REVIEW ARTICLE

LARVA MIGRANS IN CHILDREN IN INDIA - IS IT AS RARE AS WE THINK?

Sanghamitra Ray, Rajesh Kumar Meena***

Abstract

Context- Larva migrans are parasites, mainly the larvae of nematodes causing zoonotic disease. They cause broad spectrum of diseases in man depending on the organ involved. India being a developing country; overcrowding, poor level of hygiene, lack of safe drinking water and adequate sanitation, close contact with animals make our population extremely susceptible to this infection. Despite the presence of epidemiological triad of agent, host and favorable environment, incidence of larva migrans cases reported is surprisingly low in pediatric population of India. There is very little awareness among pediatricians about this entity. Hence it is possible that we are missing a lot of cases due failure to suspect, vagueness of symptoms, difficulty in diagnosis and lack of easy availability of diagnostic tests. These facts prompted the authors to review this disease which is routinely thought only to be of academic interest.

Evidence Acquisition: We conducted a detailed literature search on PubMed-Central, Google-scholar and Cochrane Database using the terms 'larva migrans' OR 'visceral larva migrans OR, ocular and cutaneous larva migrans' WITH AND WITHOUT 'India' AND "children " as references. We also searched the reference lists from such articles. Extracted manuscripts and reviews were analyzed and summarized with special emphasis on Indian scenario in pediatric population.

Result- Though world literature shows wide spectrum of manifestations of larva migrans in children, few scattered pediatric case reports from India do not corroborate with its epidemiological profile. Hence it can be concluded that we are missing a lot of cases as we fail to suspect.

Keywords : Larva migrans, Visceral larva migrans, Pediatric

Introduction

Larva migrans are parasites, mainly the larvae of nematodes causing zoonotic disease where human is the accidental host. The eggs hatch in the small intestine and enter the portal system by invading intestinal mucosa. The liver traps some larvae, but others proceed to lungs and circulatory system, from where they can disseminate to different tissues (liver, lungs, brain, eyes) causing local inflammatory and allergic reactions. (1) Although these larvae are not adapted to complete their life cycle within human body, they are capable of invading human organs in which they may survive for many months and even for years.

India being a densely populated country; overcrowding, poor level of hygiene, lack of safe water and sanitation, close proximity with domestic animals makes our population extremely susceptible to larva migrans. Dogs, wolves, foxes and other canines are also among other hosts to these nematodes. (1) World Health Organization (WHO) estimated India's stray dog population as 25 million. (2) Stray dogs play a major role in the environmental contamination with the helminth eggs. In India, presence of stray dogs, open defecation by both stray and pet dogs, improper fecal disposal are the favorable factors for the persistence of ova of nematodes in the environment. Lack of adequate public knowledge further adds to the occurrence of this disease. In a survey in Pondicherry, 21.66 % dog owners had no knowledge regarding transmission of Toxocara canis to humans. (3) Despite these facts, incidence of larva migrans cases reported is surprisingly low in pediatric population of India. There is very little awareness among pediatricians about this entity. Hence it is possible that we are missing a lot of cases due failure to suspect, vagueness of symptoms, difficulty in diagnosis, lack of easy availability of diagnostic tests.

According to the organs involved, the disease caused by larva migrans can be are divided into - visceral, cutaneous and ocular larva migrans. There are many nematodes capable of causing this disease in children, few to mention are Toxocara canis, Toxocara cati, Ancylostoma caninum, Fasciola hepatica, Gnathostoma and Necator americanus. Children especially in pre-school age group are the most susceptible due to inability or lack of compliance to maintain hygienic standards, close contact with domestic animals and also because of pica in many of them.

