

Wernicke Encephalopathy: A Complication of Parenteral Nutrition Diagnosed by Magnetic Resonance Imaging

Olivier Attard, M.D.,* Jean L. Dietemann, M.D.,† Pierre Diemunsch, M.D., Ph.D.,‡ Thierry Pottecher, M.D.,‡ Alain Meyer, M.D.,§ Bartholomeus L. Calon, M.D.§

THIAMIN (vitamin B₁) is a water-soluble vitamin involved in glucose metabolism. Its deficiency affects the cardiovascular (wet beriberi) and nervous (dry beriberi) systems, and in industrialized countries, it is commonly linked to chronic alcoholism. Wernicke encephalopathy (WE), a metabolic encephalopathy due to thiamine depletion, is clinically characterized by at least two among four features¹: nutritional deficit, oculomotor abnormalities, ataxia, and stupor. Laboratory tests (measurement of serum thiamine or erythrocyte transketolase activity) are diagnostic, but the radiologic confirmation can be achieved by magnetic resonance imaging (MRI) with abnormal hyperintense signal in the periaqueductal gray matter, the mamillary bodies, and around the third ventricle on fluid-attenuated inversion recovery and T₂ MRI scans.² We report a case of non alcoholic WE complicating postoperative total parenteral nutrition (TPN) lacking micronutrient supply and confirmed by MRI.

Case Report

The diagnosis of benign gastric tumor was established after a gastroscopy with gastric biopsy in a 30-yr-old mother of two children without any relevant medical history but prolonged gastric intolerance and 8 kg weight loss. She underwent an elective laparoscopic partial gastrectomy. On the fourth postoperative day, she had a wound dehiscence and developed peritonitis that required an emergency laparotomy with peritoneal lavage and suture. After this procedure, TPN and adapted antibiotherapy were administered. She developed a digestive tract fistula, and TPN had to be continued. After 30 days, the patient reported fatigue, and hyponatremia (127 mM) and hypophosphatemia developed and were corrected, but she had to be transferred to the intensive care unit for stupor (Glasgow Coma Scale score of 8) without any focal signs, and she was intubated and ventilated. Cerebral computed tomography scan was normal; her sodium concentration went to 150 mM. Micronutrients (polyvitamins and trace elements) were added to TPN. After 3 days, her neurologic status improved, allowing extubation, but the clinical examination showed a horizontal nystagmus and a lateral ophthalmoplegia. MRI showed no sign of central pontine myelinolysis but hyperintense lesions in the medial thalami on fluid-attenuated inversion recovery and T₂ MRI scans



Fig. 1. Fluid-attenuated inversion recovery weighted axial magnetic resonance imaging scan. Bilateral hyperintensity involving the medial thalami. Arrow indicates hyperintense lesions in the medial thalami.

(fig. 1). After inquiry, it turned out that TPN before intensive care admission had been administered without micronutrient supplementation. Thiamine administration was increased (200 mg/day), and oculomotor and MRI signs regressed, but a severe cognitive deficit along with vertigo and loss of sphincter control persisted. More than 2 yr later, these symptoms are still present, and the patient is totally dependent and disoriented with memory disturbances.

Discussion

In the Western world, thiamine deficiency is characteristically associated with chronic alcoholism, because it affects thiamine uptake and utilization. However, WE may develop in nonalcoholic conditions, as in prolonged starvation,³ hyperemesis gravidarum,⁴ bariatric surgery,⁵ and even healthy infants given the wrong formulas.⁶ Thiamine is a cofactor of several enzymes involved in glucose metabolism and cerebral energy utilization, and its depletion could lead to the neuronal damage as seen on MRI, *i.e.*, T₂ and fluid-attenuated inversion recovery hyperintense signaling in the mamillary bodies, periventricular thalamus, and periaqueductal gray matter,⁷ as well as diffusion-weighted imaging to differentiate vasogenic from cytotoxic edema.⁸ Subsequent MRIs may show regres-

* Anesthesia Student and Staff, ‡ Professor, § Physician Intensivist, Service d'Anesthésie Réanimation Chirurgicale, † Professor, Service de Radiologie 2, CHU Hôpital de Haute-pierre.

