Infectious Diseases of the Brain and Spine

Parasitic and Other Atypical Transmissible Diseases

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KEYWORDS

• Atypical CNS infections • Parasitic CNS infections • Atypical transmissible CNS infections
• Prion diseases • Creutzfeldt-Jakob disease

KEY POINTS

- Neurocysticercosis progresses through multiple stages, starting from a cyst containing a scolex, development of surrounding inflammatory reaction, and termination as a calcified nodule.
- Neurotoxoplasmosis results in mass-like lesions with targetoid or ring enhancement that mimic lymphoma in immunocompromised patients, for whom empiric treatment may prove diagnostic and therapeutic.
- Cerebral echinococcosis (neurohydatidosis) mostly appears as a solitary cyst in the brain parenchyma without enhancement or edema, but the associated mass effect can cause elevated intracranial pressure.
- Neuroschistosomiasis incites granulomatous inflammation in the brain or spinal cord, with the latter having a predilection for the conus medullaris.
- Creutzfeldt-Jakob disease typically manifests as nonenhancing DWI hyperintensity in the cerebral cortex and deep gray nuclei.

INTRODUCTION

Parasitic infections of the central nervous system (CNS) are broadly classified into two categories: unicellular protozoa and multicellular helminths (metazoan). Protozoal infections encompass toxoplasmosis, malaria, and amebiasis, whereas helminths consist of six parasitic taxa: flatworms (Platyhelminthes), tapeworms (cestodes), trematodes (flukes), roundworms (nematodes), acanthocephalans, and crustaceans. Cysticercosis and echinococcosis belong to the cestodes taxon, whereas schistosomiasis falls under Platyhelminth.[1,2] In the United States, the most common parasitic infections that lead to CNS manifestations are cysticercosis, echinococcosis, and toxoplasmosis. Less common parasitic infections include amebiasis, malaria, and schistosomiasis.[3]

Prion diseases are rare transmissible diseases that cause rapidly progressive spongiform encephalopathies, and are classified as acquired, hereditary, or sporadic types. Sporadic type is most common, whereas acquired type is extremely rare.

In this article, we provide an in-depth review of atypical infections in the brain and spine caused by parasitic and prion diseases using case examples.

PROTOZOAL INFECTIONS

Toxoplasmosis

Toxoplasmosis is caused by *Toxoplasma gondii*, an intracellular protozoan that is found worldwide.

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It is the most common opportunistic infection affecting the CNS in patients with AIDS and a CD4 count of less than 100 cells/μL.[4]

Cat is the definitive host, where the protozoa multiply in the intestinal mucosa and release oocysts in feces. Oocysts can survive for up to a year in moist soil.[4] Intermediate hosts, including humans and poultry animals, get infected by the consumption of oocysts through contaminated vegetables or direct contact with cat feces. In the intermediate hosts, parasites transform into rapidly multiplying tachyzoites in the intestine and hematogenously disseminate. In the end organ, the parasites transform into the final stage of tissue cyst containing bradyzoites. *Toxoplasma* cysts can occur in any tissue but are most common in the brain, retina, skeletal muscle, and cardiac muscle, ultimately reaching the brain and muscles transforming into the final stage of tissue cyst/bradyzoites.[4] Human hosts can also be infected by ingesting undercooked meat contaminated with this tissue cyst.

Multifocal abscesses (**Fig. 1**) with a predilection for the basal ganglia are the most common manifestation of CNS toxoplasmosis (**Table 1**). Solitary lesions are reported in about one-third of the cases. Most lesions show ring-like enhancement patterns. Although only present in 30% of the cases, the "eccentric target sign," defined as an eccentric enhancing nodule along the lesion margin,[4] is pathognomonic for toxoplasmosis. The concentric target sign is also reported in cases of cerebral toxoplasmosis, in which there are a series of concentric rings of alternating T2 hyperintense and hypointense/isointense signal characteristics.[5]

As opposed to a well-defined enhancing wall in bacterial abscess with homogenous diffusion restriction, *Toxoplasma* abscesses have poorly defined peripheral enhancement and faint peripheral diffusion restriction, believed to reflect a poor host response to the infection.[4]

In patients with HIV presenting with a brain mass lesion, a common clinical challenge is distinguishing CNS lymphoma from toxoplasma abscess (**Fig. 2**). Both have peripheral enhancement and peripheral restricted diffusion. On dynamic susceptibility contrast perfusion imaging, lymphoma has higher relative cerebral blood volume than toxoplasmosis. On MR spectroscopy, toxoplasmosis lesions typically have decreased levels of choline, whereas lymphoma generally has elevated choline levels.[6] On fluorodeoxyglucose PET, lymphoma has higher uptake, whereas toxoplasmosis has decreased activity compared with contralateral normal brain.[7] When toxoplasmosis is suspected, an empirical trial of antitoxoplasma therapy for 2 to 3 weeks may prove to be definitive. The decreased size of the lesion is considered to be sufficiently confirmatory to continue therapy and imaging surveillance until resolution. Stable or increasing size of the lesion may be indicative of an alternate diagnosis, especially CNS lymphoma, and a brain biopsy may be necessary.[4,8]

It is important to note that calcification in acquired toxoplasmosis is uncommon, although it may be seen after therapy. However, calcification

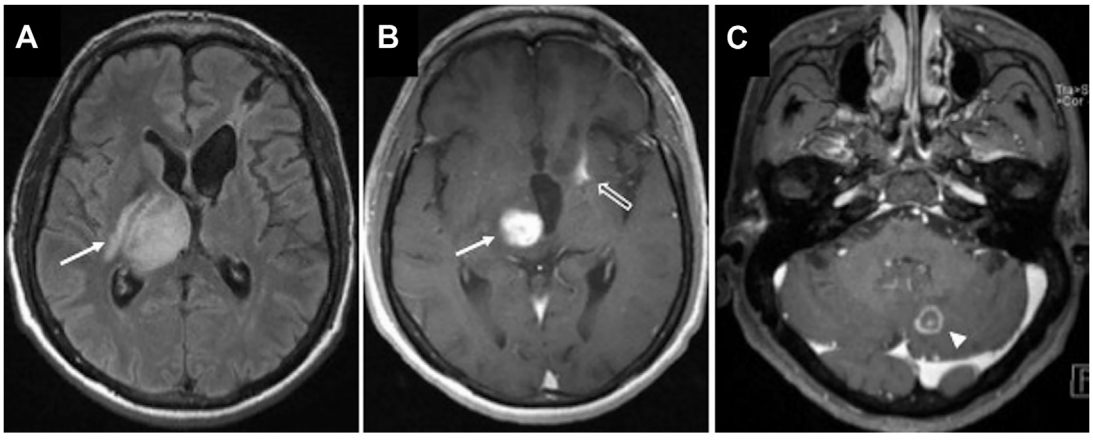

Fig. 1. CNS toxoplasmosis. Axial FLAIR (*A*) and axial T1 postcontrast (*B*, *C*) in a 45-year-old man with HIV/AIDS (noncompliant with highly active antiretroviral therapy) and previous toxoplasmosis encephalopathy who presented with altered mental status. Multifocal lesions: solidly enhancing in right thalamus with associated mass-effect and surrounding edema (*arrow*), targetoid in the left cerebellum (*arrowhead*), and flame-shaped enhancement (*block arrow*) around the left frontal encephalomalacia at prior biopsy site. There was improvement on imaging following 3 weeks of empiric toxoplasmosis therapy, confirming the diagnosis.

