

Neurocysticercosis: A new concept and insight into basic and future pharmacotherapy

Wisam Mahdi Al-Saeed, Azhar Hatif Oleiwi Al-Kuraishi, Salma Luaiby Dahash, Ali Ismail Al-Gareeb, Hayder Mutter Alkuraishy

Abstract

Neurocysticercosis is a neurological infection caused by the larva of taenia solium. The larva infection may affect different parts of the human brain and spinal cord, leading to focal neurological deficit with/without inflammatory reactions. Neurocysticercosis is one of the major causes of epilepsy in the developing countries. It is of two types. One is extra-parenchymal neurocysticercosis in which cysticerci cysts at subarachnoid space and ventricles lead to obstructive hydrocephalus and increase in the intracranial pressure. The other type is intra-parenchymal neurocysticercosis in which the cysticerci cyst grows inside the brain parenchyma, causing the feature of space-occupying lesion. The common presentation of intra-parenchymal neurocysticercosis is secondary epilepsy which is due to focal lesion and/or local inflammatory reactions. Cysticidal therapy increases the risk of seizure due to the induction of host inflammatory reactions. Therefore, co-administration of corticosteroids reduces the risk of seizure through attenuation of inflammatory reactions and brain oedema. Praziquantel alone or in combination with albendazole is regarded as the basic cysticidal therapy against neurocysticercosis. Newer drugs and agents are recommended to overcome the partial failure of standard cysticidal therapy.

Keywords: Albendazole, Praziquantel, Cysticidal therapy, Neurocysticercosis.

Introduction

Tapeworm infection was initially described in 2000BC in ancient Egypt. Aristotle in 384-322BC described pork tapeworm as 'pork measles'. Also, early Muslim physicians gave the reason for religious prohibition of pork meat. Furthermore, cysticercosis was described by Johannes Rudolph in 1555, but the association between tapeworms and cysticercosis had not been identified at that time. In the middle of the 19th century, it was clear that ingestion

of tapeworm eggs lead to cysticercosis.¹

Taenia solium (TS) is a cestode parasite common in developing countries in different rural settings. When roaming pork eat TS eggs in human stools, the larval infection develops. When humans consume and ingest pork meat infected with cystic larvae, they develop intestinal TS.²

TS adult stage is a 2-4m long, alive in the small intestine which gets attached to the intestinal mucosa. The source of eggs is the terminal part of TS which is known as gravid proglottide. The ingested egg by the intermediate host (pork) is converted into larval stage in pork muscles. Human infection occurs via ingestion of the infected meat with TS larvae which eventually grow into adult TS within four months. Also, humans may be intermediate host for TS and develop cysticercosis via ingestion of TS eggs or through faeco-oral route of infected patients (Figure-1).³

Therefore, cysticercosis should be regarded as person-to-person infection. The larvae are transmitted into different parts of the human body, including eye, brain, lung, liver and other organs.

Neurocysticercosis (NCC) is a neurological infection caused by TS larva which may affect different parts of the human brain and the spinal cord, leading to focal neurological deficit with/without inflammatory reactions. NCC is one of the most common and frequent parasitic infections of the human nervous system and is one of the major causes of epilepsy in developing countries.⁴

In humans, brain parenchyma cysticercus cyst develops in four stages. Vesicular stage is viable stage which is associated with minimal inflammatory reactions. In the colloidal stage, the larva undergoes degeneration and the cysticercus cyst is filled with gelatinous fluid. This stage is associated with profound inflammatory reactions. In the granular nodular stage, the scolex is converted into mineralised granules, while cysticercus wall gets changed and replaced by necrosis and lymphoid nodules. In the nodular calcified stage, granulation tissue is replaced by calcified and collagenous tissues which are associated with astrocytic changes.⁵

.....
Department of Clinical Pharmacology, Medicine and Therapeutic, Al-Mustansiriya University, Baghdad, Iraq.
Correspondence: Hayder Mutter. Al-kuraishy. Email: hayderm36@yahoo.com

