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Wernicke encephalopathy complicating hyperemesis gravidarum after delayed thiamine therapy for suspected thiamine allergy: a case report and review of 39 published cases

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Case Report

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Abstract

Background: Hyperemesis gravidarum (HG) is a common cause of thiamine deficiency during pregnancy and may progress to Wernicke encephalopathy (WE). Most treatment delays arise from missed diagnosis, but iatrogenic hesitation over suspected thiamine allergy has rarely been examined.

Case presentation: We report a 35-year-old woman with HG at 15+4 weeks' gestation whose thiamine replacement was withheld for more than four weeks after a positive skin test at another hospital, despite no history of allergy. She later developed altered consciousness, blurred vision, and ataxia, with brain magnetic resonance imaging (MRI) showing symmetric hyperintensities in the thalami, frontal lobes, and dorsal brainstem. After multidisciplinary review concluded that the skin test was likely a false-positive irritant reaction, high-dose intravenous thiamine was administered without any allergic response; her mental status recovered within 24 hours. We also reviewed 39 published cases of WE secondary to HG identified in PubMed, Web of Science, CNKI, and Wanfang databases from January 2016 to June 2026 (40 cases including ours). The mean age was 26.9 years; vomiting began at a mean of 8.1 weeks and neurological symptoms at 15.9 weeks, after a mean of 7.1 weeks of vomiting. Only 55% had the complete classic triad; 85.3% of MRI scans were positive. Three mothers died (7.5%), all with delayed or inadequate thiamine replacement; 20% of patients had chronic neurological sequelae, including 17.5% with Korsakoff syndrome.

Conclusions: A single positive thiamine skin test without a history of hypersensitivity must not delay parenteral thiamine in pregnant patients with persistent vomiting and neurological symptoms.

Background

Hyperemesis gravidarum (HG), the severe form of nausea and vomiting of pregnancy, affects 0.3%–3.6% of pregnant women and is characterized by persistent vomiting, weight loss greater than 5% of pre-pregnancy body weight, dehydration, and ketonuria [1]. Prolonged inadequate intake and repeated vomiting deplete thiamine (vitamin B1) stores and may lead to Wernicke encephalopathy (WE). First described by Carl Wernicke in 1881, WE is an acute neurometabolic emergency. Untreated, WE has a mortality of up to 17%, and 85% of survivors are left with irreversible Korsakoff syndrome [2, 3].

The classic WE triad of altered mental status, ocular dysfunction, and ataxia is incomplete in about half of patients. In pregnancy, these symptoms are often attributed to morning sickness or fatigue, while atypical presentations such as drowsiness, hypersalivation, sudden visual loss, or flaccid paralysis are easily missed, resulting in diagnostic delay. Initial misdiagnosis rates of 75%–80% have been reported [4]. Although case reports have increasingly shown that WE in pregnancy is not exceptional, the only systematic review of WE complicating HG to date drew on cases reported up to May 2018 [12], and none has examined iatrogenic barriers to thiamine replacement — the very mechanism that caused the preventable delay in our patient.

Delay in treatment is usually attributed to missed diagnosis, but iatrogenic hesitation can also contribute. International guidelines do not mandate a thiamine skin test before administration, yet skin testing is still routine in some settings. As a result, some patients with no history of thiamine allergy are denied thiamine on the basis of a positive skin test. Here we report a case of WE secondary to HG in which the only apparent barrier to thiamine therapy was a falsely interpreted skin test, and we review 39 published cases for comparison.

Case Presentation

A 35-year-old woman, gravida 5 para 2, was transferred to the Third Affiliated Hospital of Guangzhou Medical University on May 12, 2026, at 15^{+4} weeks' gestation because of persistent nausea and vomiting of two months' duration. The pregnancy was conceived naturally. Vomiting began at 7 weeks of gestation and progressively worsened to 7–8 episodes daily with complete inability to eat, accompanied by an approximately 10-kg weight loss. She had been treated at another hospital with intravenous fluids, antiemetics, gastric protection, and supportive care. Laboratory tests there showed TSH 0.005 mIU/L, free T4 29.90 pmol/L, AST 102 U/L, ALT 137 U/L, urinary ketones (+++), and potassium 2.9 mmol/L. At 12 weeks of gestation, the outside hospital performed a thiamine skin test with 0.1 mL of a 10-fold dilution. Local erythema was recorded, but there were no clinical features of an immediate systemic hypersensitivity reaction. The hospital nonetheless interpreted the result as thiamine allergy and stopped further thiamine supplementation. At about 14 weeks she twice experienced brief episodes of delirium, limb spasms, and deep, rapid breathing, which resolved with symptomatic treatment. She denied any prior thiamine allergy, personal atopy, or family history of allergic disease.

On admission, her temperature was 36.0°C, pulse 122 beats/min, respiratory rate 22 breaths/min, and blood pressure 101/72 mmHg. She was conscious but markedly cachectic, with sunken eyes and dry, cracked lips. The fetal heart rate was 138 beats/min. Neurological examination was unremarkable. Urinary ketones were (++++) on dipstick. ALT was 123.1 U/L, AST 66.9 U/L, potassium 3.15 mmol/L, and sodium 132 mmol/L. Arterial blood gas analysis showed pH 7.488 and bicarbonate 19.3 mmol/L. Obstetric ultrasound revealed a complete atrioventricular septal defect in the fetus, with a nuchal translucency of 2.7 mm.

The patient was admitted for intravenous rehydration, liver protection, nutritional support, and prophylactic anticoagulation. Because the fetal anomaly was severe and the maternal condition was critical, termination of pregnancy was recommended, but the patient declined.