Table 1
Imaging features characteristic of certain infectious etiologies

	Finding	MR Imaging Appearance
Parasitic infections		
Toxoplasmosis	Multifocal abscesses with a predilection for the deep gray nuclei.	Ring-like enhancement, no central restricted diffusion (unlike pyogenic abscess) but may show peripheral or mixed diffusion restriction. "Eccentric target sign" is pathognomonic.
Neurocysticercosis	Variable depending on stages (see Table 2) and location. Vesicular stage has a simple cyst containing a live larvum.	Simple cyst with scolex, giving the appearance of a "target" or "dot in a hole," counts as an absolute criterion needed for diagnosis of neurocysticercosis.
Echinococcosis	Three-layered hydatid cysts; the outer pericyst formed by host immune cells. Cyst fluid contents: proteins, glucose, ions, lipids, and polysaccharides. Multiple daughter vesicles contain scolices and grow into daughter cysts.	Solitary (most common), or multiple clustered daughter cysts. Intraparenchymal, well-defined oval or round cystic mass following CSF signal, without enhancement, edema, or calcification. The outer pericyst may show a characteristic faint T2-hypointense rim because of fibrotic change.
Prion disease		
Creutzfeldt-Jakob disease	Spongiform encephalitis, rapidly progressive and fatal. Alteration of prion protein (PrP^{C}) to abnormal folded protein (PrP^{Sc}), which self-propagates by autocatalyzing the reconfiguration of normal PrP^{C}.	DWI and T2/FLAIR hyperintensity in the cortex ("cortical ribbon sign") and basal ganglia, diffuse or focal, symmetric or asymmetric. T2/FLAIR and DWI hyperintensity in the dorsomedial thalami (double hockey stick sign) and posterior thalami (pulvinar sign) most sensitive in the variant CJD.

is common in congenital toxoplasmosis.[9] Moreover, the disease may be transmitted transplacentally, which can have devastating effects on the fetal brain because maternal antibodies passed to the child are limited by the blood-brain barrier. Seizures, microcephaly, and chorioretinitis are noted in most cases.[4]

Malaria

Malaria is the most common parasitic disease worldwide, although fatal cases are mostly restricted to sub-Saharan Africa.[10] In the United States, from 2000 to 2014, there were 22,029 malaria-related hospitalizations (4.88 per 1 million population) and 4823 severe malaria cases.[11] Cerebral malaria is almost exclusively caused by protozoan parasite *Plasmodium falciparum*, transmitted by female *Anopheles* mosquitos, which flourish in stagnant water. During a blood meal, a *Plasmodium*-infected mosquito inoculates sporozoites into the human host. Sporozoites infect liver cells, mature, and release merozoites that multiply in erythrocytes. Blood-stage parasites are responsible for the clinical manifestations of malaria, such as fever. Cerebral malaria is thought to be caused by the sequestration of infected erythrocytes in the microcirculation. Cerebral malaria is associated with a mortality rate of 15% to 25% even when appropriate treatment is given.[10]

Cerebral malaria can present with a wide range of MR imaging findings, that includes T2/FLAIR hyperintensities in the white matter, deep gray nuclei, and corpus callosum[12–14]; hemorrhagic and nonhemorrhagic infarctions[13,15]; and petechial microhemorrhages at the gray matter–white matter junctions and deep white matter (Fig. 3).[13] In serious cases of cerebral malaria, MR imaging would show diffuse cerebral edema, vasogenic and cytotoxic in origin. It is caused by an increase in cerebral blood volume because of the sequestration of parasitized erythrocytes and compensatory

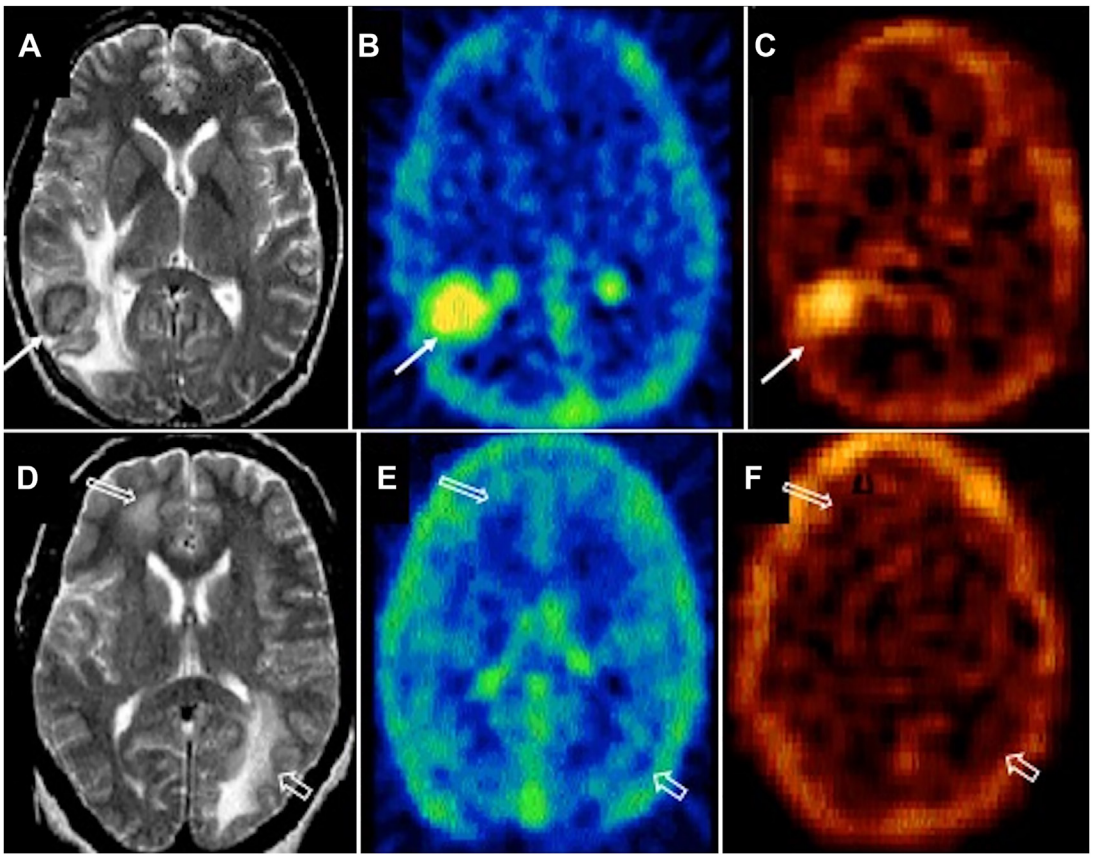

Fig. 2. Distinguishing toxoplasmosis from lymphoma in two different patients with HIV/AIDS. Axial T2 (*A*) shows a hyperintense mass with peripheral hypointensity in the right parietal lobe, corresponding to increased radiotracer uptake on ^{11}C-Thymidine (*B*) and ^{201}Thallium single-photon emission computed tomography (*C*) scans, consistent with a CNS lymphoma with increased metabolism (*arrows*). Axial T2 (*D*) shows right frontal and left parieto-occipital hyperintensity with underlying masses, corresponding to no abnormal increased radiotracer uptake on either ^{11}C-Thymidine (*E*) or ^{201}Thallium single-photon emission computed tomography (*F*), indicating an infectious/inflammatory cause (*block arrows*).

vasodilation, damage to cerebral capillary endothelium, and cerebral microvascular occlusion.[10]

Amebic Infections

Amebae are free-living protozoa that are widespread in water and soil worldwide.[16] Humans are frequently exposed to amebae, but the occurrence of the disease is rare. Although rare, amebic infections are virulent and have high mortality rates.[17] Neurologic manifestations of amebic infection come in two flavors: primary amebic meningoencephalitis (caused by *Naegleria fowleri*) and granulomatous amebic encephalitis (caused by *Acanthamoeba* spp; *Balamuthia mandrillaris*; and, in only one case to date, *Sappinia pedata*).[18] Primary amebic meningoencephalitis has no predilection for immunocompromised patients, whereas granulomatous amebic encephalitis usually affects immunocompromised patients, but rare cases in immunocompetent hosts have been reported.[17,19–22]

N fowleri, often called the "brain-eating ameba," is transmitted through the olfactory mucosa of the nasal cavity; most cases reported recent swimming or diving activities in freshwater. The other amebae can also be transmitted via the nasal route, in addition to via cutaneous lesions or inhalation of airborne cysts into the lower respiratory tract with subsequent hematogenous spread to the brain and other organs.

