

УДК 616.995.132.8-06:616.155.391]-071-053.2
DOI: 10.24061/1727-0847.16.4.2017.112

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TOXOCARIASIS WITH MARKED EOSINOPHILIC LECOCITOSIS TO A 3 YEARS OLD CHILD - CASE PRESENTATION

ТОКСОКАРОЗ З ВИРАЖЕНОЮ ЕОЗИНОФІЛЬНИМ ЛЕКОЦИТОЗОМ У 3-Х РІЧНОГО ДИТИНИ – КЛІНІЧНИЙ ВИПАДОК

Резюме. Токсокароз – важливий зооноз, викликаний другою стадією розвитку личинок *Toxocara canis* і *cati*. Його типовими синдромами є *Larva migrans visceralis*, *Larva migrans ocularis* і окультний токсикароз. Більшість випадків токсикарозу протікають безсимптомно, особливо у дорослих. Пацієнти з *Larva migrans visceralis* можуть відчувати втому, втрату ваги, втрата апетиту, лихоманку, головний біль, висипання, кашель, біль у грудях, дратівливість, біль в животі, нудоту та блювоту. *Larva migrans ocularis* є зоною запалення, задні гранулеми і ендодальміт. Гіпереозінофілія може вказувати на наявність паразитарної інфекції, в даному випадку токсикарозу. Епідеміологічне обстеження та детальний анамнез пацієнта можуть бути корисними під час встановлення цього складного діагнозу. Дуже мало досліджень було зроблено на зрізах, які були вилучені з розтинів. На розтині печінка є збільшеною. Його поверхня глянцева і гладка. У паренхімі печінки є кілька біло-сірих вузликів з діаметром 2,0 мм, хоча в деяких випадках вони можуть досягати 1-2 см. В центрі деяких з цих вузликів деколи можна знайти личинки S2. У випадках з тяжкої алергічної гіперчутливості, можна зареєструвати часті абсцеси з еозінофілами та некрозом печінки. Важливо відзначити, що присутність в серці або інших структурах серцево-судинної системи навіть невеликої кількості личинок може викликати появу особливо серйозних симптомів, таких як ексудативний міо-ендо-перикардит, подібний з ревматичних, з можливою серцевою тампонадою, коронарною аортальною аневризмою, дисемінованим васкулітом, медіастинітом тощо. Тільки в трьох з дев'яти випадків, коли проводився гістологічний аналіз (до або після розтину), були виявлені типові гранульоми або залишки паразита. В інших шести випадках результати були неспецифічними; ушкодження серця помірно було викликано прямим вторгненням личинок і імунологічними реакціями, викликаними системної гіпер-еозінофілією або наявністю личинок в тканині. Ми представляємо клінічний випадок трирічної дитини з діагнозом Токсокароз. *Larva migrans visceralis*, рецидивна хронічна форма.

Ключові слова: токсикароз, еозінофілія, виражений лейкоцитоз.

Toxocarosis is an infection produced by the ingestion of embryonated eggs of *Toxocara canis* or *Toxocara cati*, parasites found in dogs and respectively in cats. The mature parasites live in the intestine of the natural hosts, ho eliminates their eggs with faeces. The eggs become infectious after 2-5 weeks, under humid and warm environments. Human infection occurs after contact with contaminated soil or infected faeces of animal hosts [1]. Many cases with Toxocarosis are asymptomatic and may reach up to 44% prevalence [2]. Systemic Toxocarosis on the other hand occurs in approximately 15.5% of the diagnosed cases [3].

Larva migrans visceralis syndrome occurs when the parasite enter the portal circulation by penetrating intestinal wall, and reaching the liver produces a granulomatous reaction forming microgranulomas look-

ing like frosted glass at echography. If the parasite passes the hepatic filter, it will colonize other organs such as the brain, the kidneys and even the cutaneous tissue [4]. Clinical manifestations of toxocarosis are due to mechanical lesions caused by larval migration and by eosinophilic inflammatory reaction with formation of eosinophilic allergic granulomas. The spectrum of clinical manifestations ranges from asymptomatic patients randomly diagnosed by routine screening, to severe, sometimes fatal clinical forms of lung or nervous system damage [4].