On hospital day 4, at 16^{+1} weeks' gestation, she suddenly became lethargic and confused, with generalized weakness, blurred vision, and inability to sit or stand. Examination showed a somnolent patient who could be aroused, grade IV limb muscle strength, and negative pathological reflexes. Emergent brain MRI demonstrated bilateral, symmetric, patchy hyperintense lesions in the frontal lobes, thalami, and dorsal brainstem, consistent with WE (Fig. 2A). Fundoscopy was normal. A multidisciplinary team of neurologists, pharmacists, obstetricians, and intensive care specialists reviewed the case and concluded that the outside hospital's thiamine skin test was not evidence of a true allergy. The patient had no history of atopy or drug hypersensitivity, no

systemic anaphylactic features, and the local erythema was most consistent with a non-specific irritant reaction or false-positive test rather than an IgE-mediated type I hypersensitivity response. The team recommended immediate high-dose thiamine replacement under close monitoring.

With resuscitation equipment at the bedside and continuous monitoring, a 100 mg intravenous thiamine test infusion was administered slowly. The infusion was uneventful, with no allergic reaction. She then received high-dose thiamine 200 mg intravenously every 8 hours for three days. Six hours after the first dose she became alert and oriented but was still unable to get out of bed; 24 hours later her mental status had fully recovered. On the third day of treatment she still had ataxia and gait instability. In view of the severe fetal anomaly and the risk of irreversible brain injury, the patient and her family consented to medical termination (mifepristone plus misoprostol). The abortion was uncomplicated. After the procedure, nausea and vomiting improved substantially and lower-limb weakness lessened, but hypersalivation persisted. She continued thiamine 250 mg intravenously once daily for two days, then 100 mg intramuscularly once daily, together with supportive care. MRI on day 8 showed marked reduction of the thalamic lesions (Fig. 2B). On day 10 she still needed assistance to walk because of gait instability. She was discharged on day 12 on oral vitamin B1, tapered from 300 mg once daily to a maintenance dose of 30 mg once daily.

At follow-up 22 days after treatment she was walking normally and independently. MRI repeated 36 days after treatment showed complete resolution of the previous lesions (Fig. 2C). Neurological examination at follow-up revealed no residual deficit. The patient received a full explanation of her illness and provided written authorization for publication. Her clinical course is summarized in Fig. 3.

Discharge diagnoses were: (1) pregnancy with Wernicke encephalopathy; (2) hyperemesis gravidarum with metabolic disturbance; (3) liver dysfunction; (4) gestational transient thyrotoxicosis; (5) advanced maternal age, multiparity; (6) mild anemia; (7) fetal complete atrioventricular septal defect; (8) gravida 5, para 2, 16^{+3} weeks, singleton pregnancy, after medical abortion.

Methods

Search strategy and selection criteria

This is a single-center case report combined with a literature review. The index case was admitted to the Third Affiliated Hospital of Guangzhou Medical University in May 2026 and met the ACOG criteria for HG (ICD-10 code O21.0). For the literature review, PubMed, Web of Science, CNKI, and Wanfang databases were searched from January 2016 to June 2026 using combinations of the terms: "hyperemesis gravidarum", "pregnancy", "Wernicke encephalopathy", "thiamine deficiency", and "Korsakoff syndrome", without language restrictions. The search window overlaps the final years of the previous systematic review by Oudman et al. [12] (search completed in May 2018) and extends it by eight years, while the inclusion of CNKI and Wanfang captured six Chinese-language case reports not retrievable in PubMed or Web of Science. We included reports describing at least one case of WE caused by thiamine deficiency secondary to HG with reasonably complete clinical, perinatal, treatment, and follow-up data. Duplicated reports and cases with missing key data were excluded. One author performed a deliberately liberal screen of titles and abstracts, so that all potentially relevant records were carried forward; potentially eligible articles were then assessed in full text by all authors for consensus, which mitigated the single-reviewer initial screen. Thirty-three reports describing 39 cases met the inclusion criteria; together with our patient, 40 cases were analyzed.

This case report was written according to the CARE guidelines [5]; the literature review followed the PRISMA 2009 statement [6].

Data extraction

A standardized data extraction form was used to collect age, gestational week at vomiting onset, gestational week at first neurological symptoms, pregnancy outcome (termination or maternal death), clinical manifestations (prodromal symptoms, classic triad, other symptoms), imaging results, thiamine regimen, and neurological outcome.

Diagnostic criteria

HG was diagnosed using ACOG Practice Bulletin No. 189 (2018) [7] and the Chinese expert consensus on diagnosis and clinical management of hyperemesis gravidarum (2015) [8]: persistent severe nausea and vomiting in early pregnancy (extending into mid-pregnancy) with inability to eat, dehydration, electrolyte disturbance, ketosis, and pre-pregnancy weight loss of at least 5%, after excluding other causes of vomiting (ICD-10 O21.0). WE was clinically diagnosed using the EFNS 2010 criteria [9]: at least two of nutritional deficiency risk (e.g., persistent vomiting), ocular signs, cerebellar ataxia, and altered consciousness or mental abnormalities; MRI was used to support the diagnosis. Korsakoff syndrome (KS) was diagnosed using ICD-11 code 5B5A.11 [10] and the thiamine deficiency consensus (Arts 2017) [11]: severe anterograde amnesia and confabulation persisting after resolution of acute WE symptoms, not restricted to alcohol-related disease. Thiamine treatment was operationalized as an initial dose of less than 500 mg/day as low dose and 500 mg/day or more as high dose [12], following the Royal College of Physicians recommendation (500 mg parenterally three times daily for 2–3 days, then 250 mg daily) [13] and EFNS 2010 guidance (200 mg intravenously three times daily as the minimum effective high dose) [9]. Both guidelines emphasize "thiamine before glucose."

