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GROUP B *STREPTOCOCCUS MENINGITIS* IN AN ADULT WOMAN WITH TYPE 2 DIABETES AND ETHMOID ROOF DEFECT. IMPACT ON "FRONTAL" COGNITIVE FUNCTIONS.

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ABSTRACT

Background: Community-acquired bacterial meningitis in adults represents one of the most severe infectious diseases worldwide with potentially life-threatening medical complications. Several infectious agents can cause acute meningitis. Although group B *Streptococcus* is more prevalent in newborns, infection can also lead to meningitis in older adults, particularly those with underlying health issues.

Case Description: A 53-year-old woman with a body mass index of 28.7 kg/m^2, type 2 diabetes mellitus, and dyslipidaemia presented to the emergency department of Santa Maria della Stella Hospital (Orvieto, Italy) with confusion, low-grade fever, echolalia, and hyperglycaemia. Computed tomography scans of the brain revealed a hypodensity in the left anterior frontal lobe and an osteodural defect of the rhinobase. Meningitis was suspected and empiric broad-spectrum antibiotic therapy with corticosteroids and insulin were administered while the results of the cerebrospinal fluid analysis confirmed the diagnosis of group B *Streptococcus* meningitis. Repeat imaging at 48 hours revealed enlargement of the hypodense lesion. The frontal assessment battery indicated deficits in executive functions. Prompt treatment led to rapid clinical improvement. Following the restoration of euglycemic status and hemodynamic stabilization, a follow-up magnetic resonance imaging confirmed the ischaemic lesion and showed cerebrospinal fluid in the sella turcica. The patient was then transferred to neurorehabilitation.

Conclusions: The complex interactions among multiple risk factors resulted in an atypical clinical case of group B *Streptococcus* meningitis, which was promptly treated with empiric antibiotic therapy to mitigate neurocognitive deficits.

KEYWORDS

Cerebral vasculopathy, cognitive impairment, GBS meningitis, osteodural defect, type 2 diabetes

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LEARNING POINTS

- Group B *Streptococcus* can cause meningitis in adults with poorly controlled type 2 diabetes mellitus and should be promptly treated with empiric broad-spectrum antibiotics.
- An osteodural defect of the ethmoid roof together with idiopathic intracranial hypertension may result in empty sella turcica and CSF rhinorrhoea, promoting the dissemination of the pathogen.
- Meningitis patients with pre-existing diabetic cerebral vasculopathy may develop cerebrovascular complications and cognitive impairments.

INTRODUCTION

Bacterial meningitis is a life-threatening condition with an estimated annual incidence ranging from 30 to 100 cases per 100,000 individuals, contributing to approximately 200,000 deaths globally[1]. Survivors may experience long-term complications such as hearing loss, epilepsy, visual impairment, and focal neurological deficits. *Streptococcus pneumoniae* and *Neisseria meningitidis* are among the most common bacterial strains responsible for adult community-acquired meningitis[2]. Conversely, group B *Streptococcus* (GBS), or *Streptococcus agalactiae* is a leading cause of bacterial meningitis in neonates and infants but rarely causes meningitis in adults. GBS is a commensal bacterium residing in the respiratory tract, as well as the genitourinary system and intestine. However, GBS may become pathogenic in certain clinical conditions[3,4]. GBS may colonize the nasopharynx, enter the central nervous system (CNS), and invade the meninges, leading to an abnormal local inflammatory response[5]. The risk of developing GBS meningitis may increase for individuals with severe chronic conditions. Notably, the prevalence of GBS meningitis is nearly doubled in diabetic patients. Specifically, poorly controlled glycaemia, insulin resistance, systemic low-grade inflammation, and decreased cellular immunity increase susceptibility to infections in such populations[6]. Furthermore, diabetes-related endothelial dysfunction is closely linked to cerebrovascular disease, and evidence suggests that meningeal inflammation can exacerbate preexisting vasculopathy, increasing the risk of cerebrovascular complications[7,8]. Here, we present a clinical case of GBS meningitis with atypical symptomatology in an adult woman with a rare osteodural defect of the ethmoid roof and type 2 diabetes mellitus (T2DM), resulting in cerebrovascular complications and "frontal" cognitive impairment.