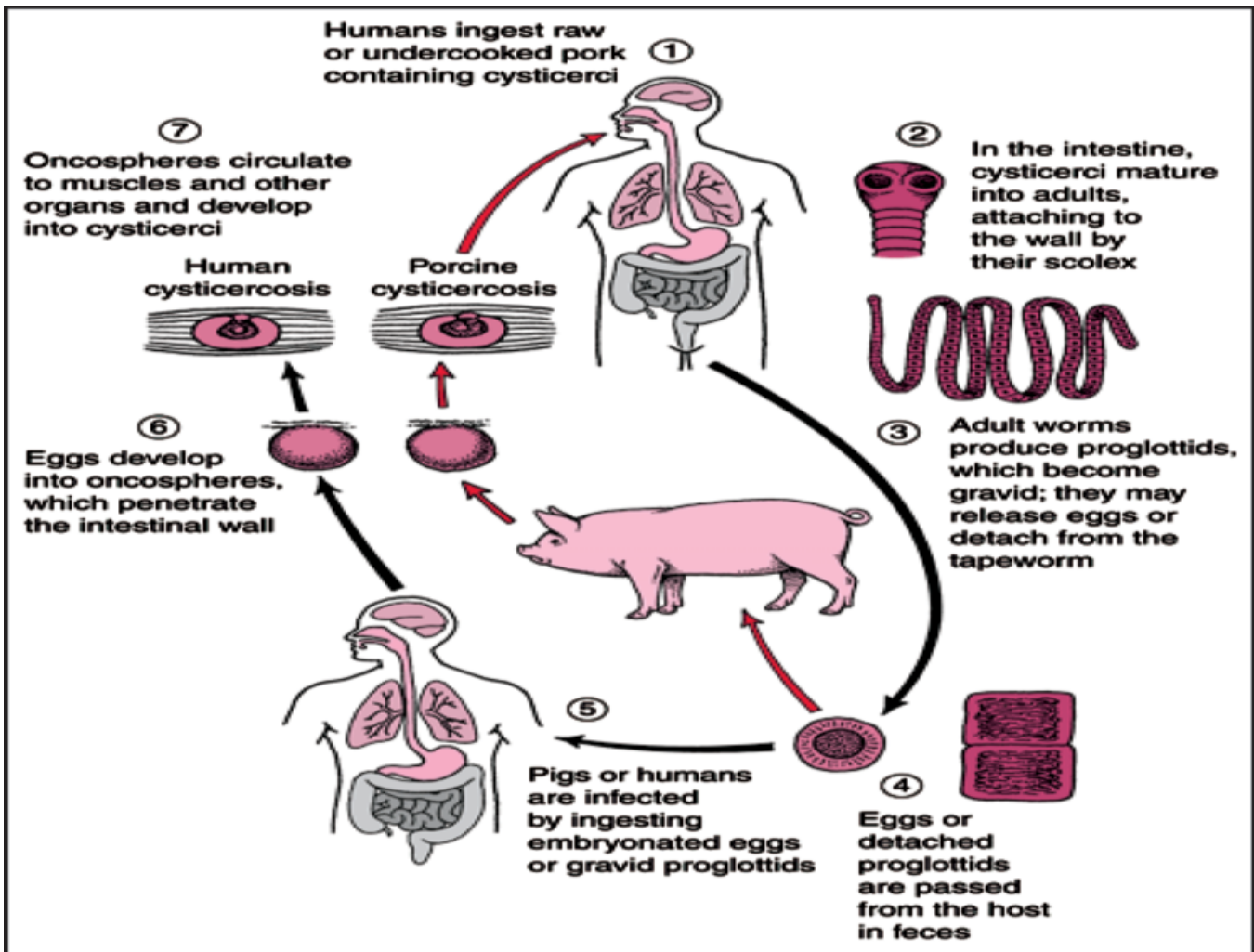


Figure-1: Lifecycle of Taenia Solium.

