

Coexistent Neurocysticercosis and Japanese B Encephalitis: MR Imaging Correlation

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BACKGROUND AND PURPOSE: An increased incidence of intestinal helminthic infections has been observed in patients with viral encephalitis in endemic areas. Both Japanese B encephalitis (JE) and neurocysticercosis (NCC) share some common socio-demographic and ecologic factors, and pigs act as the intermediate carrier for both. Our purpose was to show the coexistence of JE and NCC in brain on MR images and highlight the possible role of NCC as an amplifier of JE.

METHODS: MR images from 10 cases of coexistent JE and NCC were studied retrospectively. T1-weighted axial and sagittal, proton T2-weighted axial and coronal, and T2-weighted fluid-attenuated inversion recovery axial and coronal sections of the brain were evaluated. NCC was diagnosed on the basis of neuroimaging. Diagnostic serologic testing for JE was conducted using paired blood and CSF samples.

RESULTS: The JE changes were bilateral and asymmetrical and were more severe on the side harboring the solitary cyst or the side bearing the greater number of cysts or lodging the degenerating cyst. In each of nine of 10 cases, at least one degenerating cyst was found on the side of predominant JE pathologic abnormality.

CONCLUSION: The study suggests that the co-occurrence of JE and NCC is not just a chance coincidence. NCC apparently predisposes a person to JE infection and is a positive modulator of the encephalitic process. The study shows a spectrum of MR imaging findings of coexistent JE and NCC.

Japanese B encephalitis (JE) is a major health concern in Southeast Asian countries, including Japan, Korea, Myanmar, Thailand, and India (1, 2). The JE virus belongs to the mosquito-borne flavivirus group and has an established endemicity, with frequent seasonal epidemics. The subclinical infections by JE virus outnumber the clinically overt disease with a ratio of inapparent to clinically apparent infections ranging from 50:1 to 500:1 (3).

When clinically apparent, JE manifests as acute fulminant neurologic disease with fever, rapid development of focal neurologic signs, and unconsciousness, often resulting in death. The overall fatality rate associated with JE is 25%, and half of the survivors develop permanent neurologic and psychiatric sequelae (4). In endemic areas, a higher

prevalence of intestinal parasitic diseases has been observed in association with viral encephalitis (5, 6). Intestinal helminths are postulated to facilitate the entry of or reactivate latent neurotropic viruses, by either physically carrying them into brain or through some mechanism of alteration of host response. It is also possible that these two infectious agents do not cause altered immunologic response and are just endemic simultaneously and are not synergistic. *Cysticercus* cysts (*Cysticercus cellulosae*, an intestinal tapeworm infection) have been reportedly found in brain specimens of patients who died as a result of JE (7). The simultaneous occurrence of JE and neurocysticercosis (NCC) has been reported in few previous studies and has been noted as a poor prognosticator of the disease (7-9). The diagnosis of coexistent NCC and JE was based either on histopathology, immunohistology, diagnostic serology, or CT findings in earlier studies. The MR imaging spectrum of this association has not been reported in any previous study. MR images from 10 cases of JE referred to our institute from August 1998 to November 1999 revealed coexistent NCC in the brain. The excellent tissue contrast on MR images provided interesting correlative imaging of these two diseases in our group of patients. The purpose of our study was to show the

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coexistence of JE and NCC in brain on MR images and to highlight the possible role of NCC as an amplifier of JE.

Methods

We retrospectively studied the MR images from 10 cases of JE with associated NCC. The patients were admitted to our institute from August 1998 to November 1999. There were 10 patients (nine male and one female), whose ages ranged from 8 to 50 years (average age, 23 years; two patients were younger than 15 years). All the patients were of poor socioeconomic status and came from rural backgrounds. Agriculture was their main occupation, and pig rearing was common in their region. All the patients presented with fulminant meningoencephalitic illness of acute onset (duration of illness, 1–12 days). The common symptoms in these patients were fever, headache, and impaired consciousness. Seven patients had experienced single or multiple episodes of seizures. The mental state of the patients ranged from confusion to altered sensorium to coma. Neck rigidity was noted in six patients. The most common focal neurologic deficit was hemiparesis, which occurred in seven patients.