Statistical analysis

Descriptive statistics were calculated with SPSS 26.0. Normally distributed continuous variables are reported as mean ± standard deviation (range), and categorical variables as number and percentage.

Results

Literature search

The literature search was completed by June 30, 2026 (Fig. 1). After screening, 33 articles [14–46] describing 39 cases of WE secondary to HG were included. Three of these were multi-case reports describing four [15], three [43], and two [38] patients, respectively. Of the four cases described by Hou et al. [43], one did not meet the inclusion criteria because of incomplete clinical and outcome data, and was therefore excluded; the remaining three were included.

Baseline characteristics and pregnancy outcomes

A total of 40 patients were included, nine from China and 31 from other countries. Mean maternal age was 26.9 ± 6.4 years (range 15–42). Vomiting began at a mean of 8.1 ± 2.5 weeks (range 4–15), neurological symptoms appeared at 15.9 ± 5.5 weeks (range 7–34), and the mean duration of vomiting before neurological presentation was 7.1 ± 4.6 weeks (range 1–22).

Pregnancy outcomes were as follows: 17 patients (42.5%, 17/40) terminated the pregnancy in the first or second trimester because of critical maternal condition or fetal factors; 23 (57.5%, 23/40) continued the pregnancy to the third trimester or delivery, of whom 18 (78.3%, 18/23) delivered at term and five (21.7%, 5/23) preterm. Neonatal complications included fetal growth restriction in four (17.4%, 4/23) and Dandy-Walker malformation in one; the remaining neonates did well. Maternal death occurred in three cases (7.5%, 3/40). Details are shown in Table 1.

Table 1
Baseline characteristics and pregnancy outcomes of 40 women with Wernicke encephalopathy secondary to hyperemesis gravidarum.

Case	Source	Year	Country	Age (years)	Vomiting onset (weeks)	Neurological symptom onset (weeks)	Vomiting duration (weeks)	Pregnancy termination (1 = yes, 0 = no)	Maternal death (1 = yes, 0 = no)
1	Damaso et al. [14]	2020	Brazil	25	9	13	4	0	0
2	Jebali et al. [15]	2017	Tunisia	21	6	12	6	0	0
3	Jebali et al. [15]	2017	Tunisia	28	13	18	5	0	0
4	Jebali et al. [15]	2017	Tunisia	22	10	15	5	0	0
5	Jebali et al. [15]	2017	Tunisia	23	8	16	8	1	0
6	Bannour et al. [16]	2024	Tunisia	30	-	34	-	0	0
7	Szablewska et al. [17]	2025	Poland	21	8	15	7	0	0
8	Pagaling et al. [18]	2021	Philippines	36	6	10	4	0	0
9	Mohamed et al. [19]	2025	Malaysia	42	12	16	4	0	0
10	Gan et al. [20]	2025	Malaysia	26	11	15	4	0	0
11	Stephens et al. [21]	2019	USA	15	-	13	-	0	0
12	Patel et al. [22]	2023	USA	16	15	21	6	0	0
13	Pham et al. [23]	2023	USA	25	11	16	5	1	0
14	Olmsted et al. [24]	2023	USA	33	12	15	3	1	0
15	Punal et al. [25]	2022	USA	19	8	17	9	0	0
16	Shah et al. [26]	2020	USA	18	6	18	12	1	0
17	Spiegel et al. [27]	2022	USA	18	4	10	6	1	0
18	Stahl et al. [28]	2018	USA	27	-	17	-	1	0
19	Bensaid et al. [29]	2025	Morocco	38	-	27	-	0	0
20	Nasri et al. [30]	2020	Morocco	30	6	10	4	1	0
21	Ngene et al. [31]	2016	South Africa	28	6	11	5	1	1
22	Mahato et al. [32]	2026	Nepal	34	8	16	8	0	0
23	Mangione et al. [33]	2024	Italy	33	11	12	1	0	0
24	Tigga et al. [34]	2025	India	24	6	12	6	0	0
25	Aneja et al. [35]	2019	India	20	6	23	17	1	0
26	Kirty et al. [36]	2021	India	26	5	18	13	0	0
27	Mishra et al. [37]	2019	India	30	10	16	6	0	0
28	Grover et al. [38]	2024	India	29	6	12	6	1	0

Case	Source	Year	Country	Age (years)	Vomiting onset (weeks)	Neurological symptom onset (weeks)	Vomiting duration (weeks)	Pregnancy termination (1 = yes, 0 = no)	Maternal death (1 = yes, 0 = no)
29	Grover et al. [38]	2024	India	23	8	16	8	1	0
30	Singh et al. [39]	2024	India	20	8	17	9	0	0
31	Ye et al. [40]	2023	India	33	8	16	8	0	0
32	Jiang et al. [41]	2024	China	35	6	7	1	1	0
33	Zhang et al. [42]	2024	China	25	8	16	8	1	0
34	Hou et al. [43]	2022	China	30	5	13	8	0	0
35	Hou et al. [43]	2022	China	34	6	25	19	0	0
36	Hou et al. [43]	2022	China	24	8	30	22	0	0
37	Wang et al. [44]	2020	China	31	8	12	4	1	1
38	Liao et al. [45]	2019	China	25	8	10	2	1	1
39	Lou et al. [46]	2018	China	24	8	12	4	1	0
40	Present case	2026	China	35	7	14	7	1	0

Clinical manifestations and imaging

All 40 patients presented with nausea and vomiting as the first symptom (100%). Other prodromal symptoms included diplopia (10%, 4/40), blurred vision (10%, 4/40), vertigo (5%, 2/40), and photophobia (5%, 2/40).