The cysticercuscyst consists of two different parts; vesicular wall and the scolex. When the cysticerci enter the brain, they are in the vesicular stage which may stay viable for several years. After the development of human immunological reactions, the cysticerci undergo degeneration and calcification and move on to the granular stage which ultimately appears as mineralised nodule which is called the calcified stage.⁶

Cerebral cysticerci are surrounded by mononuclear inflammatory reactions and collagen capsule due to human immunological response. The brain inflammatory reactions lead to astrocyte gliosis, oedema, neuronal degeneration, peri-vascular lymphocyte activations and microglial proliferations. These inflammatory reactions are more pronounced at active stage of cysticerci, but when cysticerci have developed into granular and/or calcified stage, the inflammatory changes and oedema

subsides and most of the epithelioid cells coalesce to form giant cells and brain cyst.⁷

Extra-parenchymal Neuro-cysticercosis (EP-NCC)

Subarachnoid space and ventricles tend to grow and enlarge erratically which provoke inflammatory reactions. Furthermore, enlarged cysticerci cyst obstructs cerebrospinal fluid (CSF) flow, causing obstructive hydrocephalus.

Meningeal Cysticercosis: The cysticerci, on reaching the meninges, provoke severe and acute inflammatory reactions with the formation of inflammatory exudates, causing thickening of meninges. These exudates may be disseminated, leading to compression of cranial vessels and nerves with subsequent obstruction of CSF flow,

causing hydrocephalus.

Ventricular Cysticercosis: When cysticerci are attached to the brain ventricle choroid plexus, it leads to the obstruction of CSF flow, causing hydrocephalus.⁸

Intra-parenchymal Neuro-cysticercosis (IP-NCC)

Cerebral cysticerci mainly lodge at the white-grey cortical junction initially due to parasitic tegument, and do not produce any irritating effect. During parasitic penetration of cerebral parenchyma, the tegument is misplaced and the developed cysticerci create a suitable environment via immune-regulation to prevent host immunological responses.⁹ Parasitic immune-regulation processes occurs through the release of a mediator called alternate activated macrophage (AAM) that causes human immune suppression. Death of the parasitic cyst exposes hidden parasitic antigens that provoke human immunological response which is Type 1 T helper (Th1)-dependent and causes neurological damage and granuloma formation. Toll-like receptors (TLRs), chiefly TLR4, is linked with NCC immunological response and reactions, leading to complex neuropathology. Besides, cysticercal antigens provoke the production of specific antibodies, whereas other antigens activate cell-mediated immunity. It has been reported that NCC is linked with suppression of cell-mediated immunity and impairment of B-lymphocyte proliferations. This finding might explain the occurrence and incidence of NCC in patients with immunodeficiency.¹⁰

Immunological Response to NCC

Once established, IP-NCC provokes T cell activations with increase in the levels of interleukin-13 (IL-13), IL-4, IL-15 and immunoglobulin E (IgE). Human NCC is associated with mixed Th1/Th2 activation response. Th2 cytokines are responsible for asymptomatic disease course as these cytokines reduce the inflammatory response next to the cysticercal cyst. Moreover, osteopontin and sex hormones are involved in down-regulation of the immune response during IP-NCC. Besides, T-regulatory cells (Tregs) within the central nervous system (CNS) is an important anti-inflammatory mediator and may participate in this immunological response.¹¹

During the initiation of cysticidal therapy, down-regulation of immunological response is lost due to exposure of the parasitic antigens which leads to switching of T cell response from Th2 to Th1. Th1 response activates the release of tumour necrosis factor (TNF) and IL-6 which cause relentless neurological inflammatory reactions. Moreover, neutrophil adhesion

and migrations are augmented in IP-NCC. Intercellular adhesion molecule (ICAM) is increased in patients with symptomatic IP-NCC.¹²

