epidemiological, public health and gastrointestinal perspective thus there are certain limitations in the current literature that associate ascariasis with allergic diseases. The prevalence of helminth infections is decreasing in developing countries, where sanitation has been introduced [2]. On the other hand, some studies suggest that atopic diseases are becoming a rapidly growing serious public health problem. The prevalence of atopic diseases (asthma, eczema, allergic rhinitis, food allergy) has significantly increased in recent years [3, 4]. It is well known that parasite infections may stimulate total IgE production, eosinophilia and influence Th1/Th 2 balance that seems to

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Table 1. Patient data — height and weight development

Date	Age	Height	Weight
January 12, 2016 (before pyrantelum)	12 months	74 cm	9,9 kg
November 25, 2016 (after our treatment)	22 months	90 cm	14 kg
September 27, 2019	58 months	112 cm	22 kg

be involved in the clinical symptomatology. Nevertheless, the studies are inconclusive or even conflicting. In consequence opinions [5] whether helminth infections cause or protect against allergy or atopic diseases remain controversial. Some studies show that helminthic infection inhibits [6, 7], others that causes or enhances [8] and another that is unrelated to asthma and other allergic diseases [9, 10].

The effects of parasitic worms, or helminths, on the immune system has been an emerging topic of study among immunologists, parasitologists and other biologists and medical specialists

CASE REPORT

A 1.5-year-old Polish male patient suffering from 1st month of age from severe atopic dermatitis was admitted to our clinic for medical consultation in July 2016. Skin changes were localized on the whole body, especially in elbow and knee crushes. Mother referred that dermatitis appeared firstly at 1 week of age on the face and was diagnosed initially as Acne neonatorum (and later as Atopic dermatitis). Over time it progressed and took up subsequent parts of the body. Skin changes were accompanied by intense pruritus worsened with age by scratching. The infant was constantly anxious and suffered from insomnia and/ or sleep used to wake up at nights he also occasionally grinded teeth. Mother declared the use the ointment with Hydrocortisone, but with no significant improvement. Patient in the first year of life was also diagnosed with gastroesophageal reflux disease of unknown etiology and many food intolerances. In March 2016 at the age of 13 months, mother decided to empirically treat the child with the use of pyrantelum despite 3 negative results for parasites, because the results of parasitic samples were positive in other household members (mother — *Ascaris lumbricoides* and sister — *Enterobius vermicularis*). The treatment brought significant improvement of dermatitis from most parts of the body (dermatitis still remained on hands). Aditionally, GERD and food intolerances deceased. Nevertheless, the atopic symptoms gradually began to progress again and have started worsening after 3 months from the treatment. At our clinic, we observed that patient's weight and height development were delayed. Laboratory results have not shown anything relevant apart of low MCV and eosinophilia. We suspected parasitic disease so we ordered a coproscopic examination from 3 different days, which for the first time resulted positive for Ascaris lumbricoides. We proposed a treatment of nitazoxanide which brought a permanent improvement and complete resolution of skin symptoms. The patient tolerated the treatment well. After the treatment, he started to grow up and gain weight properly (Table 1). In 2019 he still developed properly and was free of skins lesions.

CONCLUSIONS

The effects of parasitic worms, or helminths, on the immune system has been an emerging topic of study among immunologists, parasitologists and other biologists and medical specialists. The effects on humans have been of special interest. The idea of a link between parasite infection and immune disorders was first suggested in 1968 [11]. The original formulation of the hygiene hypothesis dates from 1989 when David Strachan proposed that lower incidence of infection in early childhood could be an explanation for the rise in allergic diseases such as asthma and hay fever during the 20th

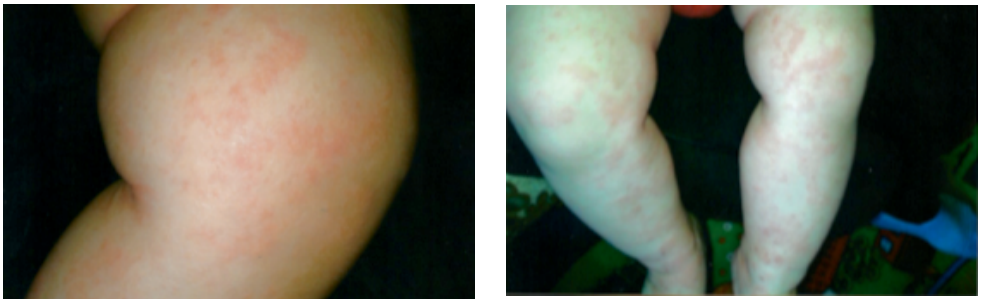

Figure 2. Clinical pictures before the treatment — 17.12.2015 (images courtesy of patient's mother)