Because of the variability of clinical signs of the disease, in 1988 the toxocarosis was divided into two main forms: *Larva migrans visceralis* (LMV) and ocular toxocarosis (LMO) [5]. Between 1992 and 1993, a third form of toxocarosis was described in seroposi-

tive patients with gastrointestinal disorders, general weakness and lethargy [6, 7] – Occult Toxocariasis [1, 8-10].

Recently, a new classification of the toxocariasis was proposed with the involvement of the patient's clinical condition, immunopathological mechanisms, serological response rate and location of the toxocara larvae. This classification divides human toxocariasis into: Classical, systemic Toxocariasis, asymptomatic Toxocariasis, occult and compartmentalized Toxocariasis (ocular and neurological). The last two forms require separate classification since the eye and the brain are the final migration sites of the toxocara larva [11].

Larva migrans visceralis is a disease that occurs predominantly in children (<5 years) [12]. Childhood prevalence varies greatly in the world, ranging from 4.6% in the US to 57.5% in Taiwanese aboriginal school children; a similar situation is seen in young children in Brazil where the prevalence varies between 8.7% and 54.8% [13].

The risk factors responsible for Toxocara disease include: geophagia; children who contact dogs that have not been dewormed; Consumption of vegetables and fruits grown in gardens contaminated with faeces [13, 14]; the consumption of insufficiently cooked meat from potentially parasitic hosts such as – birds [15], lambs [16] rabbits [17], ingestion of raw poultry liver [18] or beef; poor personal hygiene.

Acute signs of Larva migrans visceralis associated with hepatic and pulmonary larval migration include abdominal pain, loss of appetite, psychomotor agitation, fever, cough, wheezing, asthma episodes, and hepatomegaly. At this stage of infection, hyper-eosinophilia, leukocytosis and hyper-gamaglobulinemia are recorded [14]. A child with fever of unknown etiology and eosinophilia should be suspected of having Larva migrans visceralis. Certain diagnosis of toxocariasis can be established by immunological exams: ELISA IgG anti-Toxocara, and Western Blot. Albendazole is the treatment of choice of toxocariasis [8].

Material and methods. As material served the clinical case of a 3 year old child that was detected with the presence of a marked eosinophilic leukocytosis and was supervised for three years (2015-2017) with subsequent establishment of diagnosis Larvar Toxocariasis. Larva migrans visceralis with chronic recurrent evolution. In order to establish this diagnosis have been used biological (general blood analysis, biochemical blood test), bio-molecular diagnostic methods (Immunoblot test), enzyme-linked immune-sorbent assay (ELISA) and radioimaging methods (chest radiography, ultrasonography of internal organs).

Results and discussions. We present the clinical case of a 3 year old child from Ungheni, which was

first detected in November 2015 with marked leukocytosis ($60.5 \times 10^9/l$) and hypereosinophilia (68%) with no special clinical signs.

The child was born on time, physical and motor development fell within the age limits. Vaccination was performed in accordance with vaccination schedule. The pathological history of the child has no relevant data on past illnesses.

At general examination of the child there was no evidence of organ damage. The general condition of the child was satisfactory, the child was active, responded adequately to verbal and tactile stimuli, consciousness was clear. The patient's skin was pale, without rash. The mucous membranes were of normal color, without rash. The tongue is humid, without deposit. To pulmonary auscultation is determined rough breathing, with no crackles. Rhythmic, clear heart sounds. Pathological heart murmurs are not determined. Soft abdomen, indolent to palpation. The inferior limit of the liver is determined at the right costal margin, is elastic, indolent. Spleen is not palpable. Stools are without pathological inclusions. Urination is free, painless, with normal color. Giordano sign is negative bilateral. Meningeal signs are negative.