Received from Service d'Anesthésie Réanimation Chirurgicale 6369, CHU Hôpital de Haute-pierre, Strasbourg, France. Submitted for publication February 3, 2006. Accepted for publication May 15, 2006. Support was provided solely from institutional and/or departmental sources.

Address correspondence to Dr. Calon: Service d'Anesthésie Réanimation Chirurgicale 6369, CHU Hôpital de Haute-pierre, Avenue Molière, 67098 Strasbourg Cedex, France. bartholomeus.calon@chru-strasbourg.fr. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

sion of the signal abnormalities, but there is no correlation with improvement in clinical conditions.⁷ Interestingly, metabolic disturbances such as hyponatremia and hypophosphatemia have been associated with WE and can be misleading,⁹ as in our case. Lactic acidosis, however, is evocative of thiamine deficiency, especially in children.¹⁰

Our case report emphasizes the diagnostic difficulties leading astray from WE in atypical settings and the usefulness of MRI to correct the diagnosis. However, the main issue is to remind us that TPN is not a harmless and easy technique, and that micronutrients should always be administered on a daily basis during TPN.¹¹

References

1. Caine D, Halliday GM, Kril JJ, Harper CG: Operational criteria for the classification of chronic alcoholics: Identification of Wernicke's encephalopathy. *J Neurol Neurosurg Psychiatr* 1997; 62:51-60
2. Vargas MI, Lenz V, Bin JF, Bogorin A, Abu Eid M, Jacques C, Marin H, Kindo S, Zollner G, Dietemann JL: Brain MR imaging of chronic alcoholism. *J Radiol* 2003; 84:369-79
3. Merkin-Zaborsky H, Ifergane G, Frisher S, Valdman S, Herishanu Y, Wirguin I: Thiamine-responsive acute neurological disorders in nonalcoholic patients. *Eur Neurol* 2001; 45:34-7
4. Spruill SC, Kuller JA: Hyperemesis gravidarum complicated by Wernicke's encephalopathy. *Obstet Gynecol* 2002; 99:875-7
5. Toth C, Voll C: Wernicke's encephalopathy following gastroplasty for morbid obesity. *Can J Neurol Sci* 2001; 28:89-92
6. Siegel-Itzkovitch J: Police in Israel launch investigation into deaths of babies given formula milk. *BMJ* 2003; 327:1128
7. Lenz V, Vargas MI, Bin JF, Bogorin A, Grebici-Guessoum M, Jacques C, Marin H, Zollner G, Dietemann JL: Value of MRI findings in Gayet-Wernicke encephalopathy. *J Neuroradiol* 2002; 29:153-60
8. Halavaara J, Brander A, Lyytinen J, Setälä K, Kallela M: Wernicke's encephalopathy: Is diffusion-weighted MRI useful? *Neuroradiology* 2003; 45:519-23
9. Leens C, Mukendi R, Foret F, Hacourt A, Devuyt O, Colin IM: Central and extrapontine myelinolysis in a patient in spite of a careful correction of hyponatremia. *Clin Nephrol* 2001; 55:248-53
10. Remond C, Viard L, Paut O, Giraud P, Camboulives J: Severe lactic acidosis and thiamine deficiency during parenteral nutrition in a child. *Ann Fr Anesth Reanim* 1999; 18:445-50
11. Mirtallo J, Canada T, Johnson D, Kumpf V, Petersen C, Sacks G, Seres D, Guenter P: Safe practices for parenteral nutrition. *J Parenter Enteral Nutr* 2004; 28:S39-70

Anesthesiology 2006; 105:848-51

Copyright © 2006, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Compression of the Subarachnoid Space by the Engorged Epidural Venous Plexus in Pregnant Women

Tetsuo Takiguchi, M.D., Ph.D.,* Shigeki Yamaguchi, M.D., Ph.D.,* Masatomo Tezuka, M.D., Ph.D.,† Naoki Furukawa, M.D., Ph.D., † Toshimitsu Kitajima, M.D., Ph.D.‡

IT is well known that the spread of anesthetic level in spinal anesthesia is enlarged in late pregnancy.¹ Physiological^{2,3} and physiologic^{4,5} changes in late pregnancy have been suspected as being factors for this mechanism. The engorgement of the epidural venous plexus has been confirmed, and this may compress the subarachnoid space in late pregnancy. However, it remains unclear how the epidural venous plexus becomes engorged. In the current study, to clarify changes in the epidural venous plexus in late pregnancy, we observed the spinal canal using magnetic resonance (MR) images and obtained what we believe to be some valuable information.

