Wernicke encephalopathy in children and adolescents

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Background: **Wernicke encephalopathy is caused by thiamine (vitamin B1) deficiency. It is generally considered to be a disease of adult alcoholics. However, it is known to occur in the pediatric population and in non-alcoholic conditions.**

Data sources: **We searched PubMed with the key words Wernicke, thiamine, pediatric, children and adolescents and selected publications that were deemed appropriate.**

Results: **The global prevalence rates of hunger, poverty and resultant nutrient deprivation have decreased in the 21st century. However, several scenarios which may predispose to Wernicke encephalopathy may be increasingly prevalent in children and adolescents such as malignancies, intensive care unit stays and surgical procedures for the treatment of obesity. Other predisposing conditions include magnesium deficiency and defects in the *SLC19A3* gene causing thiamine transporter-2 deficiency. The classic triad consists of encephalopathy, oculomotor dysfunction and gait ataxia but is not seen in a majority of patients. Treatment should be instituted immediately when the diagnosis is suspected clinically without waiting for laboratory confirmation. Common magnetic resonance findings include symmetric T2 hyperintensities in dorsal medial thalamus, mammillary bodies, periaqueductal gray matter, and tectal plate.**

Conclusions: **Wernicke encephalopathy is a medical emergency. Delay in its recognition and treatment may lead to significant morbidity, irreversible neurological damage or even death. This article aims to raise the awareness of this condition among pediatricians.**

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Review article

Introduction

Wernicke encephalopathy is a neurological complication of thiamine (vitamin B1) deficiency. Carl Wernicke[1] first described it in 1881 as an acute encephalopathy with oculomotor dysfunction and ataxia in 3 adult cases, 2 of which were in the context of chronic alcoholism. More than 100 years after this initial report, the clinical characterization of Wernicke encephalopathy has not changed significantly and it continues to be associated with alcoholism. However, over the years it has become apparent that the classical triad of Wernicke encephalopathy is not present in all patients. The condition is now known to occur in the pediatric population due to etiologies other than alcoholism. We searched PubMed with the key words Wernicke, thiamine, pediatric, children and adolescents and selected publications that were deemed appropriate for this review.

Pathophysiology

Thiamine acts as a cofactor for various enzymes in the carbohydrate metabolism including transketolase, alpha-ketoglutarate dehydrogenase, pyruvate dehydrogenase and branched chain ketoacid dehydrogenase complex.[2,3] Thiamine requirement depends on metabolic rate and rises during high metabolic demand including after heavy glucose intake. Thiamine deficiency is hypothesized to cause neuronal injury in brain regions with high metabolic requirements. Various genetic factors have been described which increase susceptibility to the development of Wernicke encephalopathy in appropriate clinical settings, for example, decreased affinity of transketolase toward thiamine.[4,5]

Neuropathological studies have demonstrated that lesions occur in a characteristic and symmetric distribution in Wernicke encephalopathy. The lesions involve medial thalami, mammillary bodies,

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hypothalamus, colliculi, periaqueductal gray substance and the floor of the fourth ventricle in the upper pons and medulla oblongata to varying degrees depending on the severity.[6] Vascular congestion and petechial hemorrhage characterize acute lesions while chronic lesions demonstrate gliosis, destruction of neuropil and neuronal loss.

Incidence

Pediatric Wernicke encephalopathy is known to be an underdiagnosed condition.[7] It is estimated that about one third of pediatric patients with Wernicke encephalopathy may be diagnosed only by postmortem examinations.[8] Although no studies have been performed, the incidence in the pediatric population is hypothesized to be very similar to that in adults.[9]

Associated conditions

The literature describes various clinical scenarios as predisposing conditions in pediatric Wernicke encephalopathy, mostly in the form of case reports or small case series. The awareness of these conditions will help clinicians maintain a high index of suspicion for thiamine deficiency as a possible cause of encephalopathy in such patients.