Due to marked eosinophilic leukocytosis, the patient was consulted by the haematologist who excluded haematological pathology. Ultrasound of the internal organs was performed with no modification.

Due to hyper-eosinophilia and elevated total IgE (439 IU / mL), a 10-day Helmizol course with age-appropriate doses was indicated. As a result, leukocyte level decreases twice ($33.5 \times 10^9/l$), but the eosinophil level increase considerably (up to 82%). Total IgE level also increase (869 IU / mL).

Subsequent, 5 consecutive courses of larvicidal medicine were indicated between December 2015 and April 2016. During this time, the general blood analysis had different modulations with maintaining the hemoglobin level below normal limits but with a subtle increase to 100 g / l, the leukocyte level decreasing considerably from $60.5 \times 10^9/l$ to $13.1 \times 10^9/l$ in March 2016. The serum level of total IgE also decreased gradually to 508 IU / mL. Eosinophils were maintained at high level with an index of over 48% in March 2016. During this time, transaminases maintained their values within the normal limits.

The patient was investigated for Toxocariasis with detection of anti-Toxocara canis IgG positive in February 2016 with a value of 3.98, the test being repeated in March 2016 with a practically equal value of 3.80. In May 2016, after a short break in treatment, biochemical indices significantly deteriorated: leukocytosis was $17.1 \times 10^9/l$, hyper-eosinophilia – 43.1%,

hyper-transaminasemia with ALT-901 U / L, total IgE level increased to 634 IU / ML.

Due to the instability of paraclinical indices on anti-parasitic treatment, the clinical diagnosis was established: Larvar Toxocariasis. Larva migrans visceralis with chronic recurrent evolution.

Taking into account the elevated level of transaminases, were indicated markers of viral hepatitis with HBs Ag – negative, anti HBsAg-positive with high protective titre, anti HCV-negative, anti-Toxoplasma IgM and IgG-negative.

A 10 day Zentel (Albendazole) cure with 2 ml x 2 times per day per oral with repeat of the treatment over 7 days in combination with hepatoprotective

therapy was indicated. General blood and biochemical tests were examined periodically (Table 1 and Table 2).

In the following months of surveillance the condition of the child remained satisfactory, the general examination did not revealed changes at any dynamical verification. There were indicated 3 larvicidal cures with Escazol, with gradually improving biochemical indices: leukocytes – $6.8 \times 10^9/l$, eosinophils 11%, total IgE 108.9 IU / mL, in November 2016, transaminase level normalized, but they continue to grow in the absence of antiparasitic treatment. To confirm the diagnosis of Toxocariasis, in November 2016 the Western Blott test for

Table 1

Indications of general blood analysis during patient surveillance

| Indicators /data | 27.11. 2015 | 07.12. 2015 | 06.01. 2016 | 08.02. 2016 | 14.03. 2016 | 05.05. 2016 | 06.06. 2016 | 28.06. 2016 | 15.08. 2016 | 15.11. 2016 | 06.02. 2017 | 13.03. 2017 | 14.11. 2017 |
|------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Hemoglobin (g/l) | 98 | 93 | 103,0 | 99,0 | 100,0 | 118,0 | 118,0 | 112,0 | 122,0 | 114,0 | 124,0 | 124 | 112,0 |
| Erythrocytes ($10^{12}/l$) | 4,0 | 3,8 | 5,08 | 4,71 | 4,53 | 4,9 | 4,80 | 4,62 | 4,74 | 4,0 | 4,65 | 4,62 | 4,0 |
| Thrombocytes ($10^9/l$) | | | 423,0 | 321,0 | 430,0 | 542,0 | 341,0 | 393,0 | 278,0 | 448,0 | 319,0 | 360,0 | 319,0 |
| Leukocytes ($10^9/l$) | 60,5 | 33,5 | 19,7 | 10,8 | 13,1 | 17,0 | 15,3 | 10,4 | 7,3 | 6,8 | 9,5 | 9,6 | 7,6 |
| Neutrophils (%) | 5 | 3 | 15 | 39,1 | 16 | 19,1 | 13 | 21,4 | 21,5 | 42,0 | 41,9 | 34,0 | 39 |
| Eosinophils (%) | 68 | 82 | 64 | 30 | 48 | 43,1 | 55 | 37,2 | 28,6 | 11,0 | 14,0 | 13,8 | 23,5 |
| Basophils (%) | 0 | 0 | 0 | 0,9 | 2 | 1,6 | 1 | 1,2 | 2,0 | 0 | 1,0 | 1,0 | 0,9 |
| Lymphocytes (%) | 17 | 13 | 17 | 22,2 | 27 | 27,8 | 25 | 34,1 | 39,6 | 43,0 | 31,6 | 41,9 | 27,6 |
| Monocytes (%) | 10 | 2 | 4 | 7,8 | 7 | 8,4 | 6 | 6,1 | 8,3 | 4,0 | 11,5 | 9,3 | 9,0 |
| ESR (mm/h) | - | - | 30 | 15 | 30 | 20 | 15 | 22 | 12 | 10 | 30 | 7 | 5 |

