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REGRESSION OF ALLERGIC SYMPTOMS AFTER ANTIPARASITIC THERAPY: A CASE OF TOXOCARA

Medicine

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ABSTRACT

Toxocara canis is a parasitic roundworm of particular public health concern. Eggs of *Toxocara canis* may be present in dog and cat faeces, which become infectious after being deposited for some weeks in the local environment. Humans become infected after ingesting the eggs, by accident. In the human body, larvae do not become adult worms but rather can migrate to various tissues and organs, remaining either in a latent state or causing various clinical manifestations.

The clinical case here reported suggests how Toxocara canis may cause chronic symptoms, often considered allergic symptoms, the resolution of which requires corresponding anthelmintic therapy. Our allergologic evaluation therefore focused attention on those cases in which common allergologic treatments do not present a resolution, raising therefore the suspect of a possible under-lying parasitosis.

We examined a patient referred for dry cough and dyspena. The patient showed hypereosinophilia, but asthma symptoms improved after previously prescribed treatment with nasal steroid and formoterole/budesonide. Thus, tests for IGG antibodies *Toxocara canis* using ELISA and Western blot were recommended.

The patient was positive for *Toxocara canis* and, therefore, anthelmintic therapy was prescribed. After treatment, the patient showed full remission of symptoms. After treatment, we prescribed the same tests again, which were negative for *Toxocara canis*.

These findings suggest the possible role of *Toxocara canis* in inducing chronic symptoms, which may raise the suspect of a possible under-lying parasitosis, and which show remission after anthelmintic therapy.

KEYWORDS

Toxocariasis, *Toxocara canis*, helminths, asthma.

Toxocara canis is a nematode belonging to the order of Ascaridae. Eggs of *Toxocara canis* may be present in dog and cat faeces, which become infectious after being deposited for some weeks in the local environment. Humans become infected after ingesting the eggs, by accident. In the human body, larvae do not become adult worms but rather can migrate to various tissues and organs, remaining either in a latent state or causing various clinical manifestations. In humans, these larvae may remain occult or may cause different clinical manifestations depending on which tissue has been invaded. Toxocariasis may cause syndromes such as visceral larva migrans (VLM) and ocular larva migrans (OLM), in which the inflammatory response may lead to partial or total retinal detachment with visual loss. Larvae have been found in the liver, lungs, eye and brain where they cause inflammation, eosinophilia, haemorrhage and necrosis. The larvae may be encapsulated inside granulomas, in which they may remain silent for a long time (Despommier, 2003); (Schantz,1989). Infection from this helminth plays a crucial role in the development of allergic immunopathology and successive clinical manifestations; indeed, *Toxocara* infection has a role in the production of Th-2 type cytokines (IL–4, IL-5, and IL-13), in increased IgE levels and eosinophilia, persistent pulmonary inflammation, airway hyper-reactivity and production of Th-2 type cytokines (Qualizza, Incorvaia, Grande, Makri, Allegra,2011); (Qualizza, Megali, Incorvaia, 2009); (Del Prete, De Carli, Mastromauro, Biagiotti, Macchia, Falagiani, Ricci, Romagnani, 1991); (Coffman; Mosmann, 1991); (Buijs, Lokhorst, Robinson, Nijkamp, 1994) ; (Kayes, 1997); (Pinelli, Withagen, Fonville, Verlaan, Dormans, van Loveren, Nicoll, Maizels, van der Giessen, 2005); (Qualizza, Furci, Furci, 2017). Infection with helminths may alter the host immune system with the appearance of atopy, asthma, and an increased value of blood eosinophilia and total IgE (Buijs, Borsboom, Renting, Hilgersom, van Wieringen, Neijens, 1997); (Li, Gao, Yang, Wu, Bi, Zhang, Huang, Yao, 2014); (Alcântara-Neves, de S G Britto, Veiga, Figueiredo, Fiaccone, da Conceicao, Cruz, Rodriques, Cooper, Pontes-de -Carvalho, Barreto, 2014). Helminth infection induces an immune response which is distinct from other chronic pathogens (such as protozoa, bacteria and viruses) as they are characterized by a Th2 immune response. Parasitic infections present an increase of circulating CD4+ CD25+ FoxP3+ regulatory T cells (Tregs) and autoantigen-stimulated peripheral blood lymphocytes (PBLs) that produce IL-10 and TGF beta (Alcântara-Neves, de S G Britto, Veiga, Figueiredo, Fiaccone, da Conceicao, Cruz, Rodriques, Cooper, Pontes-de -Carvalho, Barreto, 2014).

