CASE REPORT

Immune-inflammatory markers in massively disseminated cysticercosis

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SUMMARY

Disseminated cysticercosis is a common endemic tropical infection. We report a 24-year-old man who presented with a single episode of focal seizure and transient depression. Imaging studies revealed disseminated vesicular cysticercosis involving almost all the body parts. In spite of severe dissemination and significantly raised immunological inflammatory markers, the patient had negligible symptoms. He was subsequently followed up with oral corticosteroid and antiepileptic drug without further complication. The extensive dissemination, relatively benign nature of the disease and clinoradiological discordance are interesting to describe. This neglected tropical infection can sometimes be alarming and needs public health awareness.

BACKGROUND

Neurocysticercosis (NCC) is caused by *Taenia solium*, a common but neglected tropical infection in developing countries like India. Humans acquire intestinal tapeworms by consuming insufficiently cooked infected pork. Humans are the definite hosts and pigs, the intermediate hosts. Humans can also become accidental intermediate hosts if they ingest *Tsolium* eggs shed in faeces by autoinfection or consuming unwashed contaminated vegetables. It is hypothesised that immune-inflammatory responses may play a role in parasite survival and dissemination. Local and systemic immune responses to the parasite could be of relevance in the outcome.¹ Clinical presentation depends on several factors including number, size, location and stages of the parasite. The severity also depends on various

inflammatory and immune responses of the host.² We report such a case of relatively clinically benign but severely disseminated cysticercosis with high titre of serum as well as cerebrospinal fluid (CSF) immune-inflammatory markers.

CASE PRESENTATION

A 24-year-old man, resident of district Ghaziabad, Uttar Pradesh in North India, has been working as a railway attendant. He had a single episode of left focal seizure with secondary generalisation in September 2012. He was treated with phenytoin (300 mg/day) with good compliance by a general practitioner with no seizure recurrence. However, he had not been investigated for the same. From January to July 2013, he developed apathy, social withdrawal and lack of motivation and preferred to stay alone for most of the day. He discontinued his job. He received treatment for the depressive symptoms (tablet escitalopram 10 mg/day) from a psychiatry clinic for a period of 3 months. He gradually improved and achieved premorbid state and rejoined his duty without further symptoms. His medical history revealed, in March 2012, trauma to the left eye which eventually led to corneal opacity despite conservative management. His dietary history was suggestive of consumption of pork for about a year in 2010. Since then, he had been a vegetarian. He was referred to us for opinion regarding history of seizure and decision regarding withdrawal of antiepileptic drug. General physical examination showed multiple mobile, non-tender, subcutaneous nodules of diameter 1–2 cm in the forehead, nape of the neck,

Figure 1 (A) MRI of the brain with T2 axial sequence showing innumerable intraparenchymal and extraparenchymal vesicular cysts containing clear fluid and scolices (arrow). (B) T2 sagittal section showing infiltration of cysts in the orbital, extraocular, neck and tongue muscles.

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Figure 2 (A and B) MRI of the whole body revealing extensive infestation of organs such as intestines, pancreas, heart, liver, pleura and genitourinary organs.

shoulders and back. Ophthalmological examination revealed corneal opacity in the left eye. Visual acuity of the left eye had negative perception of light and the right eye had 6/6 as per Snellen's visual acuity chart. Nervous system and systemic examinations were unremarkable.

NEUROIMAGING

MRI of the brain with T2 axial sequence showed innumerable intraparenchymal and extraparenchymal vesicular cysts containing clear fluid and scolices (figure 1A, arrow). T2 sagittal section showed infiltration of cysts in the orbital, extraocular, neck and tongue muscles (figure 1B). MRI of the whole body revealed extensive infestation of organs such as pancreas, heart, capsules of liver, pleura and genitourinary organs (figure 2A, B). MRI of the skeletal muscles of the shoulder, thorax, trunk, paraspinal and limb muscles showed multiple linear, hyperintense cysticercoids (figure 3A,B).