Also, matrix metalloproteinase-9 (MMP-9) is elevated when IP-NCC is complicated with blood-brain barrier (BBB) damage. Therefore, MMP-9 inhibitors, such as doxycycline, reduce leukocyte-dependent inflammation in the experimental model of NCC. As a result, doxycycline is an effective drug that lessens inflammatory tissue damage during cysticidal therapy of IP-NCC. In EP-NCC there is a strong inflammatory reaction mainly in ventricular NCC. On the other hand, in meningeal NCC there is little inflammatory reactions as the cystic fluid contains IL-10 like mediators which are responsible for down-regulation of the immune response. Once cysticidal therapy is initiated, this mediator is lost and profound immunological and inflammatory reactions commence.¹³

Clinical Presentation of EPNCC and IP-NCC

In EP-NCC, cysticerci cysts at subarachnoid space and ventricles lead to obstructive hydrocephalus and increase the intracranial pressure, causing hypertension and bradycardia.¹⁴

In IP-NCC, cysticerci cyst at the cerebral cortex may grow toward the subarachnoid space, causing obstructive hydrocephalus. But when it grows inside the brain parenchyma, it causes the feature of cerebral space-occupying lesion. The common presentation of IP-NCC is secondary epilepsy which is due to focal lesion and/or local inflammatory reactions.

Therefore, the clinical diversity of NCC is chiefly linked to individual variations, site and the severity of cysticerci cyst within CNS. Furthermore, 70% patients with NCC present with refractory seizure, which is more linked to IP-NCC than EP-NCC. Besides, NCC is regarded as the most common cause of acquired epilepsy in the developing countries.¹⁵

Hence, focal neurological deficit and signs are related to the size, site and number of parasites which is recorded in about 20% in NCC cases. The presentation of focal deficit resembles the course of brain tumour. Also, IP-NCC leads to more pyramidal than extra-pyramidal effects so patients with IP-NCC present with motor deficit, but sensory and extra-pyramidal manifestations are not uncommon. Thus, rigidity and secondary Parkinsonism might be the clinical manifestation of deep-seated IP-NCC. Cerebral stroke may be the presenting feature of IP-NCC in about 3% due to cerebral vasoconstriction or external vascular compression. Intracranial hypertension is more linked to EP-NCC which occurs due to CSF flow

obstruction or due to the inflammatory changes, including arachnoiditis, encephalitis and granular ependymitis.¹⁶

Psychiatric manifestations, low psychomotor performance and dementia may be the early features of NCC. Rarely, pituitary dysfunction and hyperprolactinaemia may be the main feature of NCC-affected a sell region.¹⁷

Regarding the differential diagnosis of NCC, the presence of headache, convulsion and focal neurological issues in endemic area with tuberculosis (TB) give a clue of tuberculoma, especially when scolex is not seen on magnetic resonance imaging (MRI) scan. When brain lesions are more than 20mm in size, are at the brain base with significant oedema and midline shifting, tuberculoma is more likely than NCC. Brain toxoplasmosis, brain metastasis, astrocytoma, chronic meningitis and brain abscess should be regarded in the differential diagnosis of NCC.¹⁸

Diagnostic Neuro-imaging of NCC

NCC is readily visualised in computed tomography (CT) and MRI scans. NCC lesions with viable parasite come into view as cystic lesions, and parasitic scolex can be visualised on MRI which becomes visible as contrast-enhancing lesions surrounded and bordered by oedema. An early sign of cystic death is hypo-intensity of the vesicular compared to CSF on two-weighted images. Calcified IP-NCC is evidence that the parasite is not viable. Therefore, MRI findings of NCC consist of multiple lesions in the thalamus, basal ganglia, cerebral white matter and at the grey-white cerebral junction. Besides, with contrast administration and direction, most NCC lesions enhance in a homogenous pattern or are ringed and nodular surrounded and boarded by oedema.¹⁹

Therefore, neuro-imaging, including CT and MRI scans, are effective for the detection of NCC. MRI is more effective than CT scan in the diagnosis and detection of posterior fossa NCC lesions also, and MRI is more proficient in the discovery and diagnosis of EP-NCC, but small calcified lesions are missed.