Several cases of Wernicke encephalopathy in infants and young children have been reported secondary to inadequate dietary intake and thiamine deficiency.[10-12] Inadequate dietary intake induced thiamine deficiency may be due to economic reasons, though the likelihood of this has significantly decreased in the developed world.[13] Other reported etiologies for dietary deficiency include starvation in anorexia nervosa and other psychiatric disorders.[14-16] In an otherwise healthy individual, body's thiamine reserve is adequate for up to 18 days. Wernicke encephalopathy occurs in as little as 2-3 weeks of unhealthy dietary practices, earlier in those with less than optimal stores.[17] Thiamine enrichment of rice and grains in many parts of the world has lowered the incidence of thiamine deficiency. Commercially available formulas have an adequate amount of thiamine and the content is often higher when compared to human milk.[18]

Gastrointestinal disorders and surgeries particularly during the postoperative period increase the risk of thiamine deficiency due to various factors such as poor oral intake, vomiting, diarrhea and malabsorption. Wernicke encephalopathy has been reported in the pediatric population in association with liver disease, necrotizing enterocolitis, food allergy, bowel obstruction and perforation, Crohn's disease, pancreatitis and pyloric stenosis.[8,19-21] Any surgical procedure leading to resection or bypass of a part of the gastrointestinal tract increases the risk of micro-nutrient deficiency. Wernicke encephalopathy is a known complication after surgical procedures for treatment of obesity in young adults. No published reports of such occurrences in the pediatric population exist. However, this scenario is likely to change as the rates of surgical interventions for obesity in adolescents have significantly increased in recent years.

Several types of cancers have been associated with Wernicke encephalopathy. Factors including increased consumption of thiamine by rapidly growing cancer cells, chemotherapeutic agent interference with function of thiamine, poor intake, vomiting and liver disease leading to decreased conversion of thiamine contribute to the active metabolite thiamine pyprophosphate. Cancers in children that have been associated with Wernicke encephalopathy include acute lymphoblastic leukemia, acute mixed lineage leukemia, acute myeloid leukemia, germ cell tumor and osteosarcoma.[22-24] Wernicke encephalopathy is considered to be a predominant complication in children undergoing chemotherapy or hematopoietic stem cell transplantation.[24]

Wernicke encephalopathy has been documented in pediatric acquired immunodeficiency syndrome, hypothesized to be due to cachexia and catabolic state. Prolonged infectious illnesses including tuberculosis also predispose to thiamine deficiency due to poor oral intake and increased demands.[8,25] Wernicke encephalopathy has been reported in the pediatric population with nephrotic syndrome and end stage renal disease requiring dialysis.[26,27]

Administration of parenteral nutrition without proper supplementation with thiamine has been widely reported as a cause of Wernicke encephalopathy especially in patients who require prolonged intensive care.[28,29] Global shortage of multivitamin has led to discontinuation of routine thiamine administration with total parenteral nutrition and in susceptible individuals. This practice has precipitated Wernicke encephalopathy because of use of glucose containing solutions.[30,31] It has been postulated that the intermittent shortage of intravenous formulation of thiamine may in part be due to low price, miniscule commercial promise and resultant production by very few pharmaceutical companies. Oral supplementation when intravenous form is in short supply may not be adequate as absorption is poor. Stores may be further compromised in cases of co-existent poor appetite, vomiting, malabsorption or non-compliance. Refeeding in the form of oral, tube or parenteral nutrition may precipitate Wernicke encephalopathy if carbohydrate rich administration is unaccompanied by thiamine supplementation because of resultant higher metabolic

rate and requirement.

Magnesium acts as a cofactor and is required in proper catalytic action of transketolase. Magnesium deficiency may lead to poor response to thiamine administration in Wernicke encephalopathy.[32] Typically seen in alcoholics and in the elderly, this deficiency may also occur in diseases that affect children such as Crohn's disease.