Primary amebic meningoencephalitis is clinically indistinguishable from acute bacterial meningitis, presenting with headache, fever, nausea, and vomiting. Incubation periods average 5 days from exposure to clinical presentation. Two-thirds of the cases would have rapid decline and death within 1 week of symptom onset, so fewer than one-third of patients in the United States have been diagnosed with primary amebic

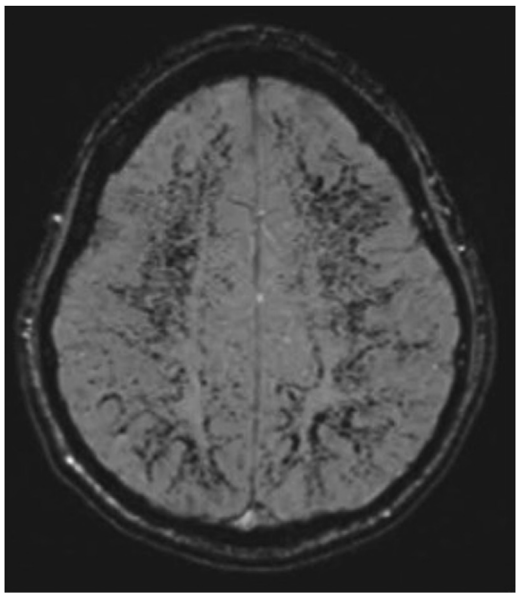

Fig. 3. Cerebral malaria. Axial susceptibility-weighted imaging demonstrates innumerable microhemorrhages at the corticomedullary junction and deep white matter of the bilateral cerebral hemispheres. (Image courtesy of Surjith Vattoth, MD.)

meningoencephalitis before death.[18] In extremely rare occasions, spinal cord involvement has been reported.[23]

Imaging findings of primary amebic meningoencephalitis are nonspecific. Early in the disease course, computed tomography and MR imaging may be normal, with the subsequent appearance of brain edema and basilar meningeal enhancement.[24] Hydrocephalus and basal ganglia infarcts have also been reported.[18] The nonspecific imaging features necessitate a high index of clinical suspicion to suggest the diagnosis before death.[24]

Granulomatous amebic encephalitis is a subacute or chronic CNS infection that presents with weeks to months of worsening headaches, fever, personality or cognitive changes, and/or focal neurologic deficits, progressing to seizures or depressed level of consciousness.[17,19–22] Despite aggressive therapy, death is common within 7 to 10 days after onset of illness.[25,26]

Granulomatous amebic encephalitis often manifests as multifocal parenchymal mass-like lesions (**Fig. 4**). These lesions represent focal edema, trophozoites, cysts, along with chronic granulomatous inflammatory cells. Leptomeningitis may accompany the parenchymal lesions.[27]

On MR imaging, these parenchymal lesions demonstrate T2 hyperintense signal and linear or superficial gyriform enhancement, which possibly represents a combination of enhancement in the overlying inflamed meninges covered with exudates and the actual enhancement of the underlying cortex. In rare occasions, granulomatous amebic encephalitis may present as multiple punctate foci of enhancement throughout the cerebral and cerebellar hemispheres. A few cases have shown evidence of intralesional hemorrhage and necrosis, which may relate to necrotizing angiitis that has been histopathologically described in severe granulomatous amebic encephalitis cases. The overall appearance is similar to that seen in other encephalitides and acute disseminated encephalomyelitis.[28] Case reports of granulomatous amebic encephalitis manifesting as a solitary mass-like lesion, hemorrhagic infarction, ring-enhancing lesions, and interhemispheric cyst have also been described.[19,24,29,30]

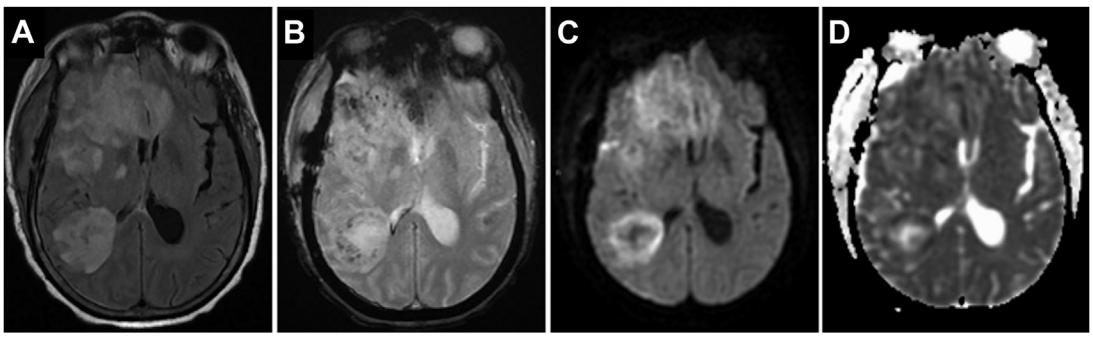

Fig. 4. Cerebral amebiasis. Axial FLAIR (*A*), axial T2*GRE (*B*), axial DWI trace (*C*), and axial ADC map (*D*) in a 59-year-old woman originally from Nigeria presenting with 2 weeks of headaches and found to have parenchymal enhancing masses thought to be glioblastoma. Resected mass was found to be amebic infection (concerning for *Naegleria fowleri* or *Entamoeba histolytica*) with pathology showing diffuse acute and chronic inflammation with a perivascular and leptomeningeal predominance. She was also found to be HIV positive. Images show multifocal FLAIR hyperintense masses, largest in the right frontal lobe with extension to the left frontal lobe. The masses have punctuate susceptibility suggesting microhemorrhages, and demonstrate peripheral restricted diffusion with centrally facilitated diffusion. Note right frontal craniotomy changes with scalp swelling.