CASE DESCRIPTION

A 53-year-old female (body mass index 28.7 kg/m^2) with a history of T2DM and dyslipidaemia with poor adherence to insulin and statin therapy, was admitted to the emergency department at Santa Maria della Stella Hospital (Orvieto, Italy) for confusion and hyperglycaemia. Her husband reported that she had symptoms of mild rhinorrhoea and low-grade fever followed by vomiting the evening before admission. Vital signs indicated hypotension with a blood pressure of 90/60 mmHg, heart rate of 100 bpm, oxygen saturation of 90%, and a body temperature of 37.5°C. The Glasgow coma scale score was 14/15. On physical examination, breath sounds were normal, and no pathological cardiac murmurs were heard. Her pupils were equal and reactive to light. No signs of focal neurological alterations or nuchal rigidity were observed. Echolalia was noticed during unstructured conversations.

Laboratory tests showed a white blood cell count of 15.65 × 10^3/µl with 93.9% neutrophils and C-reactive protein 25.65 mg/dl (normal <0.50 mg/dl). Glucose was 467 mg/dl and HbA1c was 7.1%, confirming poorly controlled T2DM. Hepatic and renal function biomarkers were unremarkable (AST 12 IU/l and ALT 14 IU/l, gamma-GT 25 IU/l, and estimated glomerular filtration rate (eGFR) 70ml/min/1.73m^3, respectively) while hyponatraemia (127 mmol/l) was detected *(Table 1)*. Arterial blood gas analysis showed: pO_2 70 mmHg, pCO_2 31 mmHg, HCO_3- 19 mmol/l, and a pH of 7.27 with lactate levels of 2.5 mmol/l, indicating metabolic acidosis. The antigenic swab for severe acute respiratory syndrome SARS-CoV-2 was negative. The bedside chest X-ray was unremarkable. Meningitis was suspected despite the atypical clinical presentation, and a lumbar puncture was performed. Within 4 hours from admission, the patient received fluid resuscitation and empiric broad-spectrum antibiotic therapy with meropenem (1g q8hr) and vancomycin (1g q12hr), along with dexamethasone (4mg q12hr). Rapid-acting insulin therapy was promptly administered subcutaneously until plasma glucose reached 200 mg/dl. A computed tomography (CT) scan of the brain at admission revealed a hypodensity of approximately 13 mm in diameter located in the left anterior frontal lobe *(Fig. 1A)*. Moreover, the sagittal plane CT scan showed an osteodural defect of the ethmoid roof, which could have served as the portal of entry for the pathogen, and an enlargement of the sella turcica *(Fig. 1B)*. The cerebrospinal fluid (CSF) analysis revealed a GBS infection confirming the diagnosis of meningitis. After 48 hours, a repeat CT scan showed further enlargement of the preexisting hypodensity in the pre-frontal cortex, evidencing an acute ischaemic event *(Fig. 1C)*. Cardioembolism was excluded via transesophageal echocardiogram.

Cognitive functions were assessed using the Frontal Assessment Battery resulting in a score of 12/18 with attention deficit and impairment of executive functions.