LABORATORY INVESTIGATIONS

The complete blood count showed marked eosinophilia with absolute eosinophil count of $13\,070/\text{mm}^3$ and the total leucocyte count of $17\,060/\text{mm}^3$. Other routine blood investigations and ELISA for HIV were unremarkable. Enzyme immune assay (SCIMEDX Kit) of serum and CSF cysticercus IgG antibody level were 2.76 optical densities (OD) units (normal (N) <0.3 OD units) and 1.62 OD units ($N < 0.3$ OD units), respectively. The CSF and serum were subjected to ELISA to determine the levels of certain cytokines using the commercially available kit (Invitrogen, USA), and the obtained values were compared with

healthy controls.³ We have tried to assess the immunological markers in our case and have looked for any symptomatic correlation. The serum cytokines markers are illustrated as: interleukin (IL) 4, 6.52 pg/mL (N 0.00–0.27); IL-10, 48.11 pg/mL (N 0.00–0.37); tumour necrosis factor (TNF), 19.43 pg/mL (N 4.62–9.86); interferon (IFN) γ , 30 pg/mL (N 0.00–38.14) and IgE level of 1130 IU/mL (N 0–380 IU/mL). The CSF immune-inflammatory markers are shown as follows: IL-4, 7.88 pg/mL (N 0.00–0.23); IL-10, 79.11 pg/mL (N 0.00–0.20); TNF, 28.08 pg/mL (N 2.73–8.92); IFN γ , 23.03 pg/mL (N 0.00–5.25). The overall cytokines values suggested that there was a high rise of serum as well as CSF titre and the comparative later value was higher.

TREATMENT AND FOLLOW-UP

In view of the high parasite load, the benefits of cyst clearance were outweighed by the potential deleterious host inflammatory response to the dying cysts. Hence cysticidal therapy was withheld. The patient was continued with anticonvulsants (tablet phenytoin 300 mg/day) and low dose of oral prednisolone (20 mg/day) for 6 months followed by 10 mg of prednisolone until the last follow-up in January 2014. He had been doing well without any further complication.

DISCUSSION

Disseminated cysticercosis has quite unpredictable presentations, which depend on host and parasite interaction. It results from parasitic infestations of the central nervous system, skeletal muscles, subcutaneous tissues, orbits and rarely thoracic and

Figure 3 (A and B) MRI of the skeletal muscles of the shoulder, thorax, trunk, paraspinal and limb muscles showed multiple linear, hyperintense cysticercoids.

abdominal organs.⁴ However, in 40% of the cases, the parasite can exist in the brain for years without any obvious symptoms and eventually disintegrate to different stages such as vesicular, colloidal, nodular and calcified.⁴ Prasad *et al*⁵ reported 29% of asymptomatic individuals among the family members of symptomatic patients. Montano *et al*⁶ also demonstrated asymptomatic cases in healthy control subjects. The literatures state that the immunological profiles in NCC depend on location of the lesion (parenchymal or extraparenchymal), stages of cysts, number of cysts, central and peripheral disseminations and intensity of host inflammatory-immune response.⁷ Interindividual variations remain an intriguing aspect of NCC. Verma *et al*⁸ demonstrated a significant association between Asp299Gly and Thr399Ile genotypes of the Toll-like receptor 4 genes in symptomatic NCC.

Alternatively, the symptoms of patients with NCC include seizure (focal or generalised), focal neurological deficit, cognitive issues and other organ-specific manifestations as well as life-threatening conditions such as raised intracranial pressure and encephalopathy. Live cysts evoke a minimal or undetectable inflammatory response. It is the dying or dead cysts that are thought to be responsible for the severe inflammatory changes that cause neurological symptoms.¹ CD4 T helper (Th) cells produce IL-4, IL-5 and IL-10; the so-called Th2 and Th1 cells produce IFN γ , IL-2 and TNF α cytokines which promote a cell-mediated inflammatory response.⁹ Previous studies showed that the Th1 response was usually found in acute symptomatic

patients and Th2 response in asymptomatic individuals or those with calcified lesions.⁹

In our case, Th1 and Th2 immune responses were activated along with the high rise of IgE and IgG levels. Further, CSF and serum immune markers were raised suggestive of severe inflammatory response. In contrast to other similar literatures, we found high immune-inflammatory markers in the CSF as compared with the serum even if there was severe peripheral dissemination.¹⁰ Eventually, the immune-inflammatory markers do not reflect the symptomatic severity of the disease state.

Contributors AKP was involved in conception and design. BKP drafted the article. AKP and BKP were involved in acquisition of the data or analysis and interpretation of the data, revising it critically for important intellectual content and final approval of the version published.

Competing interests None.

Patient consent Obtained.

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Learning points

- In an endemic area, the number, size, location and stages of neurocysticercosis and its inflammatory response may not always correlate with clinical severity.
- Th1 and Th2 immune responses were activated in our case due to peripheral as well as central nervous system dissemination.
- Public health awareness has utmost importance in the endemic region regarding consumption of infected undercooked pork and contaminated green vegetables.

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