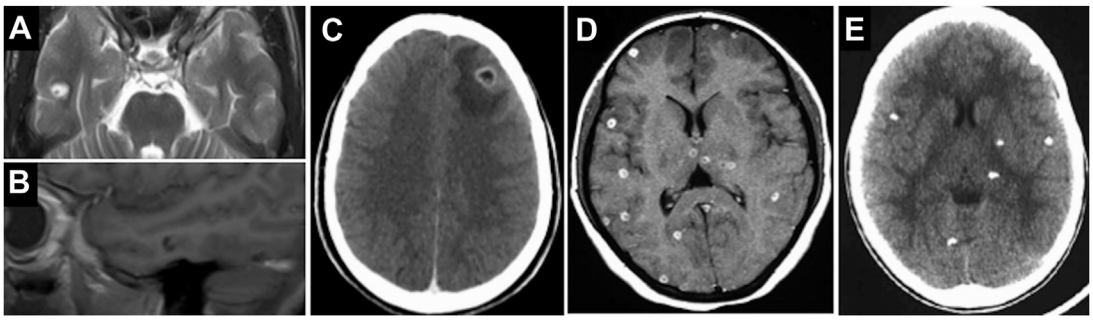

Fig. 5. Four stages of neurocysticercosis. Vesicular stage: Axial T2 (*A*) and sagittal T1 postcontrast (*B*) show a thin-walled circumscribed cyst with a mural nodule (scolex) in the right temporal lobe, without edema or cyst wall enhancement. Colloidal stage: Axial CT with contrast (*C*) shows thickened cyst wall with enhancement and prominent surrounding vasogenic edema caused by inflammatory response. Granular nodular: Axial T1 postcontrast (*D*) shows small, retracted cysts with thickened capsules and persistent edema and enhancement in a targetoid appearance. Nodular calcified: Axial unenhanced head CT (*E*) shows multiple calcified nodules. There is no contrast enhancement or edema at this stage. Note that only the vesicular stage, with evidence of cystic lesions containing scolex on CT or MR imaging, fulfills the absolute criteria for diagnosis of neurocysticercosis.

METAZOAL INFECTIONS

Cestodes

Neurocysticercosis

Neurocysticercosis is caused by encysted larvae of the tapeworm *Taenia solium*. Fecal-oral transmission of eggs is followed by the hatching of embryos that migrate through the intestinal mucosa into the circulation and lodge in the capillaries of the brain, where they develop into larvae called cysticerci. The cysts are protected from the host's immune system by the blood-brain barrier, and hence no inflammatory response is present as long as the cyst wall remains intact. However, when the parasite dies because of therapy or by a natural process, an inflammatory response with perilesional edema ensues, followed by calcification.[31]

Table 2
Stages of neurocysticercosis and their MR imaging characteristics

	Pathogenesis	MR Imaging Findings
Vesicular stage	Live larvum with thin glycoprotein-rich capsule, no inflammation.	Cyst with mural nodular enhancement (scolex), giving the appearance of a "target" or "dot in a hole." 5- to 20-mm cyst, following CSF signal with a thin imperceptible wall. Scolex isointense or hypointense relative to white matter on T1, and isointense to hyperintense on T2. No surrounding edema.
Colloidal stage	Larvum dies, capsule thickens, and larvum releases metabolites. Cyst wall disruption results in an intense inflammatory reaction to the unprotected parasite.	Cyst contents may be T1 and T2 hyperintense, reflecting proteinaceous contents. Cyst wall is thick, irregular, and enhances, with marked pericystic edema.
Granular nodular stage	The cyst retracts, capsule thickens, scolex calcifies. Granulomatous nodule formation.	Resembling a granuloma with decreased fluid content. Similar imaging appearance to the colloidal phase with persistent edema and thick enhancement.
Calcified nodular	Inactive stage. No live cysticerci, but parasite antigen may still be present. Nodule calcifies. Any residual edema or enhancement resolves during this stage.	Calcified nodules are hypointense on T1 and T2, and best depicted on susceptibility-weighted imaging. 2–10 mm in diameter. No edema or enhancement.

Neurocysticercosis is the most common parasitic disease of the CNS and the most common cause of acquired epilepsy.[32] Cysticercosis is endemic in most developing countries and closely associated with domestic pig raising. Immigration and travel have resulted in an increasing number of cases in developed countries. Incidental calcified granulomas are found in 10% to 20% of the general population in endemic settings.[33]

Neurocysticercosis is classified by location into intraparenchymal and extraparenchymal forms. In addition to the brain and spinal cord, cysticerci commonly develop in the subcutaneous tissues, muscles, and eyes.

Intraparenchymal neurocysticercosis stages of larvae development (**Fig. 5**) are well established (**Table 2**).[34] The vesicular stage is characterized by a 5- to 20-mm thin-walled cyst with no enhancement and no surrounding edema. On imaging, the presence of the scolex in the cyst appears as a "target" or "dot in a hole."[31] The vesicular colloidal or colloidal stage is characterized by the death of the scolex from either the natural processes or from therapy. Cyst wall disruption in this stage results in an intense inflammatory reaction to the unprotected parasite and clinical manifestation of diffuse encephalitis.[31] Cysts may be hyperintense on T1- and T2-weighted images, reflecting proteinaceous contents. The cyst wall is thicker than in the vesicular stage, and there is marked pericystic edema (**Fig. 6**) as reflected by surrounding enhancement and T2 signal changes.[31,35] The appearance is not specific to neurocysticercosis and may be mimicked by a neoplasm (**Fig. 7**). The granular nodular stage is characterized by cyst retraction and granulomatous nodule formation with surrounding gliosis. This phase has a similar imaging appearance of the cyst to the vesicular colloidal phase but has less edema and thicker enhancement.[31,34] The last phase is called calcified nodular, which is characterized by the calcification of this nodule. This is the nonactive stage of neurocysticercosis and any residual edema or enhancement resolves during this stage. The nodule is hypointense on T1 and T2,[31] and best depicted on susceptibility-weighted imaging. It is common to have multiple lesions at different stages.

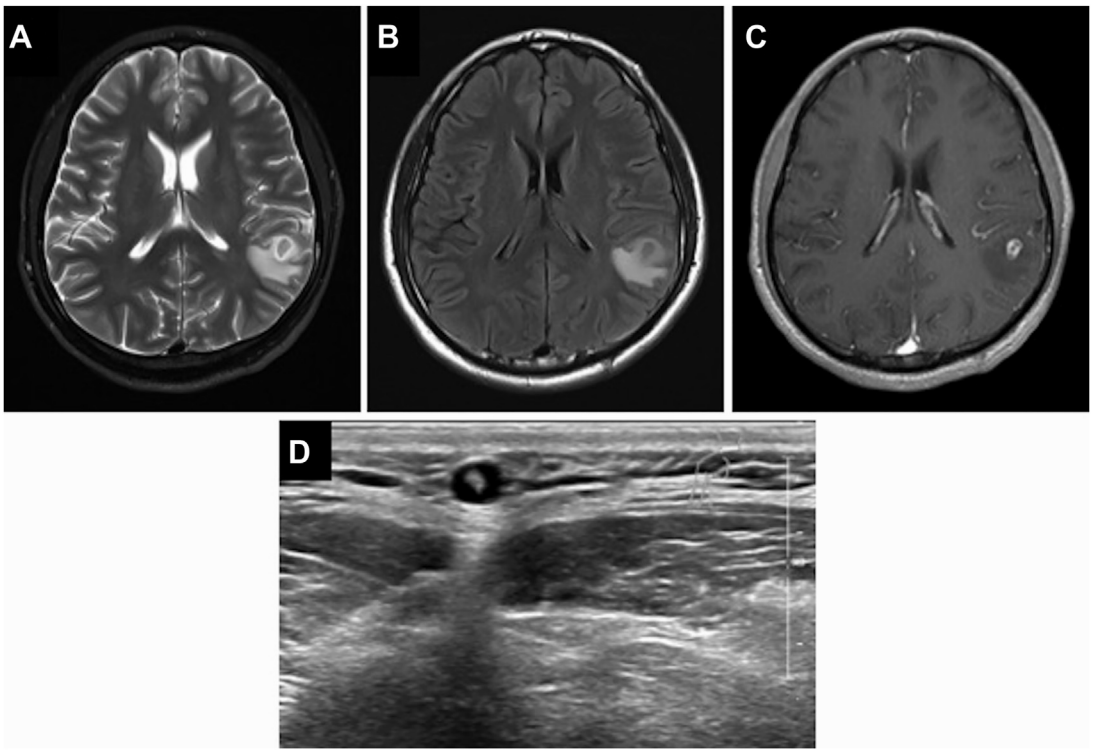

Fig. 6. A 23-year-old man presenting with first-time seizure. Axial T2 (*A*), axial FLAIR (*B*), axial T1 postcontrast (*C*) images show a left parietal subcentimeter intermediate signal lesion with peripheral enhancement and surrounding vasogenic edema. Similar lesion in the cerebellar vermis (not shown). These findings are nonspecific and could represent an infectious or neoplastic cause. Ultrasound of the nape of neck (*D*) corresponding to a palpable abnormality shows a well circumscribed, thin-walled cyst containing a nodule in the subcutaneous tissue, allowing a final diagnosis of cysticercosis in the brain (colloidal stage).