Case Report

After obtaining the approval of the hospital ethics committee (Tochigi, Japan) and written informed consent, we studied three pregnant volunteers (aged 25-34 yr; height, 155-162 cm; weight in the pregnant state, 55-62 kg; weight in the nonpregnant state, 47-50 kg). All volunteers were transferred to an MR table and placed in the supine

position. T2-weighted midsagittal, axial, and coronal slice images were obtained with the MR imaging system (GE, Fairfield, CT) operating at 1.5 T. A multiecho sequence with a repetition time of 4,500-5,000 ms and an echo time of 96-105 ms was used, with a 256 × 256 or 512 × 256 acquisition matrix.

All figures were captured at 37-39 weeks of pregnancy (pregnant state) and 3-10 months after parturition (nonpregnant state) in the same volunteers.

Figure 1 shows axial MR images at each disc level (Th12-L1 to L5-S1) in the pregnant and nonpregnant states, respectively. At each disc level, the engorged veins in the ventral epidural space were observed bilaterally in the pregnant state, but not in the nonpregnant state. The engorged veins narrowed the foramina at each disc level. Figure 2 shows axial MR images at each level of the pedicles (L1-S1) in the pregnant and nonpregnant states, respectively. At each level of the pedicles, the engorged veins crossed at the middle of the vertebra in the pregnant state, but not in the nonpregnant state. At all disc levels and levels of the pedicles that we observed, the subarachnoid space was compressed by the engorged venous plexus in the ventral epidural space in the pregnant state.

The compression of the subarachnoid space was more obvious at the lower lumbar spinal levels than at the other levels. Figure 3 shows the intervertebral disc level at L5-S1. Although the subarachnoid space was clearly observed in the nonpregnant state, there was little subarachnoid space in the pregnant state. In the pregnant state, the nerve roots of the cauda equina were compressed and adjacent in the limited subarachnoid space.

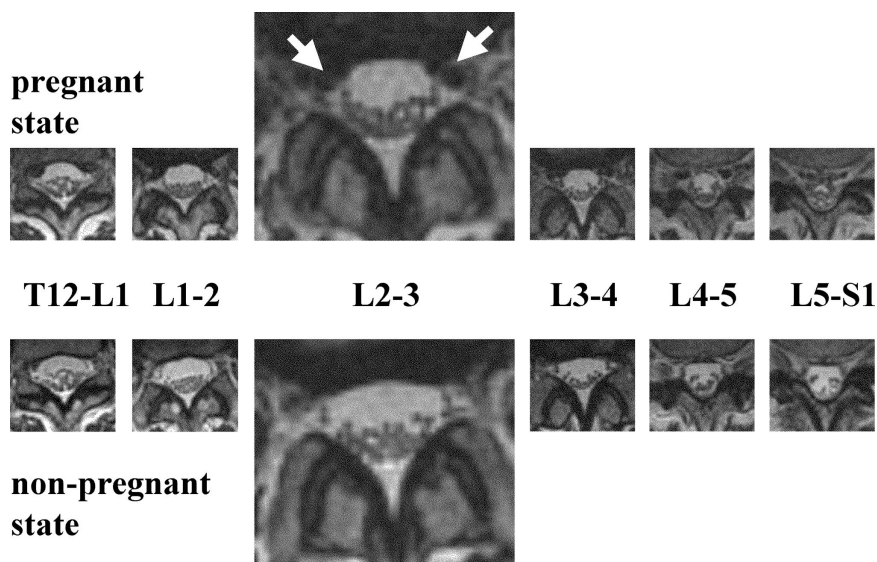
Figure 4 shows modified coronal MR images of the spinal canal, captured in the pregnant and nonpregnant states, respectively. In those images, multiple coronal images were computer-processed into one image in alignment with the curvature of the ventral epidural space (Advantage Windows version 2; GE, Milwaukee, WI). The engorged epidural venous plexus in the ventral epidural space was observed between Th12 and S1 in the pregnant state. The engorged

* Assistant Professor, † Staff Anesthesiologist, ‡ Professor and Chairman, Department of Anesthesiology.