Thiamine transporter-2 deficiency is a rare autosomal recessive disease caused by mutations in the *SLC19A3* gene.[33] Mutations in the thiamine transporter gene have been associated with episodes of Wernicke like encephalopathy syndrome though the most typical presentation is a biotin-responsive basal-ganglia disease characterized by sub-acute encephalopathy with rigidity and dystonia.[34]

Clinical features

The common presenting clinical features include alteration of sensorium, oculomotor dysfunction with ophthalmoplegia and gait ataxia. However, this classic triad will not present completely in a majority of patients with Wernicke encephalopathy. The diagnosis of Wernicke encephalopathy may be delayed in the absence of the clinical triad in a non-alcoholic pediatric patient unless a high index of suspicion is maintained in predisposing scenarios when one or more features of the triad are present. Uncommon presenting features which are not specific to this condition include hypotension, tachycardia, hypothermia, bilateral visual disturbances, papilledema, sluggish pupillary reaction, anisocoria, mydriasis, hypotonia, absence of deep tendon reflexes, tremor, seizures including status epilepticus, hearing loss, hallucinations and behavioral disturbances. Late stage features include hyperthermia, hypertonia, paresis, dyskinesia, coma, and death.[8,35,36]

Korsakoff syndrome is due to more chronic deficiency of thiamine and is characterized by anterograde and retrograde amnesia, confabulation, apathy, lack of insight and minimal content in conversation. It is classically seen in adult alcoholics and has never been reported in pediatric patients.

Laboratory investigations

The most reliable method to establish thiamine deficiency is by measuring erythrocyte transketolase activity (baseline and after addition of thiamine pyrophosphate). In patients with severe thiamine deficiency, erythrocyte transketolase activity is low and increases 25% or more after addition of thiamine pyrophosphate.[37-39] Blood thiamine levels are less reliable but more readily available.[40] Institution of treatment with thiamine before drawing blood levels contributes to a paucity of available literature of laboratory data in pediatric Wernicke encephalopathy.[8] A report out of Israel on an epidemic of 9 children with thiamine deficiency due to the use of a defective soy-based formula utilized 15% as the cut off for thiamine pyrophosphate effect.[41] Of these 9 children, only 3 had clinical signs of Wernicke's encephalopathy. The levels of thiamine pyrophosphate effect in these patients did not correlate well with the severity of clinical manifestations. All 3 patients with Wernicke encephalopathy in this series had elevated blood lactate levels. Two patients also had elevated cerebrospinal fluid lactate levels. Hyponatremia has been reported in patients with pediatric Wernicke encephalopathy. Mild pleocytosis or mild elevation of protein in cerebrospinal fluid may also be present.[8,41] It should be emphasized that once suspected clinically, Wernicke encephalopathy should be treated immediately without waiting for the results of laboratory investigations as the diagnosis is not dependent on them in appropriate clinical scenario especially if neuroimaging findings also correlate.

Radiological findings

Characteristic radiological findings in pediatric patients with Wernicke encephalopathy have been described extensively in the literature due to wider availability of magnetic resonance imaging in recent years. The sensitivity of brain computed tomography is low compared to magnetic resonance imaging. Magnetic resonance imaging commonly demonstrates symmetric T2 hyperintensities in dorsal medial thalamus, mammillary bodies, periaqueductal gray matter, and tectal plate.[41] Atypical findings include involvement of the cerebellum, cranial nerve nuclei, red nuclei, dentate nuclei head, splenium, fornix, and cerebral cortex. Low signal intensity alterations may be seen on T1 sequences. Diffusion restriction likely results from demyelination and necrosis with the development of cytotoxic edema. The lesions may enhance with gadolinium contrast. Contrast enhancement of mammillary bodies which is characteristic in Wernicke encephalopathy due to alcohol abuse occurs less frequently in the nonalcoholic population.[42] In recent years, the diagnosis of Wernicke encephalopathy has often come to light from the magnetic resonance imaging findings.[8,43,44] Magnetic resonance imaging abnormalities may resolve after successful treatment though persistent signal abnormalities have been reported.[31,45] Cortical lesions on imaging have been associated in some patients with irreversible injury