Among the classic WE triad, altered mental status was most common (95%, 38/40), followed by ataxia (77.5%, 31/40) and ocular dysfunction (72.5%, 29/40). Only 55% (22/40) presented with the complete triad. Non-classical symptoms included seizures, paresthesia, hypersalivation, rigidity, and hearing loss.

Imaging was performed in 36 patients (90%, 36/40). Thirty-four underwent brain MRI (94.4%, 34/36) and two underwent head CT (5.6%, 2/36). MRI was positive in 29 of 34 patients (85.3%, 29/34). Details are shown in Table 2.

Table 2
Clinical manifestations, imaging findings, treatment, and outcomes of 40 women with Wernicke encephalopathy secondary to hyperemesis gravidarum.

Case	Source	Prodromal symptoms	Altered mental status[a]	Ocular signs[b]	Ataxia[c]	Other symptoms	Brain MRI	High-dose thiamine (≥ 500 mg/day)**	Recovery time	Neurological sequelae
1	Damaso et al. [14]		Yes	Yes	Yes		Positive	Yes	7 days	
2	Jebali et al. [15]		Yes	Yes	No		Not performed	Unknown	1 year	
3	Jebali et al. [15]	Diplopia	Yes	Yes	Yes		Negative	Unknown	6 months	
4	Jebali et al. [15]	Diplopia	No	Yes	Yes		Positive	Unknown	2 weeks	
5	Jebali et al. [15]		No	Yes	Yes		Negative	Unknown	1 year	
6	Bannour et al. [16]		Yes	No	No	Seizures	Positive	Yes	6 months	
7	Szablewska et al. [17]		Yes	Yes	Yes		Positive	No	Postpartum	
8	Pagaling et al. [18]	Diplopia	Yes	Yes	Yes		Positive	Yes	> 1 year	KS*
9	Mohamed et al. [19]	Blurred vision	Yes	Yes	Yes		Not performed (CT negative)	Yes	Postpartum	
10	Gan et al. [20]		Yes	Yes	No		Positive	Yes	2 months postpartum	
11	Stephens et al. [21]		Yes	No	Yes		Positive	Yes	Postpartum	
12	Patel et al. [22]		Yes	No	Yes	Hearing impairment	Positive	Yes	14 months postpartum	
13	Pham et al. [23]		Yes	No	No		Positive	Yes	1 year postpartum	
14	Olmsted et al. [24]		Yes	Yes	Yes		Positive	No	Unknown	KS
15	Punal et al. [25]		Yes	Yes	Yes		Positive	Yes	Postpartum	
16	Shah et al. [26]	Vertigo	Yes	Yes	Yes		Positive	Yes	Postpartum	
17	Spiegel et al. [27]		Yes	Yes	Yes		Positive	No	5 days	
18	Stahl et al. [28]		Yes	Yes	Yes	Paresthesia	Positive	Yes	3 days	
19	Bensaid et al. [29]		Yes	Yes	Yes	Paresthesia	Positive	Yes	Unknown	
20	Nasri et al. [30]	Diplopia; Photophobia	Yes	No	Yes	Reduced lower-limb sensation	Positive	Yes	6 months	
21	Ngene et al. [31]	Headache; Photophobia	Yes	Yes	No		Not performed	No (not supplemented)	Died	
22	Mahato et al. [32]		Yes	Yes	Yes		Positive	Yes	Postpartum	
23	Mangione et al. [33]	Headache; Blurred vision	Yes	Yes	Yes		Positive	Yes	> 2 years	Residual gait instability
24	Tigga et al. [34]		Yes	Yes	Yes		Positive	Yes	Postpartum	
25	Aneja et al. [35]		Yes	No	Yes		Positive	No	6 weeks postpartum	

Footnotes: *KS, Korsakoff syndrome. **High-dose thiamine defined as ≥ 500 mg/day. aAltered mental status: changes in mental state or consciousness. bOcular signs: nystagmus, ophthalmoplegia, optic disc edema, retinal hemorrhage, or visual loss. cAtaxia: unstable standing, abnormal gait, loss of balance, or inability to walk independently.

Case	Source	Prodromal symptoms	Altered mental status[a]	Ocular signs[b]	Ataxia[c]	Other symptoms	Brain MRI	High-dose thiamine (≥ 500 mg/day)**	Recovery time	Neurological sequelae
26	Kirty et al. [36]		Yes	Yes	Yes		Positive	Yes	> 1 year	KS
27	Mishra et al. [37]		Yes	Yes	Yes		Not performed	Yes	> 1 year	KS
28	Grover et al. [38]		Yes	Yes	Yes	Hypersalivation; Rigidity	Positive	Yes	> 4 years	KS
29	Grover et al. [38]		Yes	Yes	Yes		Not performed	Yes	> 2 years	
30	Singh et al. [39]		Yes	Yes	Yes		Positive	Yes	2 weeks	
31	Ye et al. [40]	Blurred vision	Yes	Yes	Yes		Positive	No	2 weeks	
32	Jiang et al. [41]	Vertigo	Yes	Yes	Yes		Positive	Yes	1 month	
33	Zhang et al. [42]		Yes	No	Yes	Seizures	Negative	No	Postpartum	
34	Hou et al. [43]		Yes	No	No		Positive	Yes	> 1 year	KS
35	Hou et al. [43]		Yes	No	Yes		Positive	Yes	Postpartum	
36	Hou et al. [43]		Yes	Yes	No		Negative	No	> 2 years	KS and mental dullness
37	Wang et al. [44]		Yes	Yes	Yes		Not performed (CT positive)	No (delayed supplementation)	Died	
38	Liao et al. [45]	Blurred vision	Yes	Yes	No	Seizures	Negative	No (delayed supplementation)	Died	
39	Lou et al. [46]		Yes	No	No		Positive	Yes	1 month	
40	Present case		Yes	No	Yes	Hypersalivation	Positive	Yes	3 weeks	