Visceral larva migrans (VLM)

Visceral larva migrans (VLM) have a worldwide prevalence, although there is a strong predilection for the tropical countries and Southeast-Asia including India. (4) VLM is characterized by different systemic symptoms. Fever, hepatomegaly, splenomegaly, eosinophilia are among the most common presentations. (5) Cases of myocarditis caused by larva migrans are also described in literature. (6) Pulmonary involvement can result in cough, wheeze and dyspnea leading to pneumonia or reactive airway disease. (7) Signs such as seizures, neuropsychiatric symptoms, or encephalopathy could be seen in cases of central nervous system (CNS) involvement. In different reports, neurological toxocariasis has been diagnosed by finding larva in CSF, brain specimens with or without serological diagnosis. (8,9) Typical VLM usually presents in a 2-7 year old child with history of pica and history of contact with puppies. Taylor et al (10) reported abdominal pain as one of the most common symptoms, especially in children with higher titres though similar association has not been found in some other studies. Abdominal pain may be caused by lymphadenitis as a host response to larval migration. Seroprevalence studies indicated the prevalence rates of 32.86% and 6.4% of human toxocariasis from Jammu & Kashmir and Haryana states of northern India, respectively. (11,12) Sporadic cases of VLM have also been reported from many other states. (13,14)

Cutaneous larva migrans

Cutaneous larva migrans (CLM) can present as non-specific dermatitis to typical diagnostic creeping eruption. An erythematous itchy papule is observed

at first followed by formation of linear, serpentine or bizarre tracks. The larvae migrate about 2–5 cm per day. Lesions are commonly seen on the feet, lower legs and buttocks but also occur on the arms, hands and face. CLM usually heals spontaneously within weeks to months but the larvae may migrate for as long as one year. (15) If patient does not undergo treatment, complications like impetigo and local or general allergic reactions can occur.

Ocular larva migrans

Ocular larva migrans (OLM) is frequently observed in older children and young adults. OLM is usually unilateral. Most common presenting manifestations are impairment of visual acuity and leukocoria. OLM can cause uveitis, posterior and peripheral retinochoroiditis, vitritis, endophthalmitis, papillitis and other ocular lesions that often lead to loss of vision in the affected eye. (16) Few scattered case reports have been published from India. Fomda et al presented a 12 year old girl with ocular toxocariasis who presented as a case of endogenous endophthalmitis. (17) A serological study on Indian patients with ocular manifestations indicated presence of anti-Toxocara antibodies in 11 subjects of less than 15 years old (17 %) and three subjects of more than 15 years old (4 %) out of total 68 patients. (18)

Covert toxocariasis

A case control study in Ireland led to a new clinical entity called covert toxocariasis. (19) This term was coined for seropositive children detected during a population based survey which was associated with nausea, headache, behavioral and sleep disturbance with or without eosinophilia and moderate toxocara ELISA titres ≥ 1:50. (20) Another case-control study in adults in France led to the definition of common toxocariasis - a syndrome consisting of chronic dyspnea, weakness, rash, pruritus, abdominal pain with high IgE and high titres of toxocara specific antibody. Covert and common toxocariasis represent slight variation in the clinical spectrum of mild toxocara infection in children and adult. They usually have mild symptoms which do not require treatment with antihelminthic. (21) One fourth of the children with covert toxocariasis do not have eosinophilia. This entity is often confirmed by the disappearance or alleviation of symptoms and signs after treatment with anti-Toxocara medications.

Diagnosis

Diagnosis is based on peripheral hypereosinophilia, leucocytosis, hypergammaglobulinemia and positive serology. A peripheral blood eosinophilia, although has been constantly associated with VLM is often absent in patients with OLM (22) probably due to the low larval burden (often a single larva) in children with OLM. Chest X-ray may reveal miliary infiltrates, atelectasis or areas of consolidation. Liver involvement may be detected by USG (ultrasonography) as hyperechoic lesions suggestive of granulomas without liver enzymes derangements. An adult case series from India highlighted the importance of imaging modality in diagnosis. Imaging features of hepatic VLM on contrast enhanced computed tomography (CECT) include presence of small, single or multiple hypovascular eosinophilic abscesses seen enhancing only on portal venous phase (PVP) on triple phase liver study. (23) In the CNS, more sensitive magnetic resonance imaging (MRI) has revealed granulomas appearing as hyper-intense areas on T2- weighted images, primarily located cortically or sub-cortically. (24) In 11 patients with OLM, ultrasound has revealed a highly reflective peripheral mass, vitreous bands or membranes, and traction retinal detachment. (25) A definitive laboratory diagnosis of human toxocara infection can be achieved by pathology examination of various organ specimens, including the liver. (26) In the ocular form of the disease, a mobile larva can be directly observed under the retina. (27)