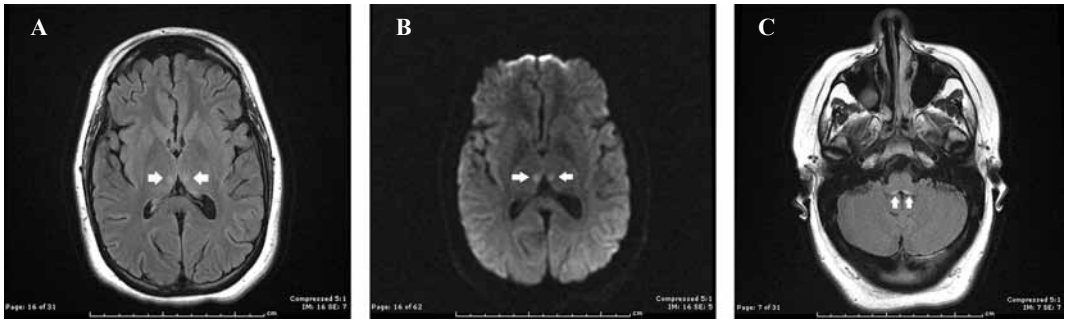

Fig. Symmetric findings on magnetic resonance imaging in Wernicke encephalopathy with arrows pointing toward the abnormalities. **A**: hyperintensities on T2 fluid attenuated inversion recovery sequence in the thalami; **B**: diffusion restriction in the thalami; **C**: hyperintensities along the posterior margins of medulla oblongata.

and poorer outcome.[33,46] Use of magnetic resonance spectroscopy has shown a large lactate doublet, decreased N-acetyl aspartate to creatinine ratio and elevated choline to creatinine ratio.[47,48] Fig. shows symmetric magnetic resonance imaging findings in a patient with Wernicke encephalopathy. Fig. A shows symmetric hyperintensities on T2 fluid attenuated inversion recovery sequence in the thalami. Fig. B shows the same lesion in the thalami with restricted diffusion. Fig. C shows hyperintensities along the posterior margin of medulla oblongata.

Treatment

Wernicke encephalopathy is a neurologic emergency. Once suspected, treatment should be instituted while confirmatory test results are awaited. Typical treatment for adults includes 500 milligrams thiamine (dissolved in 100 milliliters of normal saline or 5% dextrose to be given over 30 minutes) 3 times daily for 2-3 days followed by lowering of the dose to 250 milligrams daily for 3-5 additional days or until no further improvement is noted.[35] Patients should be followed with continued assessment of need for ongoing thiamine supplementation. The use of normal saline or 5% dextrose to dilute thiamine decreases the likelihood of a rare anaphylactic reaction. Nevertheless, provisions to treat anaphylactic reaction must be available when administering intravenous thiamine. Reports have shown significant dosing differences in the pediatric population and treatment varies according to associated conditions. In the infants identified in an Israeli epidemic, treatment with 50 milligrams daily led to improvement.[41] The infant with thiamine transporter deficiency was initiated on 100 milligrams thiamine daily and subsequently maintained on 20 milligrams per kilogram per day after genetic confirmation was obtained.[33] A 10-year-old girl with Wernicke encephalopathy secondary to food refusal responded well to 100 milligrams intravenously daily and was treated for a total of 14 days with almost complete neurologic recovery.[43] It is of utmost importance that glucose administration should never precede treatment with thiamine. Co-existent severe magnesium deficiency must be treated to prevent a poor response to thiamine. Deficiency of other vitamins including niacin and hyponatremia if present should also be addressed. Medical literature suggests that pediatric patients at risk for thiamine deficiency be supplemented with 0.35-0.5 milligrams per kilogram per day of oral thiamine to prevent development of encephalopathy.[49] However, only 4.5 milligrams from an oral dose is absorbed and hence parenteral administration may be preferred and advisable. Children with malignancies are a high risk group for the development of Wernicke encephalopathy and could be given excessive supplementation. However, this practice remains controversial as large amount of thiamine is not considered to be completely harmless in these children and may promote tumor cell growth. It is difficult to make specific recommendations regarding the treatment of Wernicke encephalopathy in children because of a paucity of the literature. However, the adult dosing mentioned above may be useful in treating adolescents especially those approaching adult weight.