MR imaging of the brain was performed on a 1.5-T unit. T1-weighted axial and sagittal, proton T2-weighted axial and coronal, and T2-weighted fluid-attenuated inversion recovery axial and coronal sections of the brain were obtained. Contrast-enhanced MR imaging was used for only one patient because the unenhanced MR imaging was diagnostic for the remaining nine patients. All the patients also underwent CT of the head. The diagnosis of NCC was based on MR imaging findings alone. The criteria used for the diagnosis was the presence of well-defined cystic lesions that were hypointense on T1-weighted images and hyperintense on T2-weighted images, representing the colloid vesicular stage of NCC. Lesions that were hypointense on both T1- and T2-weighted images were diagnosed as granular nodular NCC. Diagnostic serologic testing for JE virus was conducted using paired blood and CSF samples and an immunoglobulin M capture micro enzyme-linked immunosorbent assay technique (Pan BIO, Australia) (10) for eight patients. For two patients, serologic confirmation was not available and the diagnosis of JE was made on the basis of clinical profile and MR imaging findings alone.

Results

Viral serology revealed that the JE virus-specific immunoglobulin M antibodies could be detected in seven (87.5%) of eight cases, whereas serologic testing could not be conducted for two patients. The sensitivity (85%) and specificity (97%) of the JE virus-specific immunoglobulin M capture micro enzyme-linked immunosorbent assay test in paired blood and CSF samples have been described elsewhere (10). Negative results for one of our patients could be attributed to lower sensitivity of the test. In two patients for whom serologic confirmation was not available, JE infection was established on the basis of combination of epidemiologic, clinical, and diagnostic imaging criteria. NCC was diagnosed on the basis of neuroimaging alone. MR imaging can diagnose NCC with a high degree of certainty, particularly in endemic areas (11, 12).

For the 10 patients with JE, increased signal intensity involving the thalami bilaterally was shown in all cases. In all 10 cases, the thalamic signal changes were asymmetrical in distribution. Hyper-

intensity of substantia nigra of the midbrain was seen in eight cases. Temporal lobe involvement was noted in six. There was unilateral cortical involvement of the temporal lobe in three cases, whereas the changes were bilateral and asymmetrical in the other three. The images showed mass effect in the form of midline shift away from the side with the greater degree of involvement, except in one case.

For all patients, the presence of NCC was shown. NCC was seen as well-defined cystic lesions with hyperintense centers and hypointense rims on the T2-weighted images and hypointense centers and isointense rims on the T1-weighted images (in 13 of 15 cysts, excluding one patient with multiple cysts [patient 10]) (Table). The remaining two cysts were seen as hypointense nodular lesions. Ring enhancement of the cyst was noted in one patient who had received IV administration of contrast material. Most patients had few cysts, ranging from one to three in number. The number of cysts on the MR images was one for each of four patients (category 1), two for each of four patients (category 2), three for one patient (category 3), and more than three for one patient (category 4). All the cysts were in the supratentorial compartment, except in one patient (category 4). Of 15 cysts in nine patients, 11 showed presence of mild to moderate edema around them, indicating their degenerating nature.

In the first category with single cysts, the thalamic lesions were more pronounced on the same side as the cyst in three of four patients (Figs 1 and 2). In one patient of this group, the only cyst visualized was a fibrotic nodule without edema on the contralateral side as the predominant JE lesions (patient 3).

In the category of patients having two cysts each, the JE lesions were more marked on the side harboring both cysts in one patient (Fig 3). In two patients, the JE changes were more florid on the side bearing edematous lesions (Fig 4). In the fourth patient, the JE lesions were more marked on left side whereas the cysts inciting edema were in both hemispheres.