Received from the Department of Anesthesiology, Dokkyo University School of Medicine, Tochigi, Japan. Submitted for publication February 14, 2006. Accepted for publication May 15, 2006. Support was provided solely from institutional and/or departmental sources.

Address correspondence to Dr. Yamaguchi: Department of Anesthesiology, Dokkyo University School of Medicine, Mibu, Tochigi 321-0293, Japan. shigeki@dokkyomed.ac.jp. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

Fig. 1. Axial magnetic resonance images of the spinal canal at each disc level (Th12–L1 to L5–S1) in the pregnant and nonpregnant states, respectively. To emphasize our point of view, the images at the L2–L3 disc level were enlarged. At the L2–L3 disc level, *white arrows* indicate the veins in the ventral epidural site. The engorged veins in the ventral epidural space were observed bilaterally in the pregnant state, but not in the nonpregnant state, at each disc level.



longitudinal veins were observed bilaterally. The engorged vein crossed at each level of the pedicles, resembling a ladder. However, the engorged veins were not observed in the nonpregnant state. These findings were confirmed in all volunteers.

Discussion

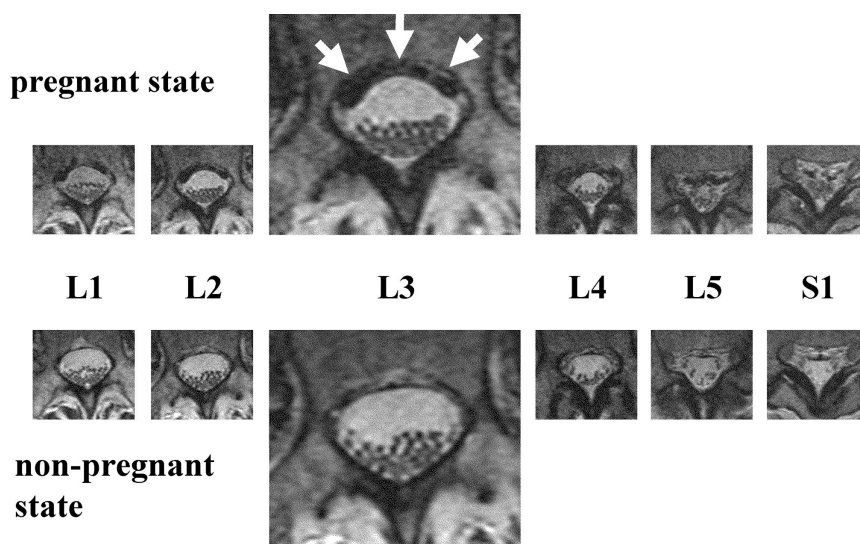
In this study, we presented interesting MR images about the engorgement of the venous plexus in the ventral epidural space in the pregnant state, resulting in narrowing of the foramen and the compression of the subarachnoid space. Those findings were extensively observed and were more obvious at the lower lumbar spinal level than at the other spinal levels. This may promote a better understanding for performing spinal or epidural anesthesia in pregnant patients.

Obstruction of the inferior vena cava by the enlarged pregnant uterus disturbs the return of venous blood from the pelvis and legs to the heart.¹ This affects the

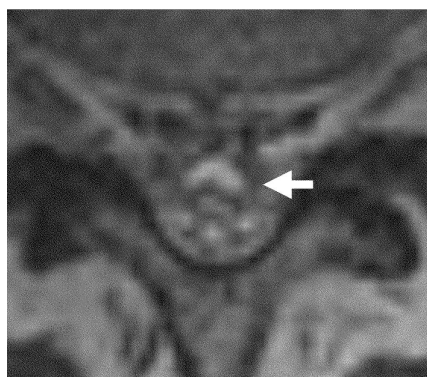
blood flow of the collateral circulation, resulting in the engorgement of the venous plexuses in the spinal canal. There has been little information about morphologic changes in the venous plexuses of the spinal canal in the late stage of pregnancy.