IP-NCC appears as small, single low-density lesion and ring. Eccentric high-density bright nodule represents the scolex, which is the pathognomic feature of NCC lesions. Starry-sky appearance is also a typical feature of small and multiple degenerative cysts of NCC on CT scans. Vesicular cyst is not surrounded by oedema, like degenerative cyst, and looks as isodense, rounded small lesion with CSF density.²⁰

Calcified cyst appears as hyper-dense without oedema; either single or multiple. Fluid attenuated inversion recovery (FLAIR) is required for the diagnosis of scolex by MRI to attenuate peri-lesional oedema that mask and obscure weighted images. Similarly, NCC cystic wall at first appear hypo-intense and finally develops into hyper-intense. Concerning EP-NCC, the cyst emerges as isointense lesions occupying CSF flow regions, including cerebellopontine angle, cisterns and Sylvian fissure. Besides, hydrocephalus and intra-ventricular cyst as well as arachnoiditis may be the presenting neuro-imaging of EP-NCC.²¹

Biochemical and Serological Investigations of NCC

Sero-diagnostic tests are used to detect antibodies against parasitic antigens, like enzyme-linked immunosorbent assay (ELISA) test which is highly sensitive and specific for multiple NCC, but less for solitary IP-NCC and calcified lesions. Enzyme-linked immunoelectrotransfer blot (EITB) assay, by using purified parasitic glycoprotein, is highly sensitive and specific for the diagnosis of active lesions. Patients' serum and CSF give the same results and, as such, CSF is not better than serum in the detection of antibodies against parasitic antigens. ELISA test is less sensitive and specific compared to EITB in the serological diagnosis of NCC. Moreover, antibody against parasitic excretory antigen is more effective in the diagnosis of active NCC which may be the base for the immune-diagnostic test. Certainly, negative serological test for NCC does not prohibit the diagnosis of NCC, while a positive test support a diagnosis without being a definite diagnosis of NCC as sero-positive individuals might not have NCC in the endemic area.

Complete blood picture illustrated eosinophilia in 30% infected patients. Also, TS in the stool does not confirm the presences of NCC.²²

CSF examination is normal in IP-NCC, but in case of EP-NCC, mainly with meningeal involvement, it shows high protein, elevated monocytes and granulocyte with significant pleocytosis.²³

The diagnosis of NCC is difficult in some patients since clinical manifestations and findings of neuroimaging are not absolutely specific. Therefore, diagnostic criteria should be involved in the diagnosis of NCC. The diagnostic criteria have four categories; absolute, major, minor, and epidemiological.²⁴

Pharmacotherapy of NCC

Symptomatic treatment should be started initially

involving analgesics, anti-inflammatory and anti-convulsant agents. Dexamethasone or prednisolone is given with anti-cysticidal therapy for the reduction of oedema. Anti-convulsant agents, like carbamazepine and valproate, should be stopped after cystic resolution, but long-term anti-convulsant drugs shall be used when seizures recur. The risk of seizure is high in NCC which is associated with viable or degenerative cyst, but continues to occur in chronic calcified cysts to a lesser extent. Host reaction and brain oedema are the main causes of seizure also, and BBB damage enhances the passages of cysticercal components into the brain. Cysticidal therapy increases the risk of seizure due to the induction of host inflammatory reactions. Therefore, co-administration of corticosteroids reduces the risk of seizure through attenuation of inflammatory reactions and brain oedema.²⁵

Increased intracranial pressure is treated by corticosteroids mainly by prednisolone, and if it does not respond or if there is an obstructive cause, ventriculo-peritoneal shunt should be employed. Indeed, calcified cyst does not need cysticidal therapy, but anti-convulsant agents should be started once recurrent seizure occurs. The recommendation for starting cysticidal therapy depends on the type of lesions. Cysticidal therapy is not urgent and is initiated after symptomatic treatment. In cystic parenchymal lesions with/without oedema with the involvement of the subarachnoid space, cysticidal therapy should be initiated which accelerates parasitic destruction.²⁶