In the third category (three cysts each), lateralization of JE lesions was on the side harboring the greater parasite load (two cysts). One patient with numerous cysts had widespread signal changes in the thalami, basal ganglia, and temporal lobes bilaterally, with marked mass effect. There was no edematous cyst in this case. However, the largest of the cysts was lying in close proximity to the predominant left-sided thalamic changes and the cyst contents showed increased signal on fluid-attenuated inversion recovery images, indicating degeneration.

Eight patients showed clinical improvement. Two died (including one with multiple cysts). No brain autopsies were performed in these two patients.

Discussion

A high incidence of intestinal parasitic infections has been reported in areas endemic to viral en-

Correlation of distribution and stage of cysts with lateralization of Japanese encephalitis lesions on MR images

Patient	No. of Cysts	Location of Cysts	Edema		Distribution of JE Lesions	Lateralization of JE Lesions	JE Serology
			Right	Left			
Category I							
01.	1	Left		+	TH, SN, BG, TL	Left	Positive
02.	1	Right	+		TH, SN, TL	Right	Positive
03.	1	Right	-		TH, SN, TL	Left	Positive
04.	1	Left		+	TH, SN	Left	Negative
Category II							
05.	2	Right	++		TH, SN	Right	Positive
06.	2	Right, Left	-	+	TH, SN	Left	Not done
07.	2	Right, Left	+	-	TH	Right	Not done
08.	2	Right, Left	+	+	TH, SN, BG, TL	Left	Positive
Category III							
09.	3	Right, Left	+	±	TH, WM, TL	Left	Positive
Category IV							
10.	M	Left > Right	-	-	TH, SN, BG, TL	Left	Positive

Note.—TH—Thalamus, SN—Substantia Nigra, BG—Basal Ganglia, TL—Temporal Lobe, WM—White matter, M—multiple.

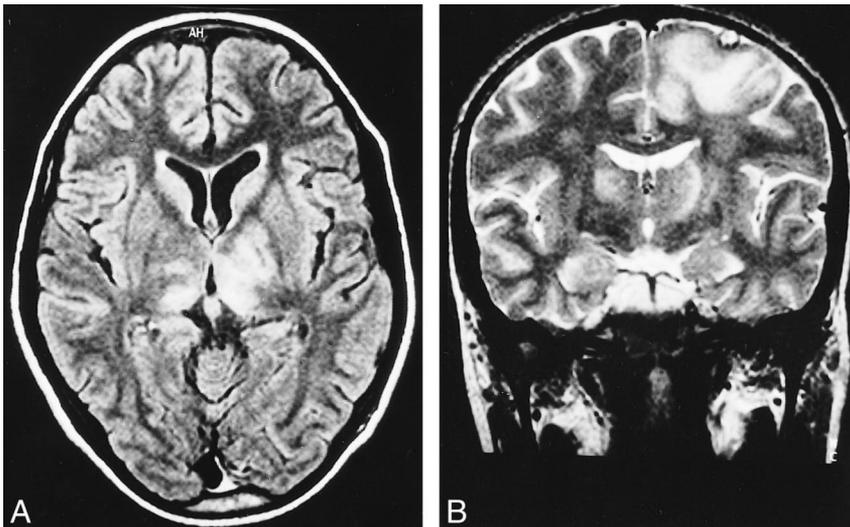


FIG 1. Images of a 16-year-old man with serologically positive JE and single coexistent NCC.

A, T2-weighted turbo fluid-attenuated inversion recovery axial section shows bilateral asymmetric thalamic hyperintensity (left more than right) with left globus pallidus involvement.

B, T2-weighted turbo spin-echo coronal section shows the degenerating cyst in the left frontal region superficially in close association with the leptomeninges with associated edema.

