Epidemiological and Clinical Dimensions, Diagnostic and Experimental Research on a Toxocariasis Case Associated with Hyperleukocytosis

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Abstract. Toxocariasis is a zoonosis caused by the ingestion of larvae *Toxocara canis* or *Toxocara cati*. In this article, the author is going to present the difficulties to diagnosis the toxocara in a child with hyperleukocytosis. He has been transferred to the pediatric care for additional investigations due to the suspicion of acute leukemia. The complete haematology investigation has shown eosinophil precursors hyperplasia (17%). Therefore, the eosinophilia has justified the additional tests, highlighting the increased titers for toxocara canis. The fecal examination, through improved methods, has identified a co-infection of parasites. The differential diagnosis has included the acute and chronic leukemia. The patient has received a treatment with albendazole which led to a prompt improvement of leukocytosis. This explains the suspicion of leukemia through a detailed presentation of the co-infection of parasites and of haematological abnormalities. The co-infection cases and their sources have been classified as socio-economic.

Keywords: co-infection, hyperleukocytosis, fecal examination, toxocariasis.


Cuvinte cheie: co-infecție, hiperleucocitoză, examen coproparazitologic, toxocaroză.

Introduction

Toxocariasis is caused by infestation with nematodes *Toxocara canis* or *Toxocara cati*, the man being just an accidental host. After the ingestion of the eggs left by the adult parasite, the larvae form and migrate in the human body. This process can take a few months. The larvae can survive for years in the host's body, but its reaction will limit their development in these organs.

There are three clinical options of the disease: visceral larvae migrans, ocular larvae migrans and latent option of the disease (“covert toxocariasis”).

*Toxocara canis*: life cycle. The adult *toxocariasis* female leaves 200,000 eggs per day (the nematode parasite is present in the intestine of small puppies and nursing bitches).
The unembryonated eggs get on the soil and, in conditions of humidity. They embryos (they are resistant to extreme temperature variations or pH). The man or the dog ingests the embryonated eggs. The larvae develop from eggs in the intestine, then pass in the blood and lymphatic vessels and migrate to different organs. It's important to remember that the man is an intermediate host, but the larvae migrate to organs where they stop their development, without becoming adult worms. The conclusion is that the man won’t leave Toxocara eggs in the intestine (the coproparasitologic examination won't show parasite eggs). The bitch is an exception (the pregnant bitch) - it passes the parasite larvae to its babies, through the placenta. After the babies’ birth, larvae continue their development, then they pass through the lungs to the digestive tube and they become adult intestinal worms, so they become the main infestation source.

The infestation sources are: the sand boxes or holes from parks are contaminated with Toxocara eggs (20-30% from playgrounds in the parks are contaminated), but also infestations cases have been reported after eating raw-dried meat, unwashed vegetables and fruit or pica.

Seroprevalence of toxocara varies from country to country and from region to region (the USA – 4-8%; Holland – 19%; Germany – 2.5%; Slovakia – 13%; Czech Republic – 5.8-36%; Brazil – 39%; Spain – 37%; Jordan – 9.8%; Romania – 44%; Republic of Moldova – 48%). It should be noted that the infestation risk is high in children aged 1-7 years old, but the seroprevalence (the titer's positivity) increases with age or the patient's development period (Nelson et al., 1996).

Methods of Study

The clinical picture will be analyzed according to the clinical option of the disease. So, visceral larvae migrans is characterized by: general clinical signs (fever, asthenia), urticarial lesions, cough, wheezing, abdominal pains, hepatomegaly, arthralgia, encephalitis etc.

Ocular larvae migrans determines a unilateral ocular involvement and it has been described in older children and teenagers. In this form of the disease there are missing the general signs and the marked eosinophilia. Besides, the patient can present leucocoria, eye pain, crossed eyes, decreased visual acuity (the differential diagnosis of retinoblastoma is required) (Bertelmann et al., 2003).

The latent form of the disease (most cases are asymptomatic) is frequently diagnosed only in the context of serological evaluations. It is manifested through abdominal recurrent pains, cough, wheezing, hepatomegaly, headaches, anorexia and growth disorders. In these cases, it is found that eosinophilia is rare, but the anti-toxocara titer is moderately increased.