About 85% of intra-parenchymal cysts are destroyed by albendazole 15mg/kg for eight days or praziquantel 50mg/kg for 15 days. Albendazole is the drug of choice due to availability, higher efficacy and bioavailability. Chaurasia et al. illustrated that three-day course of albendazole 15mg/kg was effective in resolution of solitary neurocysticercal cyst without significant effect on the rate of seizure recurrence compared to the controls.²⁷

Recently, Gonzalez et al. presented oxfendazole as an effective anthelmintic for NCC. This drug was safe in healthy human volunteers and has become an alternative agent for limited effect of standard anti-parasitic drugs.²⁸

Cysticidal therapy should be administered in hospital under close supervision as between days 2 and 5 of the initiation of cysticidal therapy, severe neurological complications may occur due to the development of severe brain oedema which is caused by local inflammatory reactions toward exposed parasitic genes following the degeneration of the neurocysticercal cyst. Therefore, intravenous (IV) corticosteroids should be

combined with cysticidal therapy. Dexamethasone administration decreases praziquantel serum levels but fortunately it happens only at high doses.²⁹

Cysticidal therapy is effective in killing 60-70% parasites, and, therefore, increased doses up to 30mg/kg might be more effective. However, this high dose may cause severe side effects, including elevated liver enzymes and pancytopenia. Furthermore, despite extensive research, an optimal regimen for NCC has not been established yet. Prospective, randomised placebo-controlled trial illustrated that combination therapy of praziquantel and albendazole does not differ from albendazole alone regarding lesion resolutions and seizure frequency.³⁰ The possible mechanisms in the cysticidal effects of tamoxifen are through induction of IL-2 expression, direct inhibiting effect on TS reproduction and induction of nitric oxide (NO) which has anti-helminth effect via induction of reactive free radicals.³⁰

Additionally, studies have tried hormonal therapy against NCC. Progesterone improves TS growth and scolex evagination in dose-independent manner due to the presence of progesterone receptors in TS. Therefore, progesterone antagonist mifepristone (RU486) has a potential role on scolex evagination and suppression of TS development. But cysticidal effect of RU486 is independent on progesterone levels since it produces cysticidal effect even when progesterone receptors are up-regulated.³¹

Furthermore, a study confirmed that dehydroepiandrosteron acetate (DHEA) or its analogue 16-bromoepiandrosterone (HE2000) has significant cysticidal effects on TS through suppression of their viability with host immuno-modulation effects.³²

Recently, Samannodi et al. reported that ivermectin is an effective cysticidal agent and should be recommended for NCC in addition to albendazole and praziquantel.³³

Palomares-Alonso et al. disclosed the potential cysticidal effect of *Prunus serotina* by its active constituent named naringenin at a dose of 300mg/kg which gave similar efficacy to that of albendazole.³⁴

An animal model study revealed that intra-nasal micro-emulsion of albendazole and curcumin combination was effective for NCC, and, thus, the intranasal route is regarded as a promising delivery system for the treatment of NCC.³⁵

Conclusion

Neurocysticercosis is a common cause of epilepsy in developing countries, mainly in rural areas. Standard

cysticidal therapy is effective in about 70% NCC patients. Therefore, search for novel and newer agents is recommended to overcome the partial failure of standard and basic cysticidal therapy.

Disclaimer: None.

Conflicts of Interest: None.

Source of Funding: None.