Some reports have described changes of the epidural venous plexus in the pregnant state. Igarashi *et al.*⁶ observed the epidural space in pregnant women using epidural fiberoptic. They showed an increase in the density of the vascular networks and engorgement of vessels in the epidural space. Hirabayashi *et al.*⁷ compared MR images of the spinal canal between nonpregnant and pregnant states, and showed the engorged anterior internal vertebral veins and displacement of the dural sac at 32 weeks' gestation. However, limited information was revealed in their reports. Therefore, the current study was designed to know more about the morphologic changes in the inside of the spinal canal.

Fig. 2. Axial magnetic resonance images of the spinal canal at each level of the pedicles (L1–S1) in the pregnant and nonpregnant states, respectively. To emphasize our point of view, the images at the L3 level of the pedicles were enlarged. At the L3 level of the pedicles, *white arrows* indicate the veins in the ventral epidural site. At each level of the pedicles, the engorged veins cross at the middle of the vertebral level in the pregnant state, but not in the nonpregnant state.



pregnant state



non-pregnant state

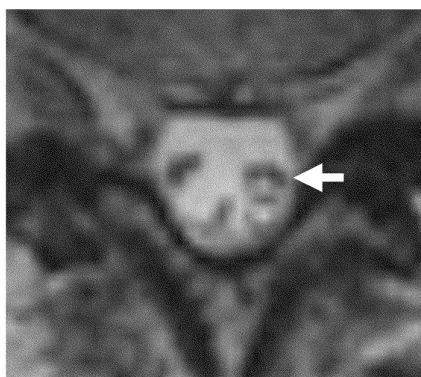


Fig. 3. Axial magnetic resonance images of the spinal canal at the L5–S1 disc level in the pregnant and nonpregnant states, respectively. In both images, *white arrows* indicate the subarachnoid space. In the pregnant state, the venous plexus in the ventral epidural space was engorged, resulting in the limited subarachnoid space. The nerve roots of the cauda equina were closely compressed and adjacent in the limited subarachnoid space. On the other hand, the subarachnoid space was clearly observed without the engorged veins in the nonpregnant state.

Some interesting findings were obtained from subjects in late pregnancy using MR images, which should be beneficial to understand how to perform spinal or epidural anesthesia in the pregnant state.

In this study, we made four important observations. The first is that the engorgement of the venous plexus was extensively seen. Hirabayashi *et al.*⁷ showed this only between the L2 and L3 levels. We, however, could confirm it from the lower thoracic to sacral levels. The second is that the engorgement of the venous plexus was obvious on the ventral side, but not on the dorsal side. The engorgement of the epidural venous plexus compressed the subarachnoid space. This can explain the mechanism of the spread of anesthetic level in spinal anesthesia for pregnant women. In our previous studies, the compression of the subarachnoid space after epidural injection was confirmed by myelography⁸ and MR imaging.⁹ However, it was compressed from the dorsal side.

The third observation is a difference in the state of the engorged veins in the epidural space between the disc level and level of the pedicles. In each level of the pedicles, the engorged veins cross at the middle of the vertebral level in the pregnant state. On the other hand, in each disc level, the longitudinal veins were engorged bilaterally in the pregnant state. This may also explain

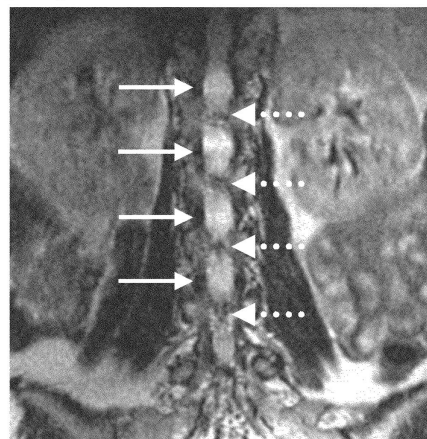
the spread of analgesic level during epidural anesthesia, because of a decrease in the leakage of local anesthetics through the foramen in pregnant women.