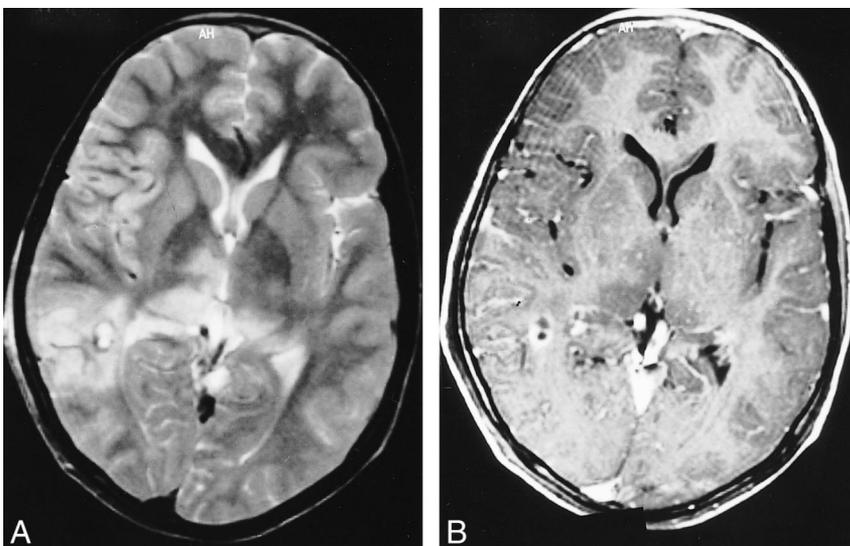


FIG 2. Images of a 13-year-old boy with a solitary cyst and JE.

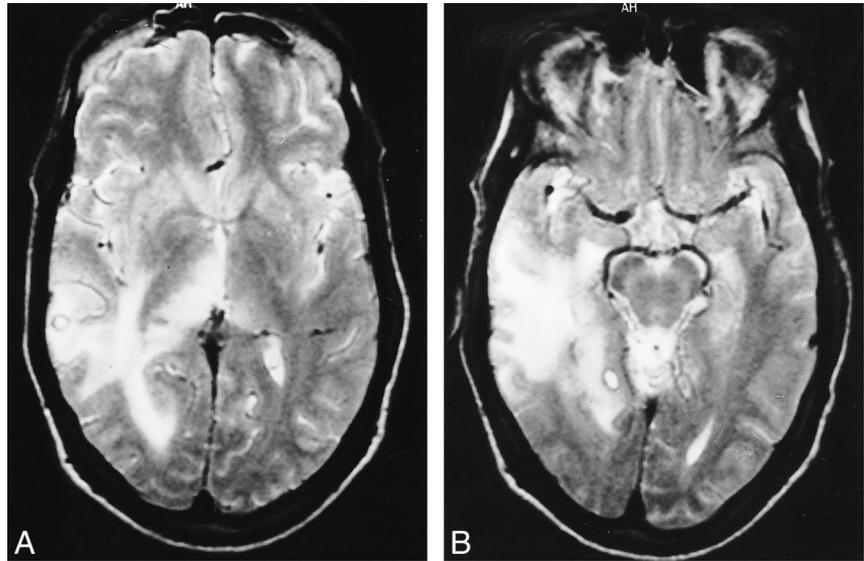
A, T2-weighted turbo spin-echo axial section of the brain shows more extensive right thalamic hyperintensity on the same side as the cyst inciting edema. The encephalitic changes in the temporal cortex also lateralize to the same side.

B, T1-weighted contrast-enhanced axial section shows the enhancement of the wall of the cyst. The thalamic lesions appear hypointense and show no hemorrhage.

FIG 3. Images of a 50-year-old man with JE and positive serology.

A, T2-weighted turbo spin-echo axial section reveals two cysticercus cysts in the right temporal lobe with thalamic lesion lateralization on the same side. The hyperintensity associated with the cysts (representing edema) involves the right temporal lobe extensively and merges with the thalamic signal changes of JE.