References

- Wadia NH, Singh G. *Taenia solium*: a historical note. In: Singh G, Prabhakar S, eds. *Taenia Solium Cysticercosis: From Basic to Clinical Science*. London, UK: CAB International, 2002; pp 157-168.
- Praet N, Kanobana K, Kabwe C, Maketa V, Lukanu P, Lutumba P, et al. *Taenia solium* cysticercosis in the Democratic Republic of Congo: how does pork trade affect the transmission of the parasite? *PLoS Negl Trop Dis* 2010;4:e817.
- Pawlowski ZS. *Taenia solium*: basic biology and transmission. In: Singh G, Prabhakar S, eds. *Taenia Solium Cysticercosis: From Basic to Clinical Science*. London, UK: CAB International, 2002; pp 1-14.
- Moazeni M, Khamesipour F, Anyona DN, Dida GO. Epidemiology of taeniosis, cysticercosis and trichinellosis in Iran: A systematic review. *Zoonoses Public Health* 2019;66:140-54.
- Duque KR, Escalaya AL, Zapata W, Burneo JG, Bustos JA, Gonzales I, et al. Clinical topography relationship in patients with parenchymal neurocysticercosis and seizures. *Epilepsy Res* 2018;145:145-52.
- Carpio A, Fleury A, Romo ML, Abraham R. Neurocysticercosis: the good, the bad, and the missing. *Expert Rev Neurother* 2018;18:289-301.
- Arora N, Tripathi S, Sao R, Mondal P, Mishra A, Prasad A. Molecular Neuro-Pathomechanism of Neurocysticercosis: How Host Genetic Factors Influence Disease Susceptibility. *Mol Neurobiol* 2018;55:1019-25.
- Mao DH, Gao S, Li YM. [Imaging characteristics of different types of cerebral cysticercosis]. *ZhongguoXue Xi Chong Bing Fang Zhi Za Zhi* 2015;27:513-6.
- Garcia HH, Del Brutto OH; Cysticercosis Working Group in Peru. Neurocysticercosis: updated concepts about an old disease. *Lancet Neurol* 2005;4:653-61.
- Chavarria A, Fleury A, Bobes RJ, Morales J, Fragoso G, Sciotto E. A depressed peripheral cellular immune response is related to symptomatic neurocysticercosis. *Microbes Infect* 2006;8:1082-9.
- Cárdenas G, Valdez R, Sáenz B, Bottasso O, Fragoso G, Sciotto E, et al. Impact of *Taenia solium* neurocysticercosis upon endocrine status and its relation with immuno-inflammatory parameters. *Int J Parasitol* 2012;42:171-6.
- Verma A, Prasad KN, Cheekatla SS, Nyati KK, Paliwal VK, Gupta RK. Immune response in symptomatic and asymptomatic neurocysticercosis. *Med Microbiol Immunol* 2011;200:255-61.
- Uddin J, Gonzalez AE, Gilman RH, Thomas LH, Rodriguez S, Evans CA, et al. Mechanisms regulating monocyte CXCL8 secretion in neurocysticercosis and the effect of antiparasitic therapy. *J Immunol* 2010;185:4478-84.
- Toledo A, Osorio R, Matus C, Martinez Lopez Y, Ramirez Cruz N, Sciotto E, et al. Human Extraparenchymal Neurocysticercosis: The Control of Inflammation Favors the Host...but Also the Parasite. *Front Immunol* 2018;9:e2652.
- Rapoport BI, Baird LC, Cohen AR. Third-ventricular neurocysticercosis: hydraulic maneuvers facilitating endoscopic resection. *Childs Nerv Syst* 2014;30:541-6.
- Srivastava S, Chadda RK, Bala K, Majumdar P. A study of neuropsychiatric manifestations in patients of neurocysticercosis. *Indian J Psychiatry* 2013;55:264-7.
- Gasparetto EL, Alves-Leon S, Domingues FS, Frossard JT, Lopes SP, Souza JM. Neurocysticercosis, familial cerebral cavernomas and intracranial calcifications: differential diagnosis for adequate management. *ArqNeuropsiquiatr* 2016;74:495-500.