According to the Global Initiative for Asthma guidelines 2015, asthma is defined as a chronic inflammatory disorder of the conducting airways and is characterized by airway hyper-responsiveness that results in recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, above all during night time or early morning (Reddel, 2015).

Interleukin-10 (IL10) is produced mainly by macrophages and T-lymphocytes, and plays a central role in both anti-inflammation and immunosuppression. Thus, genetic polymorphisms found in regulatory sites, especially the promoter region of the *IL-10* gene, are believed to affect the expression of IL-10 protein and possibly be associated with asthma susceptibility and prognosis. *IL-10* has been studied as a candidate gene for adult asthma predisposition in Iran, Macedonia and Finland, but the findings are inconclusive (Karjalainen, Hulkkonen, Nieminen, Huhtala, Aromaa, Klaukka, Hurme, 2003); (Trajkov, Mirkovska-Stojkovikj, Petlichkovski, Strezova, Efinska Mladenovska, Sandevska, 2009); (Hsia, Chang, Wang, Shen, Hsiao, Liu, Liang, Chen, Tu, Tsai, Hsu, Bau 2015). Parasitic infections are underestimated; it is estimated that ascarid infection affects 25% of the world's population. In patients with respiratory symptoms such as obstructive and restrictive syndromes, ascarid infection is not usually investigated, and symptoms, such as asthma, dry cough and dyspnea, are only treated with antibiotics and steroids. In this way, the symptoms are abated but then re-emerge as a new exacerbation, as seen in the clinical case of recurrent bronchitis by *Toxocara canis* (Qualizza et al., 2017).

Parasitic infections may cause different symptoms of allergy which are unresponsive to common therapy. Here, we describe the clinical case of a patient who presented with allergic symptoms of asthma which resolved following antiparasitic therapy.

Case report

A 44-year-old male patient, who had been suffering from seasonal rhinoconjunctivitis for 5 years, was referred for observation. There was no history of allergy in the family, no significant pathologies and he reported dry cough and dyspnea. A positive prick test for grass pollen (+++), birch pollen (+++), Dermatophagoides farinae (+++), Dermatophagoides pteronyssinus (++), total IgE 224 KU/l, eosinophilia 41.1 (n.v. < 7), and spirometry with small airway obstruction were observed (FEV1 value, 44%).

The patient was initially treated with nasal steroid, formoterol/ budesonide and deltacortene (25mg/5 days). On check-up, after 7 days, breathing was normal, with just a persistent dry cough. Nasal steroid and formoterol/budesonide was continued. After 2 months, a second spirometry showed an FEV1 value of 56%. The patient also presented with tiredness and muscular pain. Hematologic, rheumatologic and thoracic CT tests were requested, with normal outcomes. Therefore, the patient was prescribed prednisone therapy (25 mg/ 5 days), showing, at the following check, a reduction in asthma symptoms. However, eosinophilia had doubled to 41.1%. We prescribed tests for IgG and IgM for echinococcosis and *Strongyloides*, and IgG for *Toxocara canis,* using ELISA and Western blot.

The tests were positive for *Toxocara canis*: Anti Toxocara canis ELISA > 1.1 (n.v. <0.9; doubtful 0.9 – 1.1; positive > 1.1) and negative at Western Blot. Anti-parasitic therapy was started (Mebendazole, 2 x 100 mg x 3 days) and repeated after 20-50-80 days. Treatment is repeatedly until eosinophil level is normal. In this case, levels had returned to normal by 80 days.

Conclusions

Our case demonstrates how hypereosinophilia and allergic symptoms may be caused by *Toxocara canis;* in areas where Toxocarisis is not frequently found, this case highlights the importance of knowing how the presence of allergic symptoms which do not respond to common therapy, and the co-presence of hypereosinophilia, may raise a suspect of a parasitic infection the treatment of which leads to significant clinical improvement of symptoms.

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