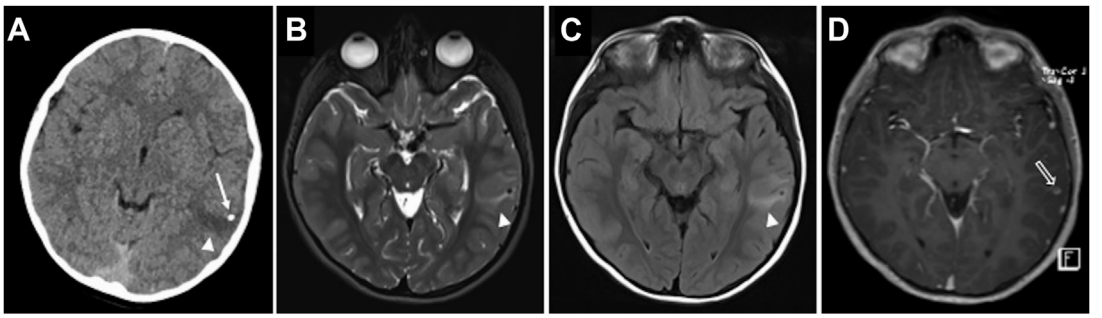

Fig. 7. Low grade glioneuronal tumor mimicking neurocysticercosis. Axial unenhanced head CT (*A*), axial T2 (*B*), axial FLAIR (*C*), axial T1 postcontrast (*D*) images in a 10-year-old girl presenting with first-time seizure. CT shows a punctate calcification (*arrow*) in the left temporal cortical region, with surrounding edema (*arrowheads*). MR imaging demonstrates peripheral enhancement (*block arrow*). Resected tissue reveals low-grade glioneuronal proliferation.

Extraparenchymal neurocysticercosis includes subarachnoid-cisternal and intraventricular locations, and can be large and multicystic clustered (so called "racemose"). Space-occupying lesions in subarachnoid space can result in hydrocephalus.[31] Intraventricular neurocysticercosis (**Figs. 8** and **9**) most commonly affects the fourth ventricle, followed by lateral ventricles, third ventricle, and aqueduct. Isolated ventricular neurocysticercosis has been reported in one-third of cases. It often presents with hydrocephalus and ventriculitis caused by ependymal inflammatory response or adhesions caused by prior ventricular infestation.[31]

Spinal neurocysticercosis (**Fig. 10**) is a result of cerebrospinal fluid (CSF) dissemination of the larvae throughout the craniospinal subarachnoid space. Spine involvement is almost always associated with concomitant intracranial involvement. Spinal neurocysticercosis is extremely rare, which might be explained by the relatively larger size of the cyst compared with the cervical CSF space.[31]

Echinococcosis

CNS cystic echinococcosis is caused by *Echinococcus granulosus* infestation. It is also known as hydatid disease or neurohydatidosis. Cystic echinococcosis is endemic in many sheep- and cattle-raising countries.[36] Dogs and other carnivores are the definitive hosts, whereas sheep, goats, and swine are the intermediate hosts. The adult worm attaches to the small intestine mucosa of the definitive host by hooklets and releases eggs in the feces. The intermediate host (mostly poultry animals) ingests these eggs. Once ingested in the duodenum of the host, the eggs lose their protective chitinous layer, and the embryo (also referred to as oncosphere) is released. The oncosphere passes through the intestinal wall into the portal and systemic circulation, developing into mature cysts within the end-organ. The lifecycle is complete when the definitive host eats the viscera of the infected intermediate host. Humans get infected by eating undercooked meat from intermediate hosts or egg-contaminated water or

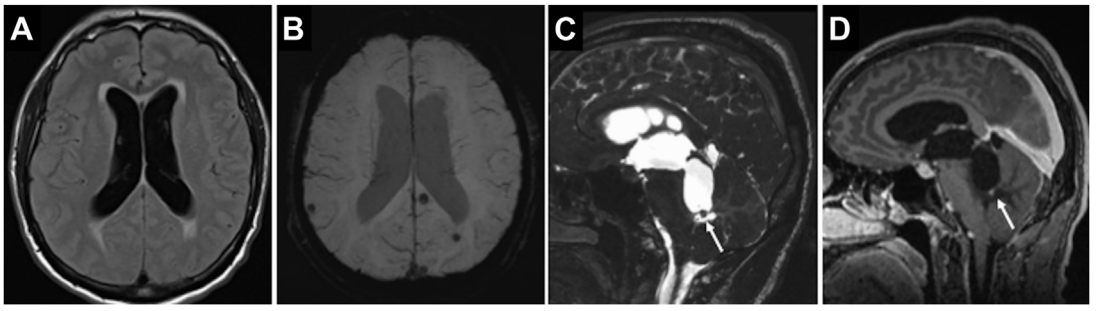

Fig. 8. A 38-year-old Spanish-speaking man presenting with 2 months of headaches followed by nausea and vomiting. (*A*) Axial FLAIR image shows moderate obstructive hydrocephalus with interstitial edema. (*B*) Susceptibility-weighted imaging shows multifocal calcifications also demonstrated on initial head CT. (*C*) Sagittal CISS shows a cystic lesion expanding the fourth ventricle with a small nodule (*arrows*) in its caudal aspect, which shows contrast enhancement in *D*. The combination of multifocal nonspecific calcified granulomas and more specific intraventricular cyst with a mural nodule allowed a clinical diagnosis of neurocysticercosis.

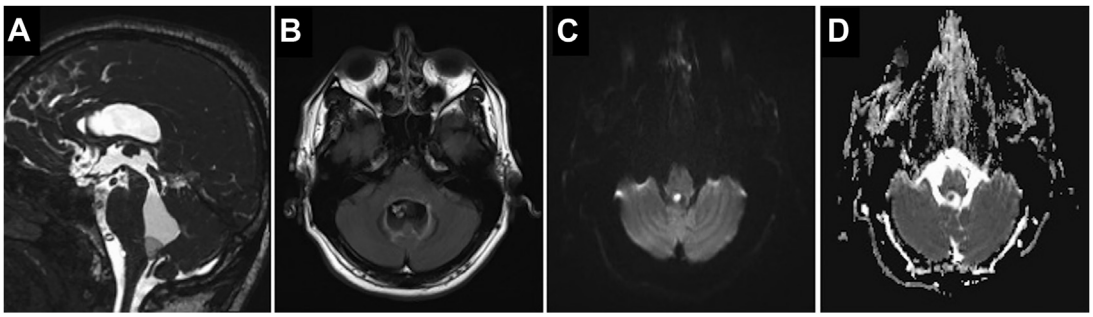

Fig. 9. Intraventricular neurocysticercosis in a 44-year-old man from Mexico with waxing waning headaches and dizziness for 2 months. (*A*) Sagittal CISS shows a cystic lesion expanding the fourth ventricle, containing an intermediate signal nodule in the caudal aspect. Note that the cyst has a T2 hyperintense signal slightly different from the ventricular and cisternal CSF. (*B*) Axial FLAIR shows expanded fourth ventricle with adjacent interstitial edema, and a nodule within the cyst. DWI trace (*C*) and ADC map (*D*) show a small area of restricted diffusion within the nodule, a feature often seen in scolex.