The laboratory diagnosis is based on:
- eosinophilic leukocytosis (to 80%);
- IgM hypergamaglobulinemia;
- serological examination (ELISA) to identify the anti-toxocara antibodies (specificity 90%, sensitivity 75%). Remember that the serological tests don't make any difference between recent and old infestations, but in the ocular the antibody titers are reduced or are in normal limits. Instead, the titer from the vitreous or from the aqueous humor can be elevated in the ocular;
- the western-blotting technique (even time-consuming) is more sensitive than ELISA;
- the PCR method (polymerase chain reaction) – an useful identification method of the parasite in tissues;
- for the latent form of the disease advocates the positive serology for *Toxocara* associated with asthenia, abdominal pains, rash and eosinophilia that aren't triggered by allergens.

In terms of imaging, the cases can be evaluated using the CXR (in case of wheezing, cough) to be able to determine the eosinophilic pneumonia, pleurisy and cardiomegaly. The cardiac ultrasound is used to evaluate the myocardial contractility and to determine pericarditis. The ultrasound of the abdomen reveals the hepatic granulomas.

Among the surgical procedures, the biopsy of the affected tissue reveals the granulomas with infiltration of eosinophils/neutrophils and (probably) debris larval.

Treatment. Most patients are treated with antiparasitic therapy associated with corticosteroids to avoid the amplification of inflammatory response after the parasite destruction. In ocular larvae migrans case the corticosteroid is recommended (without antiparasitic therapy) and if needed, the surgical therapy. In latent form of the disease, the therapeutic choice depends on patient's age, on the severity of symptoms and on the certainty of diagnosis.

The prevention includes regular deworming procedures of dogs and cats, but also implementing measures that would limit the pets’ access to playgrounds frequented by children (Pelloux & Faure, 2004).

The prognosis is good for visceral larvae migrans and latent form of the disease. In ocular larvae migrans it depends on determining the diagnosis (high risk of unilateral amaurosis in case of late diagnosis). The health education refers to hygiene measures.

**Results and Discussion**

Patient A.Z. is presented for discussions. He is a five-year-old boy who lives in the countryside. On his case it has been done a study on clinical, diagnostic and experimental aspects. He has been admitted at contagious disease ward at the county Hospital from Cahul presenting watery and mucosangvinolent seats, symptoms that have started at home for days before the admission. At home he took enterocolitis, without other medication.

Hederocollateral antecedents: healthy parents and without “blood relations”. His mother is uneducated and without a job.

From personal antecedents we remind: he is the first child in his family (he has a younger brother – 18 months – healthy). He was born at the gestational age of 36 weeks and birth weight – 3200 g, head shape; the pregnancy evolution has been physiological, without long suffering at birth, APGAR = 10/1 minutes. The mother had smoked during the pregnancy. Among the pathological antecedents we mention an admission for respiratory tract infection. The psychomotor development: corresponding to the age stages (stood at 7 months, walked when he was 1 year old). Among the living conditions we mention the source of running water, insanitary housing (4 people /1 room).

From the history of the disease we remind that the disease started 4 days before the admission with watery and mucosangvinolent seats, justifying the admission to the County Hospital from Cahul. After the investigations, he was suspected with acute leukosis and he was transferred to the pediatric ward. Here are the investigation results done in the contagious disease ward:

- CBC with microcytic anemia (Hgb = 119 g/l; RBC =3.9 x 10^{12}/L), reactive thrombocytosis (PLT 437.6 x 10^{9}/L), leukocytosis (WBC 44.6 x 10^{9}/L), leukocytes
indicating a redominance of the lymphocytes (lymphocytes 82%), and also of the eosinophils (eosinophils 8%);
- the peripheral blood smear: RBC MicroCal and hypochromia; without morphological changes in leukocytes;
- inflammatory balance: C-reactive protein and normal values of ESR;
- the amylase and the calcium phosphorus balance with normal values;
- urinalysis: without pathological changes;
- immunological balance: antinuclear antibodies, complement and immunogram serum - in normal values;
- infectious balance (pharyngeal exudate, Rotavirus antigen test/adenovirus in stool, stool): negative.