Table 2

Biochemical indices during patient surveillance

| Indicators /data | 27.11. 2015 | 06.01. 2016 | 08.02. 2016 | 14.03. 2016 | 05.05. 2016 | 12.05. 2016 | 06.06. 2016 | 28.06. 2016 | 15.08. 2016 | 14.11. 2016 | 06.02. 2017 | 13.03. 2017 | 14.11. 2017 |
|----------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| ALT (0-34 U/L) | 36,7 | 14 | 13 | 13 | 901 | 650 | 181 | 179 | 54 | 30,8 | 51,56 | 727 | 91,9 |
| AST (0-31 U/L) | 46,5 | 35 | | | | 411 | 167 | 151 | 65 | 47,6 | 48,0 | 312 | 84,9 |
| Total Ig E level (0-45 UI/mL) | 439 | 869 | 516 | 508 | 634 | | 479 | 565 | 384 | 108,9 | 256 | 306 | |
| Anti Toxocara Canis IgG (N< 1,0) | | | 3,98 | 3,80 | | | 3,70 | 5,97 | 4,40 | | 2,24 | 3,5 | |

Toxocara canis was performed with suspicious result.

At the last clinical examination, the condition of the child remained satisfactory, with no complains, organ systems unchanged, paraclinical indices close to the normal levels.

Conclusions. 1. Larvar toxocariasis in a young children encompasses various clinical manifestations ranging from classical systemic to asymptomatic, which requires a thorough diagnosis and therapeutic management. 2. The presence of such a marked eosinophilic leukocytosis requires a multilateral and meticulous differential diagnosis, and and establishing the

diagnosis of Toxocariasis can only be done using modern and accurate diagnostic methods. 3. Repeat cures of larvicidal treatment were satisfactorily tolerated by the child with increased transaminases after the 7th treatment course, indicating greater caution in the use of anti-parasitic therapy due to the knowledge of its hepatotoxic action. 4. In the cases with long-term marked hyper-eosinophilia, it is absolutely necessary to involve specialists from different fields, including histologists, to identify cardio-rheumatological repercussions in the cases with cardiovascular damage.

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ТОКСОКАРОЗ С ВЫРАЖЕННЫМ ЭОЗИНОФИЛЬНЫМ ЛЕКОЦИТОЗОМ У 3-Х ЛЕТНЕГО РЕБЕНКА - КЛИНИЧЕСКИЙ СЛУЧАЙ

Резюме. Токсокароз – немаловажный зооноз, вызванный второй стадией развития личинок *Toxocara canis* и *cati*. Его типичными синдромами являются Larva migrans visceralis, Larva migrans ocularis и оккультный токсокароз. Большинство случаев токсокароза протекают бессимптомно, особенно у взрослых. Пациенты с Larva migrans visceralis могут испытывать усталость, потерю веса, анорексию, лихорадку, головную боль, сыпь, кашель, боль в груди, раздражительность, боль в животе,