Prognosis

Early diagnosis and emergent treatment improve chances of long-term recovery. Conversely, a delay in diagnosis and treatment may lead to irreversible neurological deficits, morbidity and even death. Data suggest that half to two-thirds of those who are treated and survive will have a complete neurologic recovery.[8,41] Even those who are comatose on presentation may make a significant recovery with appropriate treatment. Residual deficits described in the literature include truncal ataxia, gait ataxia, nystagmus, memory deficits, ophthalmoparesis,

hypotonia, hypertonia, dystonia, muscle weakness and developmental delay.

Conclusions

Wernicke encephalopathy in the pediatric population is a treatable but underdiagnosed condition with potential for complete reversal of neurologic manifestations upon timely diagnosis and treatment. Our review aims to increase the awareness of this condition among pediatricians.

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References

1 Wernicke C. Die akute haemorrhagische polioencephalitis superior. In: Lehrbuch der Gehirnkrankheiten für Aerzte und Studirende, Bd II. Kassel: Fisher Verlag, 1881: 229-242.
2 Victor M, Adams RA, Collins GH. The Wernicke-Korsakoff syndrome and related disorders due to alcoholism and malnutrition. Philadelphia: FA Davis, 1989.
3 Martin PR, Singleton CK, Hiller-Sturmhöfel S. The role of thiamine deficiency in alcoholic brain disease. Alcohol Res Health 2003;27:134-142.
4 Blass JP, Gibson GE. Abnormality of a thiamin-requiring enzyme in patients with Wernicke-Korsakoff syndrome. N Engl J Med 1977;297:1367-1370.
5 Mukherjee AB, Svoronos S, Ghazanfari A, Martin PR, Fisher A, Roecklein B, et al. Transketolase abnormality in cultured fibroblasts from familial chronic alcoholic men and their male offspring. J Clin Invest 1987;79:1039-1043.
6 Torvik A. Two types of brain lesions in Wernicke's encephalopathy. Neuropathol Appl Neurobiol 1985;11:179-190.
7 Pihko H, Saarinen U, Paetau A. Wernicke encephalopathy--a preventable cause of death: report of 2 children with malignant disease. Pediatr Neurol 1989;5:237-242.
8 Vasconcelos MM, Silva KP, Vidal G, Silva AF, Domingues RC, Berditchevsky CR. Early diagnosis of pediatric Wernicke's encephalopathy. Pediatr Neurol 1999;20:289-294.
9 Zuccoli G, Siddiqui N, Bailey A, Bartoletti SC. Neuroimaging findings in pediatric Wernicke encephalopathy: a review. Neuroradiology 2010;52:523-529.
10 Guerrero RM. Wernicke syndrome due to vitamin B deficiency; report of the disease in two infants. Am J Dis Child 1949;78:88-96.
11 Davis RA, Wolf A. Infantile beriberi associated with Wernicke encephalopathy. Pediatrics 1958;21:409-420.
12 Seear MD, Norman MG. Two cases of Wernicke encephalopathy in children: an underdiagnosed complication of poor nutrition. Ann Neurol 1988;24:85-87.