Figure1. Clinical pictures before the treatment — 1.06.2015 (images courtesy of patient's mother)

century [12]. Nevertheless, the tendency of many helminths to pacify the human immune response allows parasites to mollify some diseases while worsening others. In the past, helminths were thought to simply suppress T-helper Type 1 (Th1) cells while inducing T-helper Type 2 (Th2) cells [13]. Prof. Graham Rook of Medical Microbiology of the University College London points out that this hypothesis would only explain the regulatory effects of parasitic worms on autoimmune diseases caused by Th1 cells [14]. However, helminths also regulate Th2-caused diseases, such as allergy and asthma [14]. Professor Rook postulates that different parasitic worms suppress different Th types, but always in favour of regulatory T (Treg) cells [14]. According to Hopkin [15], the author of a 2009 *Parasite Immunology* article on asthma and parasitic worms, other immunoregulatory mechanisms are also activated, including mast cells, eosinophils, and cytokines that invoke a strong immunoglobulin E (IgE) response Osada et al. [14] state that because parasitic worms may and often do consist of allergens themselves, the degree to which they pacify or agitate the immune response against allergens is a balance of their regulating effects and their allergenic components [16]. Therefore, depending on both of these variables, some parasitic worms may worsen allergies [16]. Our case report study suggests that ascariasis may cause atopic dermatitis that may be cured with helminthic therapy. Our results are consistent with another, the only found case report was written by Qualizza et al. [17]. Other known studies are either inconclusive or inconsistent and/ or contradictory. Some studies show that helminthic infection inhibits [6, 7], others that causes or enhances [8] and another that is unrelated to asthma and other allergic diseases

Our case report study suggests that ascariasis may cause atopic dermatitis that may be cured with helminthic therapy

Figure 3. Clinical pictures before the treatment — 26.02.2016 (images courtesy of patient's mother)

Figure 4. Clinical pictures 11.03.2016 — during empirical pyrantelum, after first dose (images courtesy of patient's mother)

Figure 5. Clinical pictures after pyrantelum (images courtesy of patient's mother)

Figure 6. Clinical pictures at our clinic before nitazoxanide (images courtesy of patient's mother)

[9, 10]. This discrepancy may be due to differences between the studied population, parasites involved and duration/chronicity of infection [18]. Other researchers consider Ascaris lumbricoides as a potential risk factor for atopy and asthma [19]. High IgE levels may play a significant role in the clinical presentation of such symptoms as dermatitis, urticaria, asthma among patients with ascariasis. Nevertheless, elevated serum IgE related to helminth infections does not necessarily equal an active infection because it may reflect both current and past infections [20, 21], suggesting that it is rather repeating ascariasis, than only the presence of infection a risk factor for asthma and atopy in children. It is believed that low intensity but the recurrent presence of infection might cause allergic sensitization. The risk of allergies also depends on factors such as diet, pollution, physical activity, obesity, socio-economic factors and stress. Genetic predisposition is also a factor [22–24]. Further studies are necessary to understand ascariasis related molecular and immune mechanisms. Helminthic infections should not be considered a tropical-only public health problem and physicians should start to consider resistant atopic dermatitis as an inconclusive presentation of chronic parasite infection and may treat it with anti-helminth medication.

It is believed that low intensity but the recurrent presence of infection might cause allergic sensitization

Figure 7. Clinical pictures after complete nitazoxanide treatment (images courtesy of patient's mother)

REFERENCES:

1. Santos AB, Rocha GM, Oliver C, et al. Cross-reactive IgE antibody responses to tropomyosins from Ascaris lumbricoides and cockroach. J Allergy Clin Immunol. 2008; 121(4): 1040–1046, doi: 10.1016/j.jaci.2007.12.1147, indexed in Pubmed: 18275995.
2. Barreto ML, Genser B, Strina A, et al. Impact of a citywide sanitation program in Northeast Brazil on intestinal parasites infection in young children. Environ Health Perspect. 2010; 118(11): 1637–1642, doi: 10.1289/ehp.1002058, indexed in Pubmed: 20705544.
3. Thygarajan A, Burks AW. American Academy of Pediatrics recommendations on the effects of early nutritional interventions on the development of atopic disease. Curr Opin Pediatr. 2008; 20(6): 698–702, doi: 10.1097/MOP.0b013e3283154f88, indexed in Pubmed: 19005338.
4. von Mutius E. The rising trends in asthma and allergic disease. Clin Exp Allergy. 1998; 28 Suppl 5: 45–49, doi: 10.1046/j.1365-2222.1998.028s5045.x, indexed in Pubmed: 9988447.
5. Pinelli E, Willers SM, Hoek D, et al. Prevalence of antibodies against Ascaris suum and its association with allergic manifestations in 4-year-old children in The Netherlands: the PIAMA birth cohort study. Eur J Clin Microbiol Infect Dis. 2009; 28(11): 1327–1334, doi: 10.1007/s10096-009-0785-6, indexed in Pubmed: 19644714.
6. Scrivener S, Yemaneberhan H, Zebenigus M, et al. Independent effects of intestinal parasite infection and domestic allergen exposure on risk of wheeze in Ethiopia: a nested case-control study. Lancet. 2001; 358(9292): 1493–1499, doi: 10.1016/S0140-6736(01)06579-5, indexed in Pubmed: 11705561.
7. Cooper PJ, Chico ME, Rodrigues LC, et al. Risk factors for atopy among school children in a rural area of Latin America. Clin Exp Allergy. 2004; 34(6): 845–852, doi: 10.1111/j.1365-2222.2004.01958.x, indexed in Pubmed: 15196269.
8. Palmer LJ, Celedón JC, Weiss ST, et al. Ascaris lumbricoides infection is associated with increased risk of childhood asthma and atopy in rural China. Am J Respir Crit Care Med. 2002; 165(11): 1489–1493, doi: 10.1164/rccm.2107020, indexed in Pubmed: 12045121.
9. Sharghi N, Schantz PM, Caramico L, et al. Environmental exposure to Toxocara as a possible risk factor for asthma: a clinic-based case-control study. Clin Infect Dis. 2001; 32(7): E111–E116, doi: 10.1086/319593, indexed in Pubmed: 11264048.
10. Cooper PJ, Chico ME, Vaca MG, et al. Effect of albendazole treatments on the prevalence of atopy in children living in communities endemic for geohelminth parasites: a cluster-randomised trial. Lancet. 2006; 367(9522): 1598–1603, doi: 10.1016/S0140-6736(06)68697-2, indexed in Pubmed: 16698413.
11. Maizels RM, McSorley HJ, Smyth DJ. Helminths in the hygiene hypothesis: sooner or later? Clin Exp Immunol. 2014; 177(1): 38–46, doi: 10.1111/cei.12353, indexed in Pubmed: 24749722.
12. Strachan DP. Family size, infection and atopy: the first decade of the „hygiene hypothesis". Thorax. 2000; 55 Suppl 1: S2–10, doi: 10.1136/thorax.55.suppl_1.s2, indexed in Pubmed: 10943631.
13. Rook GAW. Review series on helminths, immune modulation and the hygiene hypothesis: the broader implications of the hygiene hypothesis. Immunology. 2009; 126(1): 3–11, doi: 10.1111/j.1365-2567.2008.03007.x, indexed in Pubmed: 19120493.
14. Osada Y, Kanazawa T. Parasitic helminths: new weapons against immunological disorders. J Biomed Biotechnol. 2010; 2010: 743758, doi: 10.1155/2010/743758, indexed in Pubmed: 20169100.
15. Hopkin J. Immune and genetic aspects of asthma, allergy and parasitic worm infections: evolutionary links. Parasite Immunol. 2009; 31(5): 267–273, doi: 10.1111/j.1365-3024.2009.01104.x, indexed in Pubmed: 19388947.
16. Kamal SM, El Sayed Khalifa K. Immune modulation by helminthic infections: worms and viral infections. Parasite Immunol. 2006; 28(10): 483–496, doi: 10.1111/j.1365-3024.2006.00909.x, indexed in Pubmed: 16965284.
17. Qualizza R, Losappio LM, Furci F. A case of atopic dermatitis caused by Ascaris lumbricoides infection. Clin Mol Allergy. 2018; 16:10, doi: 10.1186/s12948-018-0088-5.
18. Smits HH, Yazdanbakhsh M. Chronic helminth infections modulate allergen-specific immune responses: Protection against development of allergic disorders? Ann Med. 2007; 39(6): 428–439, doi: 10.1080/07853890701436765, indexed in Pubmed: 17852030.
19. Hawlader MDH, Ma E, Noguchi E, et al. Ascaris lumbricoids Infection as a Risk Factor for Asthma and Atopy in Rural Bangladeshi Children. Trop Med Health. 2014; 42(2): 77–85, doi: 10.2149/tmh.2013-19, indexed in Pubmed: 25237284.
20. Dold S, Heinrich J, Wichmann HE, et al. Ascaris-specific IgE and allergic sensitization in a cohort of school children in the former East Germany. J Allergy Clin Immunol. 1998; 102(3): 414–420, doi: 10.1016/s0091-6749(98)70129-0, indexed in Pubmed: 9768582.
21. Obihara CC, Beyers N, Gie RP, et al. Respiratory atopic disease, Ascaris-immunoglobulin E and tuberculin testing in urban South African children. Clin Exp Allergy. 2006; 36(5): 640–648, doi: 10.1111/j.1365-2222.2006.02479.x, indexed in Pubmed: 16650050.
22. Rook GAW. 99th Dahlem conference on infection, inflammation and chronic inflammatory disorders: darwinian medicine and the ‚hygiene' or ‚old friends' hypothesis. Clin Exp Immunol. 2010; 160(1): 70–79, doi: 10.1111/j.1365-2249.2010.04133.x, indexed in Pubmed: 20415854.
23. Filippi CM, von Herrath MG. Viral trigger for type 1 diabetes: pros and cons. Diabetes. 2008; 57(11): 2863–2871, doi: 10.2337/db07-1023, indexed in Pubmed: 18971433.
24. Rook GAW. Hygiene hypothesis and autoimmune diseases. Clin Rev Allergy Immunol. 2012; 42(1): 5–15, doi: 10.1007/s12016-011-8285-8, indexed in Pubmed: 22090147.