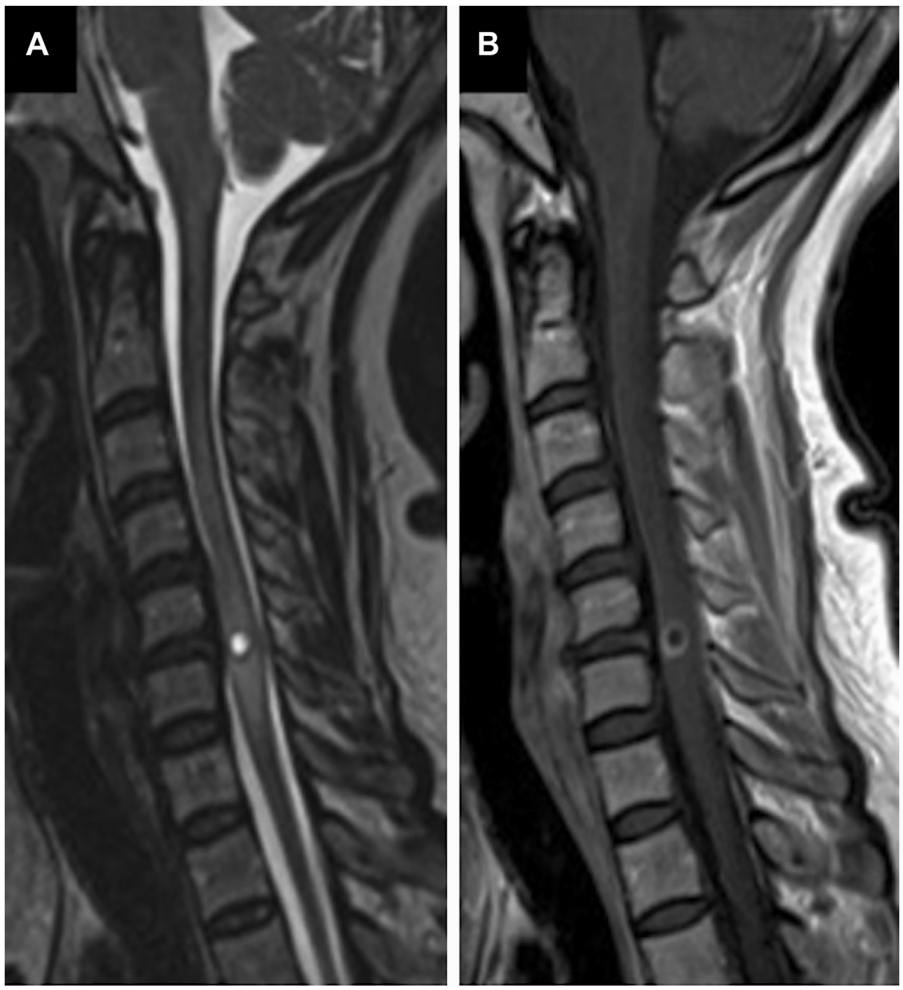

Fig. 10. Spinal intramedullary neurocysticercosis. Sagittal T2 (*A*) and sagittal postcontrast T1 (*B*) illustrate a well-circumscribed intramedullary cystic mass with thick enhancing capsule, slightly expanding the C5-6 cord and associated with surrounding edema. Findings are consistent with a colloidal stage of cysticercosis as the larva dies and incites inflammatory changes.

vegetables.[37] The viable parasite eggs subsequently penetrate the mucosa, reaching the liver (75%), lungs (15%), and CNS (2%) via hematogenous dissemination.[38] In the target end organs, they transform into mature cysts.

The hydatid cyst has three layers: (1) the outer pericyst, composed of host inflammatory cells that form a dense and fibrous protective layer; (2) the middle laminated membrane, which is an acellular membrane that allows passage of nutrients; and (3) the inner germinal layer, where the scolices (larvae) and the laminated membrane are produced. The middle laminated membrane and the inner germinal layer form the true wall of the cyst and are referred to as the endocyst. The outer layer is referred to as the ectocyst.[37] Daughter vesicles are small spherules that contain scolices, which are attached by a pedicle to the germinal layer of the mother cyst and resemble a bunch of grapes. Daughter vesicles may grow into daughter cysts and may extend through the wall of the mother cyst. Cyst fluid contains proteins, glucose, ions, lipids, and polysaccharides. The fluid is antigenic and may contain scolices and hooklets. When vesicles rupture within the cyst, scolices pass into the cyst fluid and form a white sediment known as hydatid sand.[37]

CNS cystic echinococcosis most often occurs as a simple-appearing cyst in the cerebral