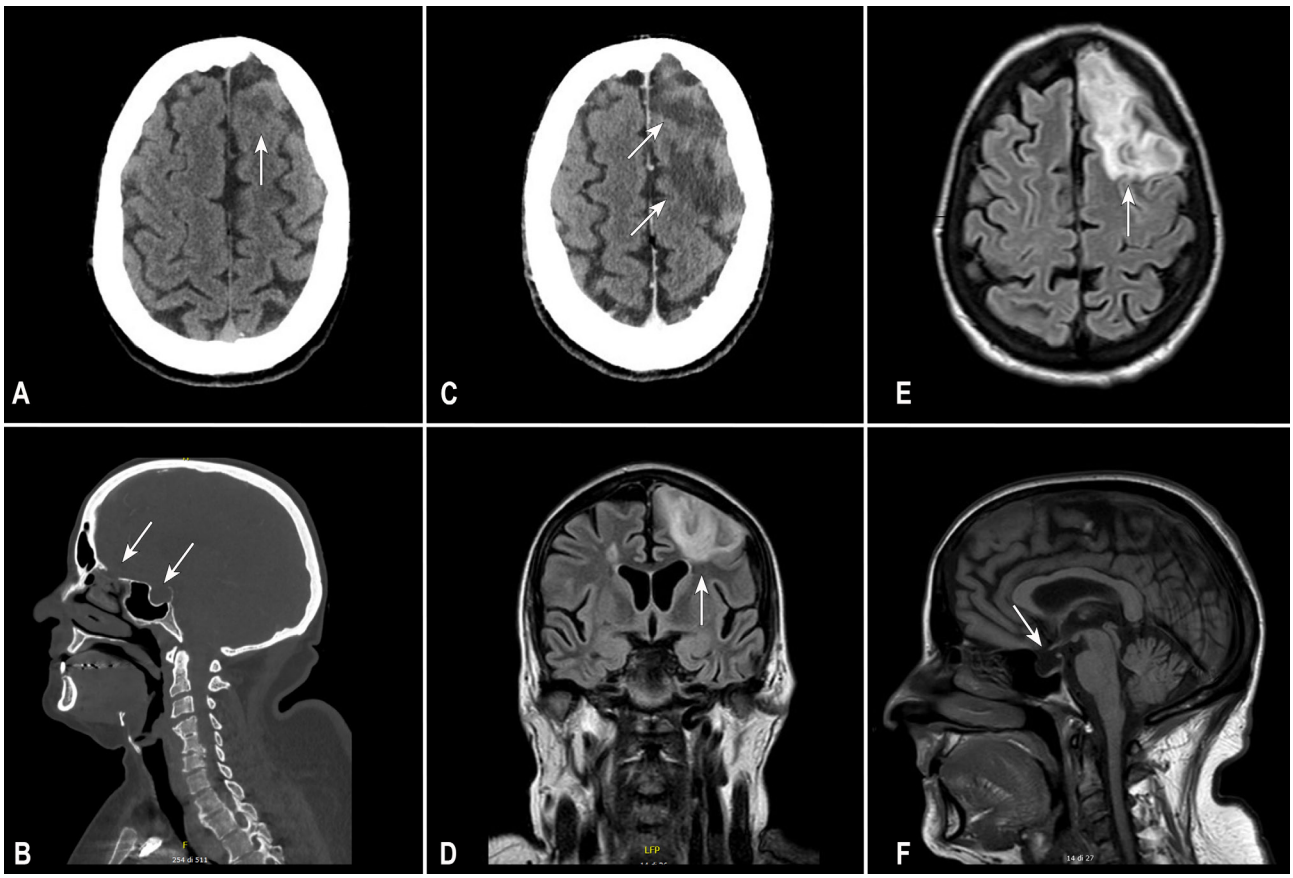

Figure 1. A) Axial CT scan of the brain revealing a small cortical-subcortical hypodensity of the left frontal lobe at admission; B) Sagittal CT scan showing the osteodural defect of the ethmoid roof and enlarged sella turcica at admission; C) Axial contrast-enhanced CT scan after 48 hours showing an increased hypodensity in the left pre-frontal cortex; D-E) 30-day follow-up: coronal and axial fluid-attenuated inversion recovery -weighted magnetic resonance imaging (FLAIR-MRI) confirming the wide hyperintense ischaemic lesion of the left pre-frontal area; F) T1-weighted MRI revealing the sella turcica filled with cerebrospinal fluid.

Furthermore, language impairment was characterized by anomia, neologisms, and semantic paraphasia.