Physical examination at admission in the pediatric ward has revealed:
- poor nutritional status (weight 12 kg, < percentile 3), afebrile;
- paleness;
- disorders of trophic function of the skin and its appendages, pediculosis of the scalp;
- without lymphadenopathy in the selected territories;
- osteoarticular transfer system with signs of rickets (Harrison ditch, parietal bone);
- examination of the respiratory system, of the cardiovascular system, urogenital system and otoscopic examination: without pathological changes;
- digestive system: throat congestion, meteorites in the abdomen, no hepatosplenomegaly;
- central nervous system: without sign of irritation of the meninges; normal pupil size and reactive to light.

Among the investigations done in the pediatric ward:
- the CBC reveals and confirms together the microcytic anemia, and also the leukocytosis, but with slightly lower values (WBC 34.1 x 10^9/L) with eosinophilia (an absolute eosinophil 6.9% value);
- the bone marrow biopsy has shown a hypercellular bone marrow with hypereosinophilia (normal values < 7%); without changes on the lymphocytic, erythroid and myeloid series, the ratio of blasts was of 2%;
- negative inflammatory balance;
- the infectious balance done to complete the original one has foreseen also the serology for infectious mononucleosis, herpes, cytomegalovirus, *Trichinella spiralis*, *Toxoplasma gondii* and HIV infection – with a negative result;
- fecal examination, using the Katoh-Miura method of concentration has shown *Ascaris lumbricoides* (*ascarid*) eggs and *Giardia* (*Lamblia*) *intestinalis* cysts;
- ophthalmologic exam: eye anterior segment without pathological changes;
- image explorations (CXR, ultrasound of the abdomen): normal aspect.

Based on the inconsistency between the peripheral blood and the bone marrow, a series of hypothesis have been developed:
- peripheral lymphocytosis is probably secondary to peripheral stimulation (at the level of the peripheral lymphoid organs);
- peripheral eosinophils have been “masked” by the partially normal percentage of eosinophils;
- eosinophilia in the central nervous system represents the true indicator for a particular eosinophils parasite.
The final diagnosis, established after an extensive and detailed investigation, has included the next entities: hyperleukocytosis, co-infection of parasite, growth retardation and fetal ponderal, anemia and rachitis sequelae.

Considering the eosinophilia of the central nervous system, the serology examination for *Toxocara canis* and the total IgE blood test have been justified: IgG antibodies to *Toxocara canis* (through ELISA method) - getting positive results for IgG antibodies to *Toxocara canis* = 26.89 UI/L (normal values < 11), and also the total IgE test = 1098 UI/L (normal values < 60) – the Toxocariasis diagnosis has been confirmed.

So, the positive diagnosis has had a co-infection of parasites (toxocariasis, ascariasis and giardiasis) in a patient with multiple biological deficiencies (iron deficiency anemia, rachitis sequelae, growth retardation and fetal ponderal).

Although it hasn't been possible to establish the acute nature versus chronic infestation with *Toxocara canis*, the antiparasitic treatment has been initiated (Albendazole 400 mg per day for 4 days). We mention that before initiating the antiparasitic treatment, the total number of leukocytes was decreasing (WBC 28.7 x 10^9/L).

**Conclusions**

The studies have confirmed the fact that Toxocariasis larvae produces glycosylated antigen. This antigen determines a cellular immune response, after that the B cells switch to IgE production. So, the hyper-lymphocytosis and the high levels of IgE are detectable changes in this case, changes that are similar to those from Toxocariasis.

Given that the serological tests cut the correlation between the current parasitic infestation and the previous one (the old one), but especially between infestation and co-infection the treatment is still available, but the doses are calculated depending upon the clinician's decision (depending on the patient's age and weight);

Toxocariasis is, with high probability, responsible for the hyperleukocytosis, but from a practical-therapeutic point of view the co-infection with other species of parasites is masking even more the leukemic syndrome, but also determining the titer positivity on *Toxocara* antibodies.

Among the particularities of the case we mention: the total number of leukocytes reached the limit of 44.6 x 10^9/L; the concomitant infestation with three parasites species (*Toxocara canis*, *Ascaris lumbricoides* and *Giardia intestinalis*); the co-infection is explained in the light of the low socio-economic level and a reduced hygiene degree.

**References**