13 Cochrane WA, Collins-Willims C, Donohue WL. Superior hemorrhagic polioencephalitis (Wernicke disease) occurring in an infant-probably due to thiamine deficiency from use of a soya bean product. Pediatrics 1961;28:771-777.
14 Peters TE, Parvin M, Petersen C, Faircloth VC, Levine RL. A case report of Wernicke's encephalopathy in a pediatric patient with anorexia nervosa-restricting type. J Adolesc Health 2007;40:376-383.
15 Watanabe S, Yamakura S, Hirano K, Okumura Y, Aiba H. Case of infantile autism with pediatric Wernicke's encephalopathy due to severe eating disorder. No To Hattatsu 2009;41:43-46. [In Japanese]
16 Gropman AL, Gaillard WD, Campbell P, Charya SV. Wernicke's encephalopathy due to self starvation in a child. Lancet 1998;351:1704-1705.
17 Tanphaichitr V. Thiamine. In: Shils ME, Olson JA, Shike M, Ross AC, eds. Modern nutrition in health and disease, 9th ed. Baltimore: Williams & Wilkins, 1999: 381-389.
18 Friel JK, Andrews WL, Simmons BS, L'Abbe MR, Mercer C, MacDonald A, et al. Evaluation of full-term infants fed an evaporated milk formula. Acta Paediatr 1997;86:448-453.
19 Zeljko K, Darija VB, Dina LK, Marko B. Wernicke's encephalopathy during parenteral nutrition in a Crohn's disease patient. Nutrition 2011;27:503-504.
20 Basit S, Elsås T, Kvistad KA, Høsøien LS. Wernicke's encephalopathy because of pancreatitis in a young boy. Acta Ophthalmol 2011;89:e656-e657.
21 Bohnert B. Wernicke's encephalopathy in gastropancreatic disease with pyloric stenosis. Dtsch Med Wochenschr 1982;107:1722-1725. [In German]
22 Shah N, Wolff JA. Thiamine deficiency: Probable Wernicke's encephalopathy successfully treated in a child with acute lymphocytic leukemia. Pediatrics 1973;51:750-751.
23 Onodera N, Nakahata T, Tanaka H, Ito R, Honda T. Successful treatment of Wernicke's encephalopathy in a boy with acute mixed lineage leukemia. Acta Paediatr Jpn 1998;40:271-274.
24 Lim YJ, Kim HJ, Lee YJ, Seol IJ, Lee YH. Clinical features of encephalopathy in children with cancer requiring cranial magnetic resonance imaging. Pediatr Neurol 2011;44:433-438.
25 Mintz M. Clinical comparison of adult and pediatric NeuroAIDS. Adv Neuroimmunol 1994;4:207-221.
26 Nishida M, Sato H, Kobayashi N, Morimoto M, Hamaoka K.Wernicke's encephalopathy in a patient with nephrotic syndrome. Eur J Pediatr 2009;168:731-734.
27 Baracco R, Ku L, Adabala M, Jain A, Valentini RP, Mattoo TK, et al. An adolescent on peritoneal dialysis with acute encephalopathy. Pediatr Nephrol 2013;28:1221-1225.
28 Han JW, Lim S, Shin HS, Park HJ, Jung WJ, Kwon SY, et al. Two cases of Wernicke encephalopathy in young age patients receiving allogeneic hematopoietic stem cell transplantation. Yonsei Med J 2012;53:1049-1053.
29 Muwakkit S, Al-Aridi C, Saab R, Hourani R, Yazbeck N, Abboud M. Wernicke encephalopathy during total parenteral nutrition in a child with acute lymphoblastic leukemia and acute pancreatitis. Neuropediatrics 2009;40:249-251.
30 Hahn JS, Berquist W, Alcorn DM, Chamberlain L, Bass D.