The patient improved rapidly following the initiation of antibiotic therapy which was administered for 21 days. After haemodynamic stabilization and resolution of the infection, with subsequent improvement of inflammatory biomarkers and hyperglycaemia, as shown in *Table 1*, the patient was transferred to neurorehabilitation. A 30-day follow-up MRI confirmed the ischaemic lesion of the pre-frontal cortex *(Fig.1 D and E)*, supporting the described cognitive phenotype. MRI also revealed an enlargement of the sella turcica filled with CSF *(Fig. 1F)*. Manifestations of impaired executive functions persisted throughout hospitalization and at discharge. The patient was instructed to strictly adhere to the prescribed treatment plan to effectively manage plasma glucose levels, thereby reducing the risk of recurrent infections.

DISCUSSION

The pathogenesis of GBS meningitis in adults is influenced by various predisposing factors[9]. Poorly controlled glycaemia in diabetic patients may adversely affect the immune response and foster an environment conducive to opportunistic pathogens. Furthermore, a state of systemic low-grade inflammation associated with T2DM may exacerbate the inflammatory cascade that accompanies the onset and progression of such infections. Experimental models also suggest that the diabetic milieu promotes GBS survival, eliciting a greater inflammatory response compared to non-diabetic patients[10].

In the case of the diabetic 53-year-old woman presented here, clinical manifestations included hyperglycaemia, hypotension, low-grade fever, rhinorrhoea, and confusion, along with impaired language and executive functions, without signs of meningeal irritation. The preexisting diabetic cerebral vasculopathy, evidenced by the prefrontal hypodensity shown on the CT scan at admission, likely exacerbated the inflammatory response to the infection. These factors might have synergistically contributed to the development of acute cerebrovascular ischaemia, as indicated by the enlargement of the hypodensity 48 hours after admission. The damage to the prefrontal cortex likely resulted in executive function deficits and language impairment. In such clinical circumstances, empiric broad-spectrum antibiotic therapy was imperative to mitigate the risk of further neurological sequelae, considering the rapid progression of the pre-existing lesion. It is worth noting that although the poorly controlled T2DM acted as a predisposing and aggravating factor for both GBS infection and the cerebrovascular inflammatory response, the patient's rare ethmoid defect likely played a crucial role in

	Admission	96 hours	Discharge
Haemoglobin (g/dl)	15.2	13.0	12.1
Haematocrit (%)	44.2	38.2	35.6
White blood cells (×10^3/l)	15.65	14.67	7.73
Neutrophiles (%)	93.9	86.8	68.6
Lymphocytes (%)	2	6.7	24.5
Sodium (mmol/l)	127	145	137
Potassium (mmol/l)	4.7	3.9	3.7
AST (UI/l)	14	14	13
ALT (UI/l)	12	10	12
Gamma-GT (UI/l)	20	17	36
Creatinine (mg/dl)	0.88	0.54	0.47
eGFR (ml/min/1.73m^3)	70	-	-
Blood urea nitrogen (mg/dl)	52.9	50	48
C-reactive protein (mg/dl)	26.93	17	2
Procalcitonin (ng/dl)	1.47	0.43	0.05
Glucose (mg/dl)	467	201	90
HbA1c (%)	7.1	-	-

Abbreviations: AST, aspartate transferase; ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate; Gamma-GT, Gamma-glutamyl transferase.

Table 1. Laboratory results at admission, after 96 hours, and at discharge: results showed the resolution of hyperglycaemia and the normalization of electrolytes and inflammatory biomarkers.

the pathophysiology of such infection, by providing a portal of entry to the CNS[11]. To the best of our knowledge, data on such osteodural defects are limited, with the literature primarily consisting of case reports. Furthermore, the presence of idiopathic intracranial hypertension, as shown by the CSF in the sella turcica in the follow-up MRI, may have resulted in CSF rhinorrhoea and likely facilitated the intracranial dissemination of the pathogen[12].

CONCLUSIONS

A complex interplay among multiple pathophysiological factors synergistically contributed to an atypical case of GBS meningitis resulting in "frontal' neurocognitive sequelae. Therefore, the prompt initiation of empiric antibiotic therapy was imperative to prevent further deterioration of the executive function deficits.

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