The most commonly utilized diagnostic serologic test is the enzyme-linked immunosorbent assay (ELISA) with TES-Ag (excretory-secretory antigens isolated from second-stage larvae of Toxocara canis. (28) The use of excretory-secretory antigens from T. canis larvae maintained in vitro further increases the specificity of the ELISA. A positive ELISA for Toxocara can be confirmed by western blot, which is as sensitive as ELISA, and quite specific when lower molecular weight bands, from 24 to 35 kilo- Daltons are considered. (29) Some authors have also demonstrated ELISA on intraocular fluids as a useful diagnostic aid. It is important to emphasize that while infection with A. lumbricoides can be diagnosed by examination of feces for the ova or adult worm, the larvae of Toxocara do not commonly complete their life cycle in man. Therefore, fecal examinations are non-contributory to the diagnosis of VLM in humans. For diagnosis in dogs, fecal examination is done to observe ova of the parasite.

Treatment

Treatment in children depends on type and severity of symptoms and also the site involved. Anti-helminthics are the main stay of treatment. Systemic therapy is generally done with benzimidazole derivatives such as albendazole, mebendazole, thiabendazole and also diethylcarbamazine. Albendazole has been used in various studies at a dose of 10mg/kg/day with a course ranging from 5, 10, 15, and 21 days. (30,31) The recommended dose of albendazole is 15 mg/kg body weight daily for five days, and in some cases with VLM syndrome, the treatment needs to be repeated.(32,33) Less side effect and better availability of albendazole makes it the first line of treatment in most clinical settings. Cutaneous larva migrans is readily treated and the treatment of choice is ivermectin. A single oral dose (200 microgram/kg body weight) kills the migrating larvae effectively. If the first treatment fails, a second dose usually provides a definitive cure. A single dose of ivermectin is more effective than a single dose of albendazole. An alternative choice of treatment is the topical application of 10 percent topical thiabendazole suspension 4 times a day for at least 2 days after the last sign of burrow activity. Albendazole (400 mg a day

for 3 days) is also effective. Asymptomatic subjects presenting with a chronic eosinophilia and those with covert toxocariasis in the absence of eosinophilia, do not normally require any specific therapy. (34)

Patients with myocarditis or central nervous system disease should always be treated with corticosteroids. Among the available drugs, albendazole is the most commonly used. Anti-helminthic drugs and corticosteroids have been used to treat OLM. Anti-helminthic therapy is not worldwide accepted because of the possibility that larvae death may increase the inflammatory reaction. In OLM, steroids can be given topically, peri-ocularly, intra-ocularly and systemically. Pars plana vitrectomy is useful and indicated to remove vitreous opacities and epiretinal membranes, to relieve the vitreoretinal traction, to prevent and treat retinal detachment. Among other methods, laser photocoagulation is indicated when a larva can be identified by direct visualization in the eye. Ocular granulomas can be treated with cryopexy. Treatment in dog includes dichlorvos, pyrantel pamoate and mebendazole. (35-37)

Prevention

This disease is preventable by simple public health measures. Improving day to day practices of hygiene and sanitation are the most important among these. Primary prevention of larva migrans can be done by reduction of exposure to infected animals and contaminated environments and elimination of infections in dogs, puppies, and cats. Children should be discouraged from putting dirty fingers in their mouth and eating dirt. Regular de-worming of dogs is also equally important. The recommendation of deworming for older animals is 1-2 times per year. (38) Reduction of the canine population is also one of the measures. World Health Organization (WHO) recommends that the canine population in each location should correspond to at most 10% of the human population. (39)

Conclusion

Children with VLM infections are often diagnosed as having allergies, infection related eosinophilia, tropical eosinophilia. Some cases are diagnosed accidentally in biopsy sample. Most of them remain asymptomatic and many symptomatic cases are also missed due to lack of suspicion by the treating pediatrician. Awareness of the different forms of manifestations of larva migrans - especially in children and young adults is needed and larva migrans in the differential diagnosis of systemic or localized disorders with eosinophilia should be considered.