B, T2-weighted turbo spin-echo axial section reveals the second cysticercus cyst in the right temporal lobe.



cephalitis (5), and the first report describing a significant association of intestinal helminthic infections and JE in humans was presented by Liu et al (6). A relationship between larva migrans and viral diseases is known. Experimental studies were reported in 1954 and 1975, describing the synergistic role of *Toxocara canis* in the evolution of JE (13, 14). The helminths show larval migration and, as do neurotropic viruses, have a propensity for the CNS (15). The virus may be carried by the parasites to the CNS or may involve some other mechanism that facilitates the entry of the virus. It is also possible that the coexistence of the two infectious agents may be due to their endemicity in the population.

The observation that NCC and JE occur together is not new and has been made as far back as 1940 (8). Few reports are available that describe the coexistence of NCC and JE in animal models and fewer still in humans. MR imaging findings in cases of coexistent NCC and JE have not previously been described. In our series, we found interesting atypical imaging features for cases of coexistent JE and NCC that suggest that one infectious agent encourages the development of the other. A few autopsy studies have shown that nearly a third of the brains of those who died as a result of JE also harbored NCC (7, 9). Desai et al (9) conducted a prospective study in 1997 to ascertain the frequency of coexistent NCC and JE in patients who survive encephalitis and found that the frequency was notably higher (37.42%) than the prevalence of NCC in the general population (4%).

The reason behind the higher incidence of NCC among patients with JE has been theorized to be multiple common factors in the etiopathogenesis of the two pathogens, the most common being the rearing of pigs. Pigs are efficient amplifiers of the JE virus in its natural cycle and are the intermediate host of *Taenia solium*. Other factors shared by the two illnesses are socio-demographic and include a

relatively higher incidence of intestinal parasitic infections, poor socioeconomic status, and hygienic conditions as well as malnutrition. These factors are known to predispose a patient to diseases by neurotropic viruses. All our patients were of poor socioeconomic status and came from rural agricultural areas known for pig rearing, where epidemiologic studies had already established an endemicity of JE.

The characteristic MR imaging findings in cases of JE without NCC have been described as symmetrical bilateral lesions in the thalamus and the basal ganglia (16). In all 10 cases in our study, the signal changes in the thalamus were asymmetrical. Importantly, the distribution and stage of evolution of the cysts apparently influenced the lateralization of distribution and severity of signal changes of JE in eight patients in our series. The encephalitic changes were more severe on the same side harboring the cysts (in cases of one or two cysts confined to one hemisphere). In cases with bilateral distribution of cysts, the severity of JE correlated with the side bearing the greater number of cysts or the side lodging the cyst showing features of degeneration and inciting brain inflammation. The thalamic and temporal lobe lesions were much larger on the ipsilateral side and revealed greater hyperintensity on T2-weighted images. A relatively widespread distribution and greater number of pathologic necrolytic JE lesions were noted by Desai et al (9) in their autopsy specimens of patients with encephalitis with NCC compared with those without NCC. Further, changes were more severe on the side bearing the cyst in their study. Thus, MR imaging features of our patients support this observation and directly indicate greater necrosis on the side harboring the cyst. In two patients, the severity of encephalitic changes did not correlate with NCC. Another important observation was that in nine of 10 patients, at least one degenerating cyst was located on the same side as the predominant