The fourth observation is that the compression of the subarachnoid space was more obvious at the lower lumbar spinal levels than at the other levels. It has been thought that the rate of paresthesia during spinal puncture is high in pregnant women.¹⁰ In our MR images, there was only limited subarachnoid space, and the nerve roots of the cauda equina were closely compressed and adjacent at the lower lumbar disc levels. This might contribute to the high incidence of paresthesia during spinal puncture in late pregnancy.

Furthermore, in the current study, we showed an interesting image, computer-processed into one image in alignment with the curvature of the ventral epidural space from multiple coronal images. This may be useful to understand the morphology of the spinal canal for spinal or epidural anesthesia or both.

Because the number of subjects studied in the current study was limited, we did not measure the area of the subarachnoid space at each level. However, the above findings were observed in all subjects. Our findings can promote a better understanding for performing spinal or epidural anesthesia or both in the pregnant state.

pregnant state



non-pregnant state



Fig. 4. Computerized coronal magnetic resonance images of the spinal canal between T12 and S1 in the pregnant and nonpregnant states. Multiple coronal images are computer-processed into one image in alignment with the curvature of the ventral epidural space. Those images show the curved surface with the ventral epidural space. The engorged epidural venous plexus in the ventral epidural space was observed between Th12 and S1 in the pregnant state, but not in the nonpregnant state. In the pregnant state, *arrows* indicate the engorged plexus in the ventral epidural space (*white arrows* = longitudinal veins; *dotted arrows* = crossed veins). The situation of the engorged epidural venous plexus resembles a ladder.

The authors thank Sumio Washiya, M.D. (President, Washiya Hospital, Ut-sunomiya, Toshihi, Japan), for generous support.

References

1. Barclay DL, Renegar OJ, Nelson EW Jr: The influence of inferior vena cava compression on the level of spinal anesthesia. *Am J Obstet Gynecol* 1968; 101:792-800
2. Greene NM: Distribution of local anesthetic solutions within the subarachnoid space. *Anesth Analg* 1985; 64:715-30
3. Scott DB: Inferior vena caval occlusion in late pregnancy and its importance in anaesthesia. *Br J Anaesth* 1968; 40:120-8
4. Datta S, Hurley RJ, Naulty JS, Stern P, Lambert DH, Concepcion M, Tulchinsky D, Weiss JB, Ostheimer GW: Plasma and cerebrospinal fluid progesterone concentrations in pregnant and non pregnant women. *Anesth Analg* 1986; 65:950-4
5. Hirabayashi Y, Shimizu R, Saito K, Fukuda H, Igarashi T: Acid-base state of cerebrospinal fluid during pregnancy and its effect on spread of spinal anaesthesia. *Br J Anaesth* 1996; 77:352-5
6. Igarashi T, Hirabayashi Y, Shimizu R, Saitoh K, Fukuda H, Suzuki H: The fiberoptic findings of the epidural space in the pregnant women. *ANESTHESIOLOGY* 2000; 92:1631-6
7. Hirabayashi Y, Shimizu R, Fukuda H, Saito K, Igarashi T: Soft tissue anatomy within the vertebral canal in pregnant women. *Br J Anaesth* 1996; 77:153-6
8. Takiguchi T, Okano T, Egawa H, Okuda Y, Saito K, Kitajima T: The effect of epidural saline injection on analgesic level during combined spinal and epidural anesthesia assessed clinically and myelographically. *Anesth Analg* 1997; 85:1097-100
9. Yamaguchi S, Takiguchi T, Tezuka M, Kitajima T: Epidural injection markedly compresses the subarachnoid space (abstract). *ANESTHESIOLOGY* 2004; 101:A1115
10. McAndrew CR, Harms P: Paraesthesiae during needle-through-needle combined spinal epidural *versus* single-shot spinal for elective caesarian section. *Anaesth Intensive Care* 2003; 31:514-7