Funding : None

Conflict of Interest : None

References :

1. Otranto D, Dantas-Torres F, Brianti E, Traversa D, Petrić D, Genchi C, Capelli G. Vector-borne helminths of dogs and humans in Europe. Parasit Vectors. 2013; 6: 16
2. Menezes R. Rabies in India. CMAJ. 2008 Feb 26; 178(5): 564–566.
3. Das SS, Kumar D, Sreekrishnan R. Assessment of awareness of dog owners about public health importance of Toxocara cani infection in Pondicherry. J Vet Parasitol. 2007; 21:69–70
4. Chang S, Lim JH, Choi D, Park CK, Kwon NH, Cho SY, Choi DC. Hepatic visceral larva migrans of Toxocara canis: CT and sonographic findings. AJR Am J Roentgenol 2006;187:W622–9.
5. Jain R, Sawhney S, Bhargava DK, Panda SK, Berry M. Hepatic granulomas due to visceral larva migrans in adults: appearance on US and MRI. Abdom Imaging.1994; 19:253–256
6. Dao AH, Virmani R. Visceral larva migrans involving the myocardium: report of two cases and review of literature. Pediatr Pathol.1986;6:449–456.
7. Cianferoni A, Schneider L, Schantz PM, Brown D, Fox LAM. Visceral larva migrans associated with earthworm ingestion: clinical evolution in an adolescent patient. Pediatrics.2006; 117:336–339
8. Komiyama A, Hasegawa O, Nakamura S, Ohno S, Kondo K. Optic neuritis in cerebral toxocariasis. J Neurol Neurosurg Psychiatry. 1995;59:197–198.
9. Duprez TPJ, Bigaignon G, Delgrange E, Desfontaines P, Hermans M, Vervoort T et al. MRI of cervical cord lesions and their resolution in Toxocara canis myelopathy. Neuroradiology. 1996;38:792–795.
10. Taylor MR, Keane CT, O'Connor P, Mulvihill E, Holland C. The expanded spectrum of toxocaral disease. Lancet. 1988;1:692-5.
11. Malla N, Aggarwal AK, Mahajan RC. A serological study of human toxocariasis in north India. The Nat Med J Ind. 2002; 15:145–147.
12. Dar ZA, Tanveer S, Yattoo GN, Sofi BA, Wani SA, Dar PA, Fomda BA. Seroprevalence of Toxocariasis in children in Kashmir, J&K State, India. Iranian J Parasitol. 2008; 3:45–50.
13. Thakkar PA, Dahat A, Shukla O, Javadekar. An interesting case of visceral larva migrans (VLM). Int J Med Sci Public Health. 2012;1:101–104.
14. Dao AH, Virmani R. Visceral larva migrans involving the myocardium: report of two cases and review of literature. Pediatr Pathol. 1986; 6:449–456.
15. Chaudhry AZ, Longworth DL. Cutaneous manifestations of intestinal helminthic infections. Dermatol Clin. 1989; 7:275–290.
16. Steward JM, Cubillan LD, Cunning ET Jr. Prevalence, clinical features and causes of vision loss among patients with ocular Toxocariasis. Retina. 2005; 25:1005-13.
17. Fomda BA, Ahmad Z, Khan NN, Tanveer S, Wani SA. Ocular toxocariasis in a child: A case report from Kashmir, north India. Indian J Med Microbiol. 2007;25:411-2.
18. Mirdha BR, Khokar SK. Ocular toxocariasis in a North Indian population. J Trop Pediatr. 2002; 6:328–330
19. Taylor MR, Keane CT, O'Connor P, Mulvihill E, Holland C. The expanded spectrum of toxocaral disease. Lancet. 1988;1:692-5.
20. Smith H, Holland C, Taylor M, Magnaval JF, Schantz P, Maizel R. How common is human toxocariasis? Towards standardizing our knowledge. Trends Parasitol. 2009;25:182-8.
21. Rubinsky-Elefant G, Hoshino-Shimizu S, Jacob CMA, Sanchez MCA, Ferreira AW. Potential immunological