Footnotes: *KS, Korsakoff syndrome. **High-dose thiamine defined as ≥ 500 mg/day. aAltered mental status: changes in mental state or consciousness. bOcular signs: nystagmus, ophthalmoplegia, optic disc edema, retinal hemorrhage, or visual loss. cAtaxia: unstable standing, abnormal gait, loss of balance, or inability to walk independently.

Treatment and prognosis

Recovery time varied widely, from a few days to several years. Chronic neurological sequelae persisted in eight patients (20%, 8/40): seven (17.5%, 7/40) had persistent memory impairment 1–4 years after delivery, fulfilling the criteria for Korsakoff syndrome; one (2.5%, 1/40) still had gait instability more than 2 years postpartum.

Thiamine dose was recorded in 36 cases. Twenty-six (72.2%, 26/36) received high-dose thiamine (≥ 500 mg/day), nine (25.0%, 9/36) received low-dose thiamine (< 500 mg/day), and one (2.8%, 1/36) received no thiamine. All three maternal deaths were associated with inadequate thiamine replacement: one received none, and two received clearly insufficient doses.

Fatal cases

Case 21

[31], at 11 weeks' gestation, had WE that was not diagnosed in time and received no thiamine. The disease progressed rapidly with severe electrolyte disturbance and multi-organ damage, and she died of respiratory failure.

Case 37

[44], at 12 weeks' gestation, had delayed WE diagnosis and an inadequate thiamine dose, and eventually died of multi-organ failure.

Case 38

[45], at 10 weeks' gestation, had early diagnostic and treatment delay. At diagnosis there was already extensive cerebral cortex damage. She received a markedly insufficient thiamine dose, and large volumes of glucose were infused before adequate thiamine replacement, causing rapid deterioration. Autopsy

revealed fatty liver, hyperemesis gravidarum-related metabolic dysfunction, enteritis, and interstitial pneumonia, leading to cardio-respiratory failure.

Discussion

Mechanism of WE in hyperemesis gravidarum

Wernicke encephalopathy is rare in pregnancy, and most cases are preventable with early thiamine replacement. Thiamine is an essential cofactor for energy metabolism (pyruvate dehydrogenase, α-ketoglutarate dehydrogenase); body stores last only about 18 days, and deficiency can develop within 2–3 weeks of interrupted intake [2]. Pregnancy is a state of physiological hypermetabolism, with thiamine requirements increasing from 1.1 mg/day in the non-pregnant state to 1.4 mg/day [47]. HG causes sustained inadequate intake and usually exhausts stores within three weeks. When the tricarboxylic acid cycle is blocked, ATP production falls, lactate accumulates, and high-metabolic brain regions such as the mammillary bodies, medial thalamus, and periaqueductal gray are preferentially affected, leading to WE [48].

Clinical manifestations of WE in pregnancy

The early features of WE complicating HG are non-specific and easily overlooked. All 40 patients in this series first presented with nausea and vomiting (100%), and diplopia or blurred vision was seen in 10% each, consistent with Oudman and colleagues' systematic review showing a high frequency of prodromal visual symptoms [12]. These visual symptoms may be the first clue to impending WE.

Previous data show that only 8%–38% of WE patients have the complete classic triad [49], and mental status changes are the most common single feature. In our series, only 55% had the full triad, but altered mental status was present in 95%, ataxia in 77.5%, and ocular signs in 72.5%. The prominence of mental symptoms may reflect pregnancy-related metabolic vulnerability of the mammillary bodies and medial thalamus. Because peripheral neuropathy, seizures, hearing loss, and hypersalivation can also occur, any pregnant patient with HG and unexplained neuropsychiatric symptoms should receive empirical thiamine immediately, even when the triad is incomplete.

Diagnosis and early recognition

WE diagnosis rests primarily on characteristic clinical features. The EFNS guidelines require at least two of the following: (1) nutritional deficiency risk factor (e.g., alcohol misuse, persistent vomiting); (2) ocular signs (e.g., nystagmus, gaze palsy); (3) cerebellar ataxia; and (4) altered consciousness or mild mental abnormalities [9]. In pregnancy, WE is most often seen in HG, especially after 3–4 weeks of inability to eat or drink. Altered mental status should raise strong suspicion; if accompanied by nystagmus or ataxia, the diagnosis is usually clear.

The time course of WE in HG is fairly consistent. In our series, vomiting began at a mean of 8.1 weeks and neurological symptoms at 15.9 weeks, after about 7 weeks of vomiting, closely matching Oudman and colleagues' systematic review, in which thiamine depletion developed between 10 and 15 weeks of gestation after a median of 7 weeks of vomiting [12]. This pattern is consistent with thiamine stores lasting only 2–3 weeks. Our data suggest that clinicians should be most alert once vomiting has lasted beyond 7 weeks and gestation approaches 15 weeks. Because neurological symptoms usually appear 2–7 weeks after vomiting onset and the triad is often incomplete [50], clinical recognition is often delayed. Any patient with persistent vomiting beyond 10 weeks and unexplained neurological findings should receive empirical thiamine without waiting for the full triad.