Wernicke encephalopathy and beriberi during total parenteral nutrition attributable to multivitamin infusion shortage. Pediatrics 1998;101:E10.
31 Perko R, Harreld JH, Helton KJ, Sabin ND, Haidar CE, Wright KD. What goes around comes around? Wernicke encephalopathy and the nationwide shortage of intravenous multivitamins revisited. J Clin Oncol 2012;30:e318-e320.
32 McLean J, Manchip S. Wernicke's encephalopathy induced by magnesium depletion. Lancet 1999;353:1768.
33 Pérez-Dueñas B, Serrano M, Rebollo M, Muchart J, Gargallo E, Dupuits C, et al. Reversible lactic acidosis in a newborn with thiamine transporter-2 deficiency. Pediatrics 2013;131: e1670-e1675.
34 Kono S, Miyajima H, Yoshida K, Togawa A, Shirakawa K, Suzuki H. Mutations in a thiamine-transporter gene and Wernicke's-like encephalopathy. N Engl J Med 2009;360:1792-1794.
35 Sechi G, Serra A. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol 2007;6:442-455.
36 Cefalo MG, Ioris MA, Cacchione A, Longo D, Staccioli S, Arcioni F, et al. Wernicke encephalopathy in pediatric neuro-oncology: presentation of 2 cases and review of literature. J Child Neurol 2013 Nov 28. [Epub ahead of print]
37 Leigh D, McBurney A, McIlwain H. Erythrocyte transketolase activity in the Wernicke-Korsakoff syndrome. Br J Psychiatry 1981;139:153-156.
38 Doolman R, Dinbar A, Sela BA. Improved measurement of transketolase activity in the assessment of "TPP effect". Eur J Clin Chem Clin Biochem 1995;33:445-446.
39 Kuriyama M, Yokomine R, Arima H, Hamada R, Igata A. Blood vitamin B1, transketolase and thiamine pyrophosphate (TPP) effect in beriberi patients, with studies employing discriminant analysis. Clin Chim Acta 1980;108:159-168.
40 Ming X, Wang MM, Zee D, Katz RM, Freeman JM. Wernicke's encephalopathy in a child with prolonged vomiting. J Child Neurol 1998;13:187-189.
41 Fattal-Valevski A, Kesler A, Sela BA, Nitzan-Kaluski D, Rotstein M, Mesterman R, et al. Outbreak of life-threatening thiamine deficiency in infants in Israel caused by a defective soy-based formula. Pediatrics 2005;115:e233-e238.
42 Zuccoli G, Santa Cruz D, Bertolini M, Rovira A, Gallucci M, Carollo C, et al. MR imaging findings in 56 patients with Wernicke encephalopathy: nonalcoholics may differ from alcoholics. AJNR Am J Neuroradiol 2009;30:171-176.
43 Zuccoli G, Pipitone N. MR Imaging: an increasingly important tool in the early diagnosis of Wernicke encephalopathy. AJNR Am J Neuroradiol 2012;33:E92.
44 Coe M, Carfagnini F, Tani G, Ambrosetto P. Wernicke's encephalopathy in a child: case report and MRI findings. Pediatr Radiol 2001;31:167-168.
45 Sparacia G, Banco A, Lagalla R. Reversible MRI abnormalities in an unusual paediatric presentation of Wernicke's encephalopathy. Pediatr Radiol 1999;29:581-584.
46 Zhong C, Jin L, Fei G. MR Imaging of nonalcoholic Wernicke encephalopathy: a follow-up study. AJNR Am J Neuroradiol 2005;26:2301-2305.
47 Kornreich L, Bron-Harlev E, Hoffmann C, Schwarz M, Konen O, Schoenfeld T, et al. Thiamine deficiency in infants: MR findings in the brain. AJNR Am J Neuroradiol 2005;26:1668-1674.
48 Rodan LH, Mishra N, Tein I. MR spectroscopy in pediatric Wernicke encephalopathy. Neurology 2013;80:969.
49 Seear M, Lockitch G, Jacobson B, Quigley G, MacNab A. Thiamine, riboflavin and pyridoxine deficiencies in a population of critically ill children. J Pediatr 1992;121:533-538.

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