- Rudie JD, Rauschecker AM, Nabavizadeh SA, Mohan S. Neuroimaging of Dilated Perivascular Spaces: From Benign and Pathologic Causes to Mimics. *J Neuroimaging* 2018;28:139-49.
- Zapata CH, Vargas SA, Uribe CS. [Racemose neurocysticercosis: Neuroimaging guides the diagnosis]. *Biomedica* 2017;37:26-32.
- Chawla S, Husain N, Kumar S, Pal L, Tripathi M, Gupta RK. Correlative MR imaging and histopathology in porcine neurocysticercosis. *J MagnReson Imaging* 2004;20:208-15.
- Gabriël S, Blocher J, Dorny P, Abatih EN, Schmutzhard E, Ombay M, et al. Added value of antigen ELISA in the diagnosis of neurocysticercosis in resource poor settings. *PLoS Negl Trop Dis* 2012;6:e1851.
- Abraham R, Livramento JA, LeiteCda C, Pardini AX, Vaz AJ, Machado Ldos R. Neurocysticercosis: relationship between *Taenia* antigen levels in CSF and MRI. *ArqNeuropsiquiatr* 2010;68:7-11.
- Del Brutto OH, Nash TE, White AC Jr, Rajshekhar V, Wilkins PP, Singh G, et al. Revised diagnostic criteria for neurocysticercosis. *J Neurol Sci* 2017;372:202-10.
- White AC Jr, Garcia HH. Updates on the management of neurocysticercosis. *Curr Opin Infect Dis* 2018;31:377-82.
- Garcia HH, Del Brutto OH; Cysticercosis Working Group in Peru. Antiparasitic treatment of neurocysticercosis - The effect of cyst destruction in seizure evolution. *Epilepsy Behav* 2017;76:158-62.
- Kumar A, Mandal A, Sinha S, Singh A, Das RR. Prevalence, response to cysticidal therapy, and risk factors for persistent seizure in Indian children with neurocysticercosis. *Int J Pediatr* 2017;2017:e8983958.
- Chaurasia RN, Garg RK, Agarwall A, Kohli N, Verma R, Singh MK, et al. Three day albendazole therapy in patients with a solitary cysticercus granuloma: a randomized double blind placebo controlled study. *Southeast Asian J Trop Med Public Health* 2010;41:517-25.
- Gonzalez AE, Codd EE, Horton J, Garcia HH, Gilman RH. Oxfendazole: a promising agent for the treatment and control of helminth infections in humans. *Expert Rev Anti Infect Ther* 2019;17:51-6.
- Rajshekhar V. Neurocysticercosis: Diagnostic problems & current therapeutic strategies. *Indian J Med Res* 2016;144:319-26.
- Escobedo G, Palacios-Arreola MI, Olivos A, López-Griego L, Morales-Montor J. Tamoxifen treatment in hamsters induces protection during taeniosis by *Taenia solium*. *Biomed Res Int* 2013;2013:e280496.
- Escobedo G, Camacho-Arroyo I, Hernández-Hernández OT, Ostoa-Saloma P, García-Varela M, Morales-Montor J. Progesterone induces scolex evagination of the human parasite *Taenia solium*: evolutionary implications to the host-parasite relationship. *J Biomed Biotechnol* 2010;2010:e591079.
- Hernández-Bello R, Escobedo G, Carrero JC, Cervantes-Rebolledo C, Dowding C, Frincke J, et al. A new parasiticidal compound in *T. solium* cysticercosis. *Biomed Res Int* 2013;2013:e505240.
- Samannodi MS, Zhao A, Hasbun R. Use of Ivermectin in Neurocysticercosis: A Case Report. *Am J Case Rep* 2018; 19:1378-81.
- Palomares-Alonso F, Rojas-Tomé IS, Palencia Hernández G, Jiménez-Arellanes MA, Macías-Rubalcava ML, González-Maciel A, et al. In vitro and in vivo cysticidal activity of extracts and isolated flavanone from the bark of *Prunus serotina*: A bio-guided study. *Acta Trop* 2017;170:1-7.
- Shinde RL, Bharkad GP, Devarajan PV. Intranasal microemulsion for targeted nose to brain delivery in neurocysticercosis: Role of docosahexaenoic acid. *Eur J Pharm Biopharm* 2015;96:363-79.