Brain MRI is an important supportive investigation. Its reported sensitivity is about 53% and its specificity 93% [51]. Typical T2/FLAIR sequences show bilateral symmetric hyperintensity in the mammillary bodies, around the third and fourth ventricles, medial thalamus, and midbrain tectum. CT has a low early detection rate (13%) [51]. In our series, 90% had imaging and 94.4% of those had MRI; MRI was positive in 85.3%. This supports the EFNS position that WE is a clinical diagnosis and a negative MRI does not exclude it. Imaging should not delay treatment in a pregnant patient with severe vomiting and neurological symptoms.

Outcomes

In this series, 42.5% of patients terminated the pregnancy in the first or second trimester because of critical maternal condition or fetal factors; 57.5% continued to the third trimester, with 78.3% term and 21.7% preterm deliveries. Neonatal complications were mainly fetal growth restriction (17.4%) and one case of Dandy-Walker malformation; most other neonates did well. The maternal mortality rate was 7.5% (3/40), similar to Oudman and colleagues' systematic review (about 5% mortality and 50% pregnancy loss) [12]. The slightly higher live-birth proportion in our cohort may reflect the benefit of earlier thiamine replacement in recent reports. Pregnancy terminations clustered around the WE peak window (about 15 weeks and > 7 weeks of vomiting), suggesting that maternal store depletion and diagnostic delay together increase the risk of adverse outcomes.

Recovery time varied widely. Chronic neurological sequelae persisted in 20% of patients, including 17.5% with Korsakoff syndrome and 2.5% with gait instability beyond 2 years. EFNS guidelines state that although acute ocular signs and altered consciousness can be reversed with thiamine, neuronal necrosis in the mammillary bodies and medial thalamus is often irreversible [9]. Korsakoff syndrome and chronic gait ataxia are, to a large extent, consequences of diagnostic delay. The Korsakoff rate in our cohort (17.5%) is lower than that reported in classic alcohol-related WE, possibly because pregnant patients tend to receive thiamine relatively promptly once symptoms are recognized; however, the persistence of gait and memory problems indicates that some structural damage extends beyond the window of metabolic repair. Patients who received prompt high-dose intravenous thiamine generally had better perinatal and neurological outcomes. Early recognition and adequate dosing largely determine whether WE resolves or progresses to chronic Korsakoff syndrome.

Thiamine replacement and suspected thiamine allergy

Adequate thiamine replacement is the key to stopping disease progression. In this series, the thiamine dose was recorded in 36 patients: 26 (72.2%, 26/36) received high-dose (≥ 500 mg/day) intravenous thiamine, nine (25.0%, 9/36) received low-dose (< 500 mg/day), and one (2.8%, 1/36) received none. All three deaths occurred in the low-dose or no-thiamine group, although the severity of underlying illness is an unavoidable confounder.

Thiamine dosing is not standardized. For acute WE, common regimens include the Royal College of Physicians recommendation of 500 mg parenterally three times daily for 2–3 days, then 250 mg daily until symptoms plateau [13], and the EFNS 2010 recommendation of 200 mg intravenously three times daily as a therapeutic dose [9]. Both guidelines stress that glucose-containing fluids should be given only after thiamine.

Our index case illustrates the problem of suspected "thiamine allergy." Thiamine was withheld for more than four weeks after a positive skin test, ultimately leading to WE. True thiamine allergy is extremely rare. Although skin testing before parenteral thiamine is not required by any international guideline, it remains routine practice in some hospitals, including our patient's referring hospital; this patient had no personal or family atopy, no history of drug rash or anaphylaxis, and no systemic features after the test. Thiamine skin tests remain controversial; thiamine can cause non-specific local irritation, producing false-positive results that do not reflect type I hypersensitivity. Current international guidelines (EFNS, Royal College of Physicians) do not mandate routine skin testing, and in suspected WE the priority is early thiamine replacement. Compared with the high risk of death or permanent disability from untreated WE, the theoretical risk of an unproven allergy is small. In this case, a graded-dose strategy with anaphylaxis precautions and continuous monitoring allowed safe infusion of high-dose thiamine.

In practice, thiamine should not be withheld because of a remote possibility of allergy; doing so risks permanent maternal neurological injury and adverse fetal outcomes.

Conclusions

Wernicke encephalopathy is an uncommon but treatable complication of hyperemesis gravidarum; delayed diagnosis and treatment often leave permanent neurological sequelae. For high-risk pregnant women with persistent vomiting and severe malnutrition, prophylactic thiamine should be considered. Once vomiting exceeds 7 weeks or neurological symptoms appear, high-dose intravenous thiamine must be started immediately to avoid permanent brain injury or death. A single positive thiamine skin test without a history of hypersensitivity should not be allowed to delay life-saving thiamine replacement.