тошноту и рвоту. Larva migrans ocularis представляет собой зону воспаления, заднюю гранулему и эндофтальмит. Гиперэозинофилия может указывать на наличие паразитарной инфекции, в данном случае токсокароза. Эпидемиологическое обследование и подробный анамнез пациента могут быть полезными при установлении этого сложного диагноза. Очень мало исследований было сделано на срезах происходивших с вскрытий. На вскрытии печень появляется увеличенной. Его поверхность глянцевая и гладкая. В паренхиме печени имеется несколько бело-серых узелков с диаметром 2 мм, хотя в некоторых случаях они могут достигать 1-2 см. В центре не-

которых из этих узелков иногда можно найти личинки S2. В случаях с тяжелой аллергической гиперчувствительности, можно зарегистрировать частые абсцессы с эозинофилами и некроз печени. Важно отметить, что присутствие в сердце или других структурах сердечно-сосудистой системы даже небольшого числа личинок может вызвать появление особенно серьезных симптомов, таких как экссудативный мио-эндо-перикардит, схожий с ревматическим, с возможной сердечной тампонадой, коронарная аортальная аневризма, диссеминированный васкулит, медиастинит и т. д. Только в трех из девяти случаев, когда проводился гистологический анализ (до или после вскрытия), были обнаружены типичные гранулемы или остатки паразита. В остальных шести случаях результаты были неспецифическими; повреждение сердца в равной степени было вызвано прямым вторжением личинок и иммунологическими реакциями, вызванными системной гипер-эозинофилией или наличием личинок в ткани. Мы представляем клинический случай трехлетнего ребенка с диагнозом Токсокароз. Larva migrans visceralis, рецидивирующая хроническая форма.

Ключевые слова: токсокароз, эозинофилия, выраженный лейкоцитоз.

TOXOCARIASIS WITH MARKED EOSINOPHILIC LECOCITOSIS TO A 3 YEARS OLD CHILD - CASE PRESENTATION

Abstract. Toxocarosis is a significant zoonosis caused by the second stage of development of the larvae of *Toxocara cani* and *cati*. Its typical syndromes are larva migrans visceralis, larva migrans ocularis and occult toxocarosis. Most cases of toxocarosis are asymptomatic, especially in adults. Patients with Larva migrans visceralis may experience fatigue, weight loss, anorexia, fever, headache, rash, cough, chest pain, irritability, abdominal pain, nausea and vomiting. Larva migrans ocularis it is presented as an area of inflammation, posterior granuloma and endophthalmitis. The hypereosinophilia may suggest the presence of a parasitic infection, in this case of the toxocarosis. The epidemiological examination and a detailed anamnesis of the patient may be useful in establishing this difficult diagnosis. Very few investigations were made on pieces from necropsies. At necropsy the liver appears enlarged. Its surface is glossy and smooth. In the parenchyma of the liver, there are several white-gray-colored nodules with 2 mm in diameter, although in some cases they may reach 1 to 2 cm. At the center of some of these nodules, S2 larvae can sometimes be found on serial sections. In cases of severe allergic hypersensitivity, frequent abscesses with eosinophils, liver necrosis can be recorded. It is important to note that the presence in the heart or other structures of the cardiovascular system of even a small number of larvae usually causes the appearance of particularly severe signs of suffering such as exudative mio-endo-pericarditis similar to rheumatic, with possibility of cardiac tamponade, coronary or aortic aneurysm, disseminated vasculitis, mediastenitis etc. Only in three of the nine cases where histological analysis (either pre- or post-mortem) was performed, were detected granulomas or remnants of the parasite. In the other six cases, the results were non-specific; heart damage was equally caused by direct larvae invasion and immunological reactions, either caused by systemic hyper-eosinophilia or by the presence of larvae in the tissue. We present the clinical case of a three year old child diagnosed with Toxocarosis. Larva migrans visceralis, recurrent chronic form.

Key words: toxocarosis, eosinophilia, marked leukocytosis.

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Надійшла 02.11.2017 р.
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