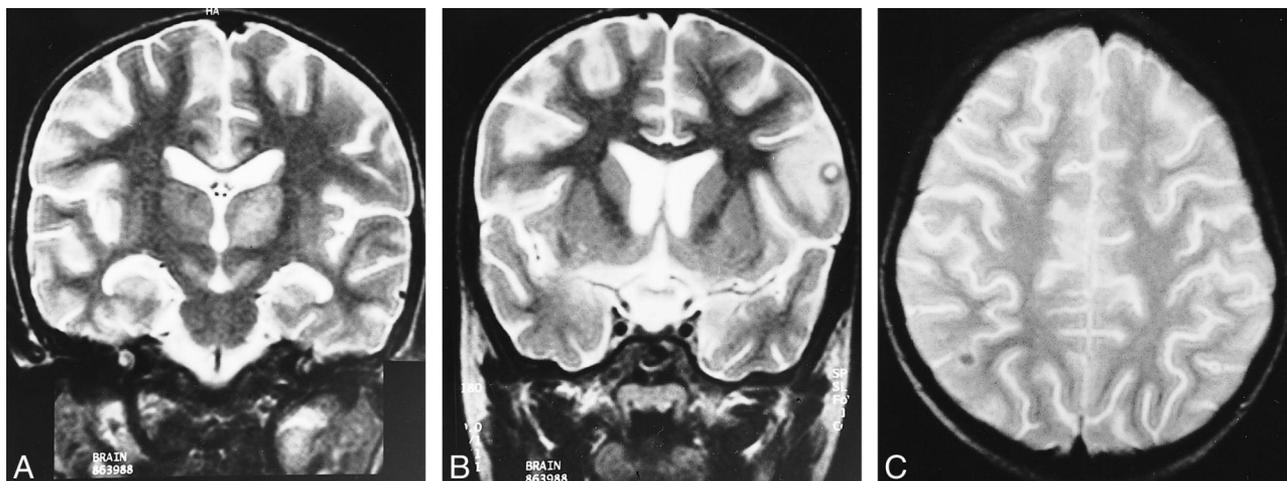


FIG 4. Images of an 8-year-old boy with JE and two cysticercus cysts.

A, T2-weighted turbo spin-echo coronal section of the brain reveals predominant signal changes in the left thalamus.

B, T2-weighted turbo spin-echo coronal section shows degenerating cyst with edema in the left frontal cortex, which correlates with the side of dominant JE lesion.

C, T2-weighted turbo spin-echo axial section shows the other cyst on the contralateral side in granular nodular stage with no inflammation in the surrounding brain.

JE pathologic abnormality. A total of 11 of 15 cysts were associated with white matter edema (excluding one patient with multiple cysts). This implicates a blood-brain-barrier disruption or an altered immune response induced by these cysts in the surrounding brain parenchyma. Experimental studies have indicated that a break in the blood-brain barrier may be responsible for predisposition to JE. The leaky blood-brain barrier may facilitate the entry and/or replication of the virus in susceptible hosts. This may be particularly true during an outbreak of JE, when the pathogen load is high. Metabolic products of the larvae, immune response of the host against surface antigens of the parasite, and suppression of cell-mediated immunity induced by the parasite have all been implicated for more fulminant JE infections (15, 17).

We do not have a group of patients in whom JE was unassociated with NCC; therefore, the comparison of severity of the disease in the two groups and the role of NCC as a prognostic modulator could not be ascertained. Apparently, the 20% (two of 10) mortality rate in our group is not very high when compared with previously reported rates (4). One of the two patients who died had multiple cysts and marked mass effect. It is possible that a larger number of cysts may be a bad prognosticator. The flaw of our study was that the exact incidence of coexistent disease could not be ascertained at our center because there were suspected isolated cases of JE revealed by imaging that did not have serologic proof of the pathology. Because 65% of patients with NCC present with acute encephalitic form (18), MR images should be obtained with careful examination for thalamic lesions to exclude associated JE. We suspect that some patients with this diagnosis may actually be harboring a viral encephalitis, especially in the endemic areas, because

the clinical presentation of both illnesses is very similar.

Conclusion

The analysis of our retrospective study brings out certain salient features. JE changes were more severe on the side harboring the solitary cyst or on the side bearing the greater number of cysts or lodging the degenerating cyst. Conversely, in nine of 10 patients, at least one degenerating cyst was present on the same side as the predominant JE pathologic abnormality. Despite common inherent predisposition to JE and NCC infection in endemic areas due to the socio-demographic and ecologic factors, NCC seems to be a predisposing factor for JE infection and a modulator of the encephalitic process. Prospective studies need to be conducted to determine the exact incidence of coexistent disease and the degree of association to prove the modulatory role of NCC on JE. In endemic areas, radiologists should be aware of this association and seek evidence of cysts on MR images of brains of patients with JE.

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