Abbreviations

ACOG
American College of Obstetricians and Gynecologists
CT
Computed tomography
EFNS
European Federation of Neurological Societies
FLAIR
Fluid-attenuated inversion recovery
HG
Hyperemesis gravidarum
ICD
International Classification of Diseases
KS
Korsakoff syndrome
MRI
Magnetic resonance imaging
PRISMA
Preferred Reporting Items for Systematic Reviews and Meta-Analyses
T2WI
T2-weighted imaging
WE
Wernicke encephalopathy

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of The Third Affiliated Hospital, Guangzhou Medical University[IRB-2026-034]. Written informed consent for participation was obtained from the patient. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Written informed consent for publication of this case report and the accompanying brain MRI images (Fig. 2A–C) was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

CPK and LLL are co-first authors and contributed equally to this work. CPK conceived the case report and drafted the manuscript. LLL, together with YW and DHF, collected the clinical data and imaging images. DJC supervised the obstetric management and critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Data Availability

The raw clinical dataset supporting the index case is not publicly available because of patient privacy restrictions; de-identified summary data may be obtained from the corresponding author upon reasonable request. All data analyzed in the accompanying review of 39 published cases are extracted from previously published reports, which are cited in the reference list; no new primary data were generated for that part of the work.

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Figures

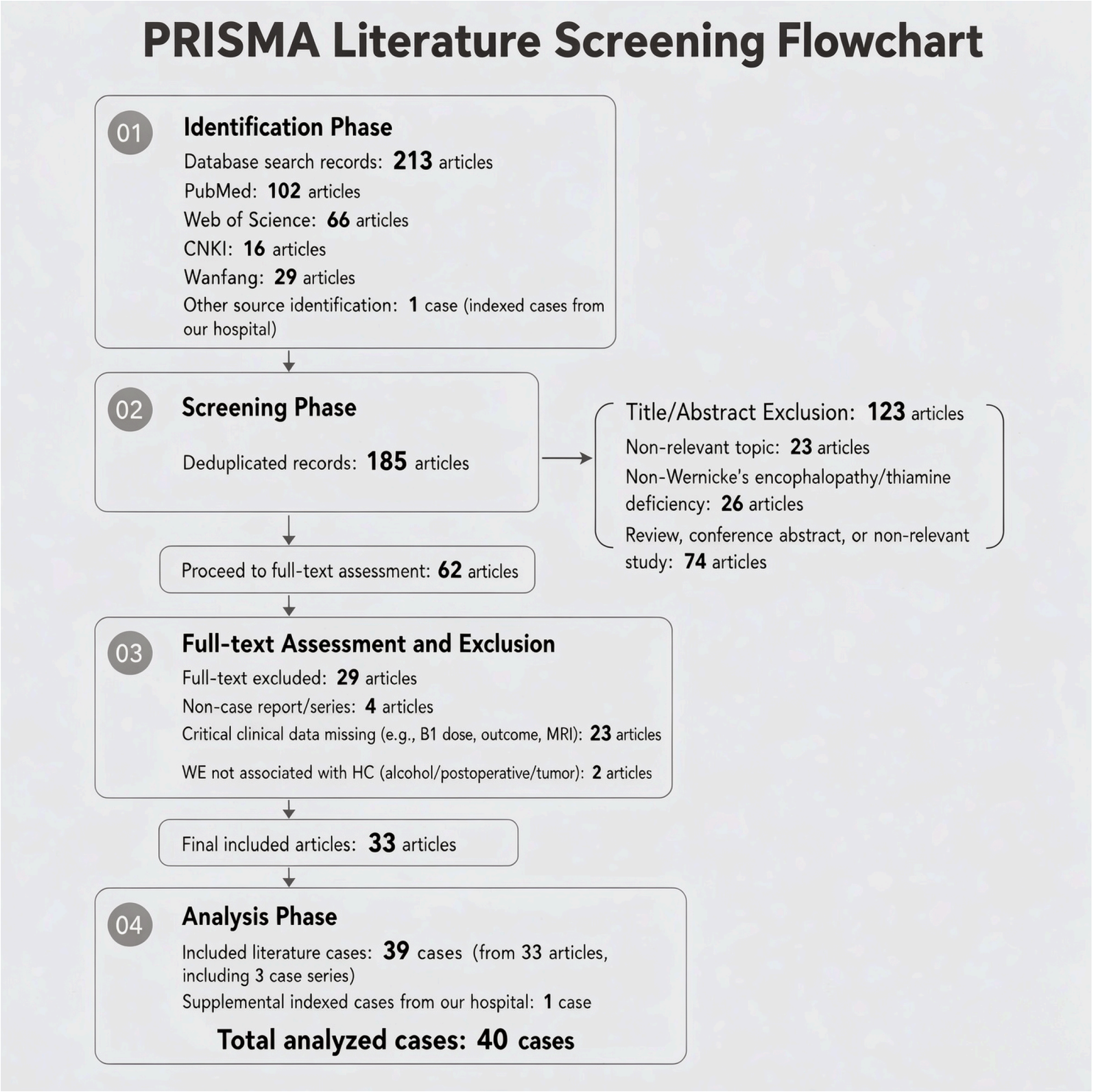


Figure 1

PRISMA 2009 flow diagram of the literature search. Databases searched were PubMed, Web of Science, CNKI, and Wanfang (January 2016–June 2026). A total of 213 records were identified, 185 remained after de-duplication, 62 were assessed in full text, and 33 reports (39 cases) were included for analysis. The index patient is reported separately.