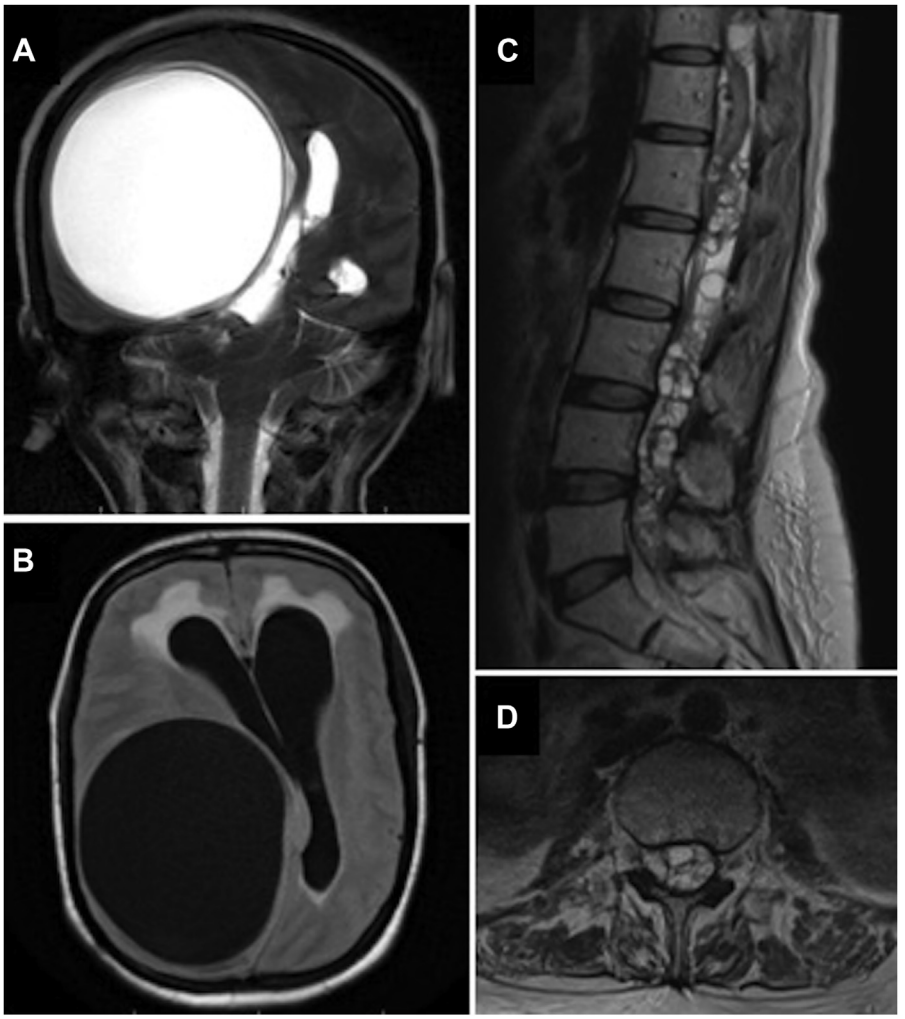

Fig. 11. Echinococcosis in the brain and spine in two different patients. Patient 1 is a sub-Saharan African woman pregnant at 30 weeks of gestation, blind and hemiplegic for 2 to 3 years (unknown cause), now presenting with convulsions. (*A*) Coronal T2 shows a large unilocular cyst with a thin wall in the right parietal lobe causing obstructive hydrocephalus and leftward midline shift. (*B*) Axial FLAIR shows complete signal suppression within the cyst, without surrounding edema, but there is interstitial edema from hydrocephalus. Patient 2 is a 32-year-old woman from China. (*C*) Sagittal and (*D*) axial T2 images of lumbar spine show innumerable cysts in the intradural extramedullary compartment with mass effect on the distal cord and cauda equina nerve roots.

hemispheres (**Fig. 11**). Rarely, cysts have been reported in the cerebellar hemispheres and may involve the dura, subarachnoid space, ventricular system, brainstem, and spinal canal.[38–42] Most of the cysts are solitary; few cases report multiple cysts, sometimes caused by rupture of a prior single cyst.[36] These cysts are well-defined, oval or round collections in the brain parenchyma, isointense to CSF without associated enhancement, edema, or calcification.[36,39] Occasionally, a faint halo of T2 hypointensity is present, which is believed to represent the fibrotic pericyst.[39] This layer may demonstrate calcification.[37]

Platyhelminths

Schistosomiasis

Schistosomiasis is caused by trematodes (a type of flatworm called flukes) of the genus *Schistosoma*. Five species are known to infect humans, three of which cause almost all reported cases of neuroschistosomiasis: *Sappinia mansoni*, *Sappinia haematobium*, and *Sappinia japonicum*. Schistosomiasis is a major public health hazard in developing countries. More than 200 million people in Africa, Asia, and South America are infected.[43] Different species have different geographic predilections: *S haematobium* and *S mansoni* are both found in Africa and the Middle East; *S mansoni* is also endemic in parts of Brazil, Venezuela, and the Caribbean; and *S japonicum* occurs in China and Southeast Asia.[44] Almost all reported cases of CNS schistosomiasis are caused by *S mansoni*, *S haematobium*, or *S japonicum*.[45]

Infected freshwater snails shed cercariae (larvae) into the water. The larvae penetrate the skin of the human host and then the adult worms enter the circulatory system. Complications result from the chronic granulomatous reaction to aberrant adult worm migration and egg deposition in end organs, such as the intestines, liver, urinary tract, and CNS.[46] Cerebral involvement in the form of acute encephalitis of the cortex, subcortical white matter, basal ganglia, or internal capsule is the most common manifestation of neuroschistosomiasis from *S japonicum*.[47] Spinal cord involvement in the form of acute transverse myelitis and subacute myeloradiculopathy is the most common manifestation of neuroschistosomiasis from *S mansoni* or *S haematobium*.

Cerebral schistosomiasis at computed tomography typically shows mass lesions (granulomas) with surrounding edema and variable contrast enhancement. MR imaging would depict small nodular or "silt-like" enhancements scattered or clustered at the cortical or subcortical areas (**Fig. 12**).[45] Sanelli and colleagues[48] reported an "arborized" enhancement pattern with a central linear enhancement that, when present, may be specific for schistosomiasis. Spinal schistosomiasis typically reveals edema and patchy contrast enhancement of the spinal cord, most often at the conus medullaris. Long-standing cases may result in cord atrophy.[45] In cerebral and spinal locations, it is difficult to differentiate granulomatous inflammation from neoplasms.[49,50]

In addition to the findings related to granulomatous lesions, the presence of bilateral symmetric T1 hyperintensity of the globus pallidi and substantia nigra (reflecting manganese deposition) have been reported as a sequala of portosystemic shunting in hepatic schistosomiasis (even in the absence of liver dysfunction).[51]

The presence of eggs in the stool or a positive serology provides only supportive evidence of neuroschistosomiasis. Definitive diagnosis requires histopathologic confirmation of *Schistosoma* eggs and granulomas.

OTHER TRANSMISSIBLE DISEASES

Creutzfeldt-Jakob Disease

Creutzfeldt-Jakob disease (CJD) is a human prion disease. It represents a heterogeneous group of rapidly progressive neurodegenerative diseases that are always fatal, usually within 1 year of onset. Fortunately, all prion diseases remain rare, at an

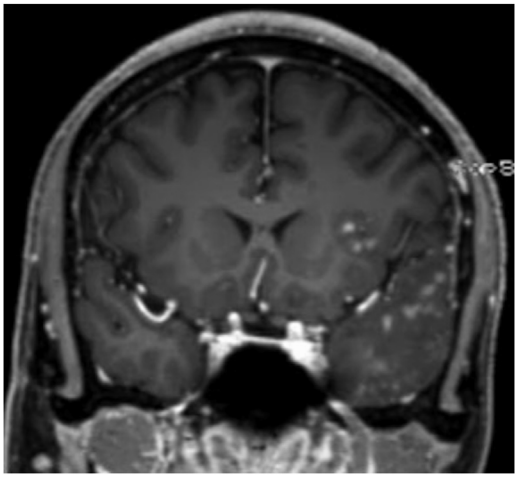

Fig. 12. Cerebral schistosomiasis. Coronal postcontrast T1 shows characteristic cluster of small nodular enhancement in the cortical and subcortical regions of the left temporal and frontal lobes, with surrounding edema most notable in the left temporal lobe. The diagnosis was confirmed on biopsy. (Image courtesy of Surjith Vattoth, MD.)