markers for diagnosis and therapeutic assessment of toxocariasis. Revista do Instituto de Medicina Tropical de São Paulo. 2011;53:61-5
22. Glickman LT, Schantz PM. Epidemiology and pathogenesis of zoonotic toxocariasis. Epidemiol Rev. 1981;3:230–250.
23. Laroia ST, Rastogi A, Sarin S. Case series of visceral series of visceral larva migrans in the liver: CT and MRI findings. International Journal of Case Reports and Images 2012;3(6):7–12
24. Ruttinger P, Hadidi H. MRI in cerebral toxocaral disease. J Neurol Neurosurg Psychiatry. 1991;54:361–362.
25. Wan WL, Cano MR, Pince KJ, Green R. Echographic characteristics of ocular toxocariasis. Ophthalmology. 1991;98:28–32.
26. Kirchner T, Altmann HW. Parasitenlarven als Ursache umschriebener Leberherde. Morphologie und Differentialdiagnose. Pathologe. 1987;8:31–36.
27. Meyer-Riemann W, Petersen J, Vogel M. Extraktionsversuch einer intraretinalen Nematode im papillomakularen Bundel. Klin Monatsbl Augenheilkd. 1999;214:116–119.
28. De Savigny DH, Voller A, Woodruff AW. Toxocariasis: serological diagnosis by enzyme immunoassay. J Clin Pathol. 1979;32:284–288.
29. Magnaval J-F, Fabre R, Maurieres P, Charlet J-P, De Larrard B. Application of the western-blotting procedure for the immunodiagnosis of human toxocariasis. Parasitol Res. 1991;77:697–702
30. Bathia V, Sarin SK. Hepatic Visceral larva migrans: evolution of the lesion, diagnosis, and role of high-dose albendazole therapy. Am J Gastroenterol. 1994;89:624-7.
31. Pawlowski Z. Toxocariasis in humans: clinical expression and treatment dilemma. J Helminthol. 2001;75:299-305.
32. Magnaval JF. Comparative efficacy of diethylcarbamazine and mebendazole for the treatment of human toxocariasis. Parasitology. 1995;110:529–33.
33. Magnaval JF, Dorchies P, Glickman LT. Toxocara species. In: Liu VL, Weber R, editors. In: Antimicrobial therapy and vaccines. Lippincott: William and Wilkins; 2000.
34. Magnaval JF, Glickman LT, Dorchies P, Morassin B. Highlights of human toxocariasis. Korean J Parasitol. 2001;39:1–11
35. Dinning WJ, Gillespie SH, Cooling RI, Maizels RM. Toxocariasis: a practical approach to management of ocular disease. Eye.1998; 2:580–582.
36. Maguire AM, Zarbin MA, Connor TB, Justin J. Ocular penetration of thiabendazole. Arch Ophthalmol.1990; 108:1675.
37. Werner JC, Ross RD, Green WR, Watts JC. Pars plana vitrectomy and subretinal surgery for ocular toxocariasis. Arch Ophthalmol. 1999; 117:532-534.
38. Maizels RM, Meghji M. Repeated patent infection of adult dogs with Toxocara canis. J Helminthol. 1984;58:327-33.
39. World Health Organization. Guidelines for dog population management. Available at URL: http://apps.who.int/iris/bitstream/10665/61417/1/WHO_ZOON_90.166.pdf. Accessed on 25th February 2017.

From: *Department of Pediatrics, Cantonment General Hospital, Delhi Cantt, New Delhi, India, **Department of Paediatrics, ESIC Hospital, New Delhi, India.

Address for Correspondence: Dr Sanghamitra Ray, Flat no-176, Pocket- 1, sector- 1, Dwarka, New Delhi 110075, India.

Email : dr.sanghamitra.ray@gmail.com

DOI : 10.7199/ped.oncall.2017.35