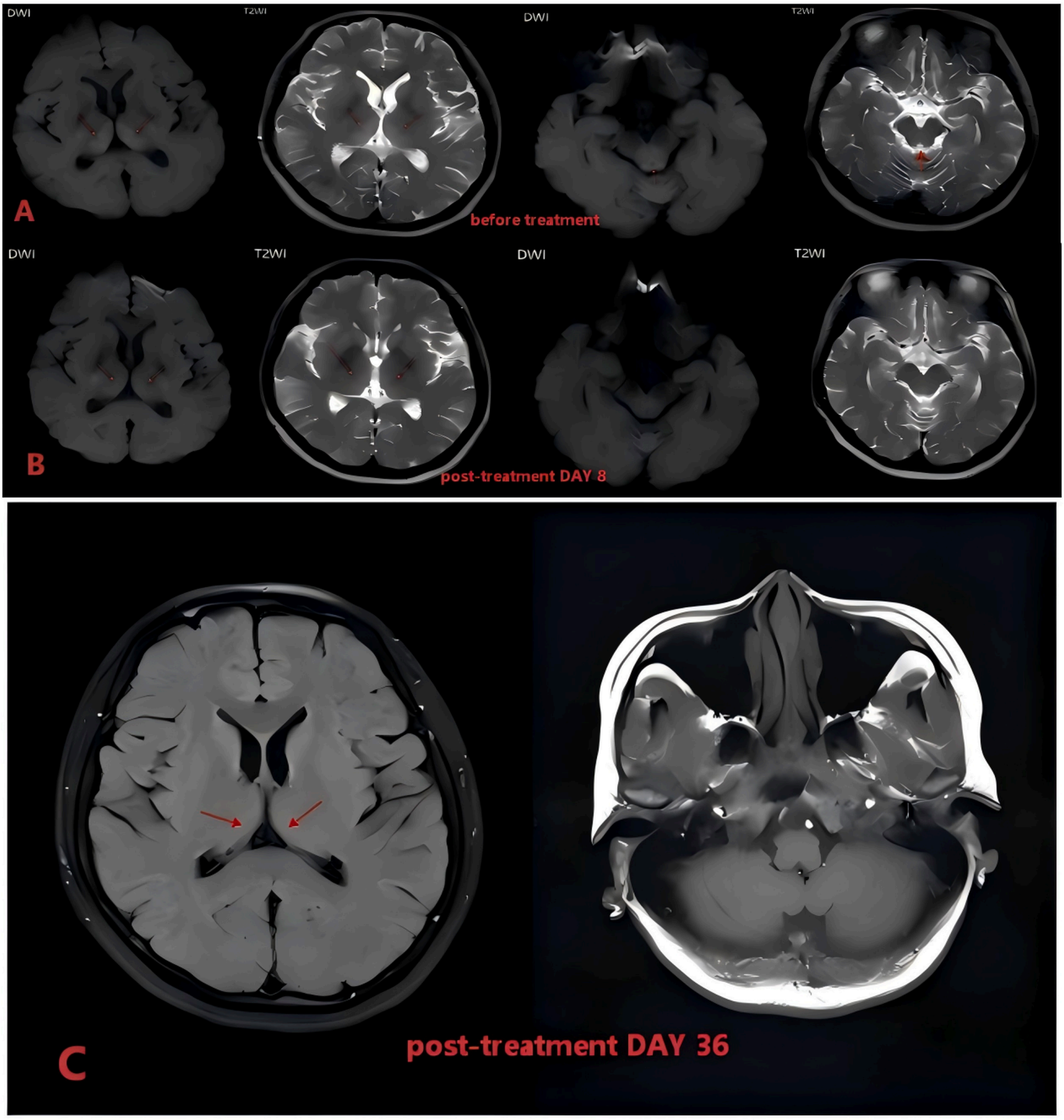


Figure 2

Brain MRI of the index patient. (A) Before treatment: bilateral symmetric hyperintense lesions in the frontal lobes, thalami, and dorsal brainstem (DWI and T2WI sequences). (B) After 8 days of treatment: marked reduction of thalamic lesions. (C) After 36 days: complete resolution of the previous abnormal high-signal lesions in the thalami and brainstem.

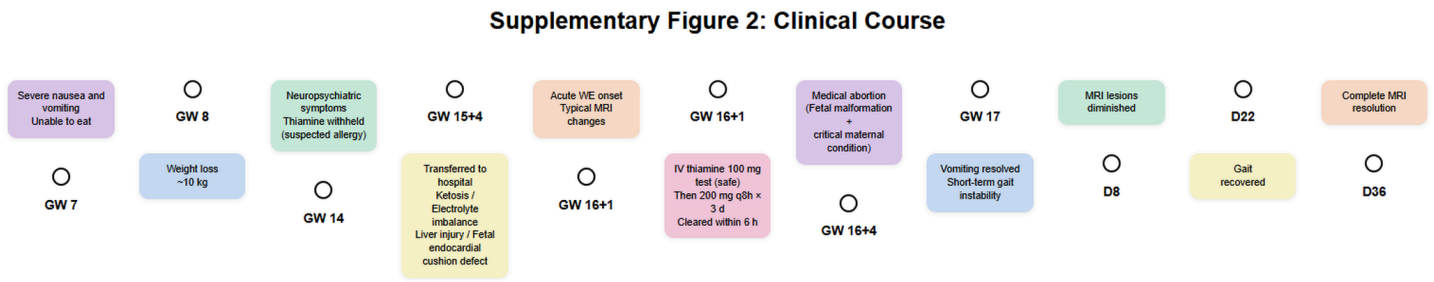


Figure 3

Timeline of the clinical course of the index patient with hyperemesis gravidarum and Wernicke encephalopathy. GW, gestational week; IV, intravenous; MRI, magnetic resonance imaging; WE, Wernicke encephalopathy.

Supplementary Files

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- CAREchecklist20261012.docx