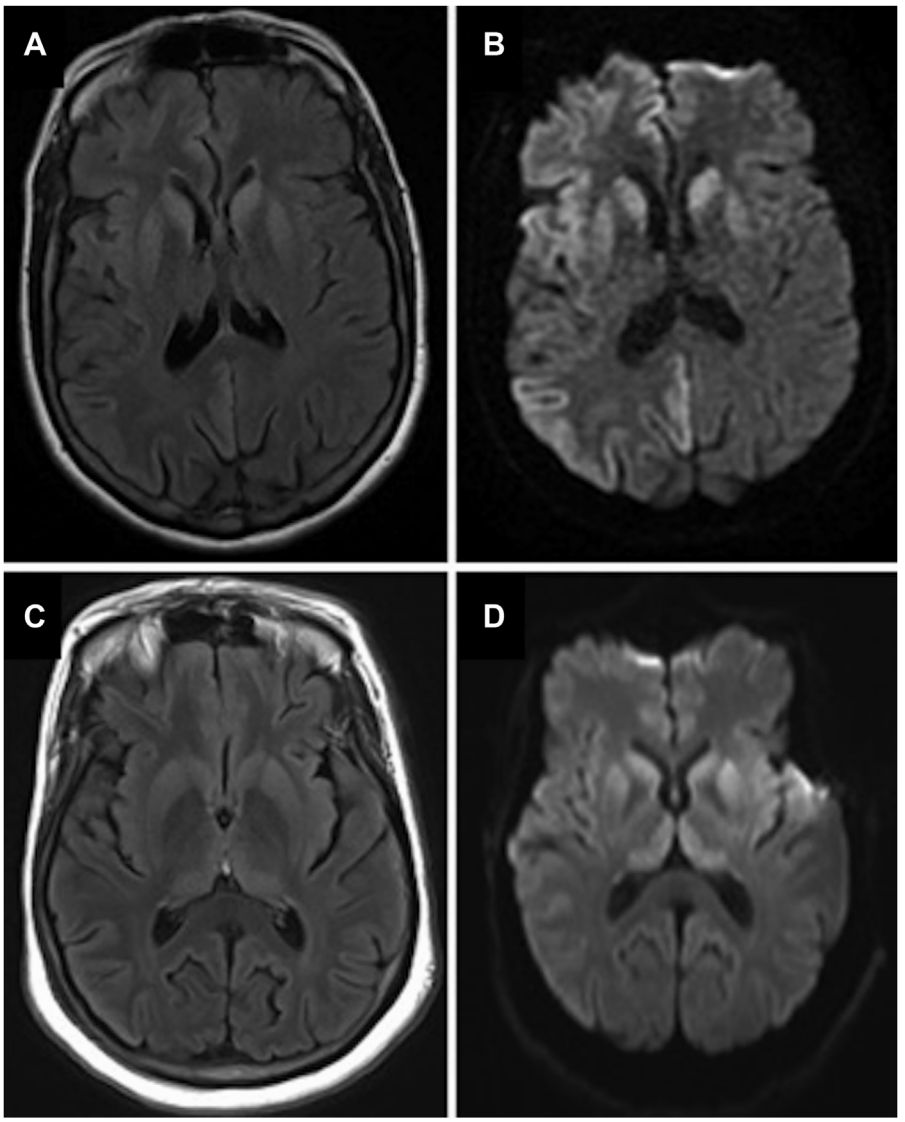

Fig. 13. CJD in two different patients in different forms. Patient 1 is a 58-year-old woman with profound cognitive decline, mood swings, fatigue, and insomnia. (*A*) Axial FLAIR and (*B*) axial DWI trace images show abnormal hyperintensity involving bilateral corpus striatum and right cortical ribbons, often described in "sporadic type." Patient 2 is a 68-year-old woman with rapidly progressive dementia. (*C*) Axial FLAIR and (*D*) axial DWI trace images show abnormal hyperintensity involving bilateral caudate and putamina and bilateral thalami in a hockey stick configuration, described in "variant type."

incidence around one case per 1 million people per year.[52] Prion disease results from the alteration of prion protein (PrP^{C}), normally present and most abundant in the brain, to an abnormally folded protein (PrP^{Sc}) that self-propagates by autocatalyzing the reconfiguration of normal PrP^{C}.

Depending on the pathogenesis, prion diseases are classified as acquired, hereditary, or sporadic. The largest group of prion diseases is idiopathic, accounting for 85% of the cases, and is generally referred to as sporadic. Hereditary prion disease is the second most common subtype, accounting for 10% to 15% of cases. It is further categorized according to their distinctive clinical and pathologic features, and includes genetic CJD, Gerstmann-Sträussler-Scheinker syndrome, and fatal familial insomnia. The acquired diseases are extremely rare and are further subclassified into kuru, iatrogenic CJD, and variant CJD. Kuru was isolated in a small tribe in New Guinea because of ritual cannibalism and has become almost extinct after the

interruption of this practice. Iatrogenic transmission has been described from various medical procedures that used infected human tissues. Variant CJD, or the human form of bovine spongiform encephalopathy ("mad cow disease"), is transmitted from infected beef to humans.[52]

The classic presentation includes rapidly progressive dementia with the presence of myoclonus, visual or cerebellar signs, pyramidal/extrapyramidal signs, and akinetic mutism.[53]

Diffusion-weighted imaging (DWI) changes can precede the clinical onset, even in unsuspected cases with unremarkable/atypical electroencephalogram and CSF examination, making this technique the cornerstone to support early diagnosis (see **Table 1**). Although there is a wide range of radiologic patterns, "typical" findings of early stage CJD consist of diffuse or focal, symmetric or asymmetric DWI and T2/FLAIR hyperintensity involving the cortex and basal ganglia (**Fig. 13**). Involvement of the peri-Rolandic area and cerebellum is less common but has been reported.

The physicochemical basis for DWI abnormalities remains unclear. Histopathologic studies have shown vacuolization of the neurophil, astrogliosis, and, in a few subtypes, amyloid deposition. DWI abnormalities may be attributed to diffusion restriction related to compartmentalization within vacuoles or alternatively deposition of prion protein. As the disease progresses, there is an increase in the degree and extent of T2/FLAIR and DWI hyperintensity in subcortical gray matter regions, which reflects the degree of spongiform degeneration. Signal changes in the cortex may fluctuate with disease progression. Normal DWI signal in advanced disease has been attributed to neuronal loss and atrophy.[52]

Atypical findings include T2/FLAIR and DWI changes in the peri-Rolandic cortex, dorsomedial thalami (double hockey stick sign) (see **Fig. 13**), posterior thalami (pulvinar area), and cerebellum. The "pulvinar" and double hockey stick signs have been reported as the most sensitive radiologic markers for variant CJD but are not pathognomonic for variant CJD and have also been reported in the more common sporadic CJD. Bilateral basal ganglia T1 hyperintensity without DWI changes has also been reported in some cases, which is characterized by prion protein deposition in this area. Although putamen has an even higher prion protein content, the T1-shortening effects of protein in this area are presumed to be canceled out by the coexistent high degree of spongiform degeneration, leading to an overall T1 relaxation time longer than that of the globus pallidus.[52]

SUMMARY

On neuroimaging atypical infections caused by parasites and prion diseases may resemble other infections, and neoplasms, metabolic or immune-mediated processes, or other noninfectious inflammatory conditions. Clinical history and presentation are important guiding differential diagnoses. Imaging plays a pivotal role in assessing the infection's extent, identifying complications, and potentially indicating the specific type of infection when characteristic features are present.

CLINICS CARE POINTS

- In patients with HIV, CNS lymphoma and toxoplasma abscess are challenging to differentiate; both have peripheral enhancement and peripheral restricted diffusion. When toxoplasmosis is suspected, an empirical trial of antitoxoplasma therapy for several weeks is considered sufficiently confirmatory. MR perfusion, MR spectroscopy, and fluorodeoxyglucose PET have been used with varying success.
- There are four stages of neurocysticercosis, and only the vesicular stage would have the characteristic cystic lesions containing scolex on computed tomography or MR imaging that fulfills the absolute criteria for diagnosis of neurocysticercosis.
- A few imaging characteristics can aid in distinguishing certain unusual infectious agents. For instance, the presence of an eccentric target sign could be indicative of cerebral toxoplasmosis, the presence of a mother cyst containing internal daughter cysts might suggest echinococcosis, and an arborized enhancement with a central linear enhancement may be specific for schistosomiasis.
- Creutzfeldt-Jakob disease is characterized by rapidly progressive dementia with the presence of myoclonus, visual or cerebellar signs, pyramidal/extrapyramidal signs, and akinetic mutism. MR imaging may show DWI hyperintensity in the cerebral cortex and deep gray nuclei.

DISCLOSURE

None

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