

# ***Streptococcus agalactiae* meningitis presenting with cerebral infarction in an adult patient: Clinical case and review**

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## **Abstract**

Bacterial meningitis is an inflammation of the meninges associated with the invasion of bacteria. The etiologic agents vary by age group. Bacterial meningitis due to group B streptococcus (GBS) is common for the neonatal period but is deemed to be rare in adult patients. Since 2000, more than two-thirds of all cases occur in adults, which is becoming a growing problem worldwide. We present a rare case of GBS meningitis presented with cerebral infarction in an adult patient and briefly review the etiology and incidence of GBS infections in adults. There is an increasing incidence of cases in elderly patients, particularly in those with more medical comorbidities. Cerebral infarction as an adverse effect in bacterial meningitis is both a sign of severity and a predictor of a poor clinical outcome with a high mortality rate. Early recognition of the infection, a search for deep-seated infection, and early antimicrobial therapy are vital moments for successful management of the GBS disease.

**Keywords:** Group B Streptococcus, *Streptococcus agalactiae*, neuroinfection, meningitis, stroke, ischemic stroke, cerebral infarction

## **INTRODUCTION**

Bacterial meningitis is an inflammation of the meninges, particularly the arachnoid and the pia mater, associated with the invasion of bacteria into the subarachnoid space. Usually, the inflammatory process is not limited to the meninges surrounding the brain but also affects the brain parenchyma – meningoencephalitis.<sup>1</sup>

The etiologic agents responsible for bacterial meningitis vary by age group. Among neonates and children, most cases of bacterial meningitis are due to group B Streptococcus (GBS) *agalactiae* and *Listeria monocytogenes*. In adults, the most common pathogens are *Streptococcus pneumoniae* and *Neisseria meningitidis*.<sup>2</sup> *Haemophilus influenzae* is a typical pathogenic agent for both age groups.<sup>3</sup>

Acute bacterial meningitis can have various presentations and adverse effects, such as ischemic stroke in 10–29% of the cases.<sup>4</sup> A cerebrovascular

accident can mask the underlying neuroinfection and is both a sign for the severity of the condition and an independent predictor of a poor clinical outcome.<sup>5</sup>

Despite modern antibiotic treatment and improved intensive care, bacterial meningitis is still an unresolved problem in clinical neurology. The mortality rates are up to 50% when the infection is unrecognized and untreated. Even when diagnosed early and treated adequately, mortality rates are still high – about 34%.<sup>6</sup>

We present a rare case of group B streptococcus (GBS) meningitis in an elderly female presented as acute ischemic stroke in the left cerebral hemisphere. Written informed consent was obtained from all subjects before the study.

## **CASE REPORT**

A 62-year old female was brought to the Second Clinic of Neurology of the University Hospital

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“St. Marina”, Varna, Bulgaria, after she was found in her home disorientated, with incomprehensive speech and weakness of the right limbs. She had chills, fever up to 37.5°C, and lower-back pain.

The patient had a previous history of hypertension, atrial fibrillation, and previous operation for cervical carcinoma with radiotherapy.

On admission, she was in poor general condition, with a blank stare and lack of awareness of her environment. She had normal body habitus, a petechial rash on her lower limbs, a temperature of 37.2°C, an irregular pulse at 88 beats per minute, blood pressure 100/70 mm/Hg (Figure 1).

On neurological examination, the patient was somnolent, with general confusion and limited command response due to partial sensorimotor aphasia. There were no signs of meningism. The pupils were equal, with slow reaction to light, unaffected eye movements. There was a central lesion of the right facial nerve and mild hemiparesis on the right. Tendon reflexes were unremarkable, and Babinski’s sign was negative bilaterally. The neurological findings were noted to be consistent with cerebral infarction in the left middle cerebral artery territory.

Initial laboratory tests were significant or elevated leukocyte count -  $16.89 \times 10^9$ , high C-reactive protein (CRP) - 149 mg/l, and low platelet count -  $119 \times 10^9$ . Renal and hepatic enzymes were moderately elevated.

Computed tomography (CT) scan of the head without contrast showed a hypodense lesion in

the left hemisphere suspicious for acute ischemic stroke (Figure 2).

Because of the presence of neurological symptoms with leukocytosis, fever and skin changes, infectious meningoencephalitis was suspected and a lumbar puncture was performed. Analysis of the cerebrospinal fluid (CSF) revealed several abnormalities- (++) positive Pandy reaction, marked leukocytosis-  $2470/\mu\text{l}$ , proteinorachia with 3.44 g/L protein and glucose was barely detectable - less than 0.6 mmol (Table 1). The diagnosis of acute bacterial meningitis was made. Furthermore, group B *Streptococcus agalactiae* was isolated from the CSF, the urine, and the blood culture tests. The patient was treated with a triple combination of broad-spectrum antibiotics combined with dexamethasone.

On the third day, the patient presented in severe general condition, comatose with right-sided hemiplegia, intubated and fed through a nasogastric tube. There was an improvement in the control lumbar puncture -  $894/\mu\text{l}$  leucocytes, 1.46 g/L protein, and 2.0 mmol/l glucose (Table 1).

Because of the worsening of the neurological symptoms on the fourth day, a magnetic resonance imaging (MRI) of the head was performed with multiple supra and supratentorial hyperintense lesions on T2 and T2-flair, suspicious for multiple septic embolisms (Figure 3). In addition, there was no leptomeningeal enhancement, ventriculitis,



Figure 1. Petechial rash on the lower limbs of the patient described as a toxic-allergic reaction due to an infectious disease

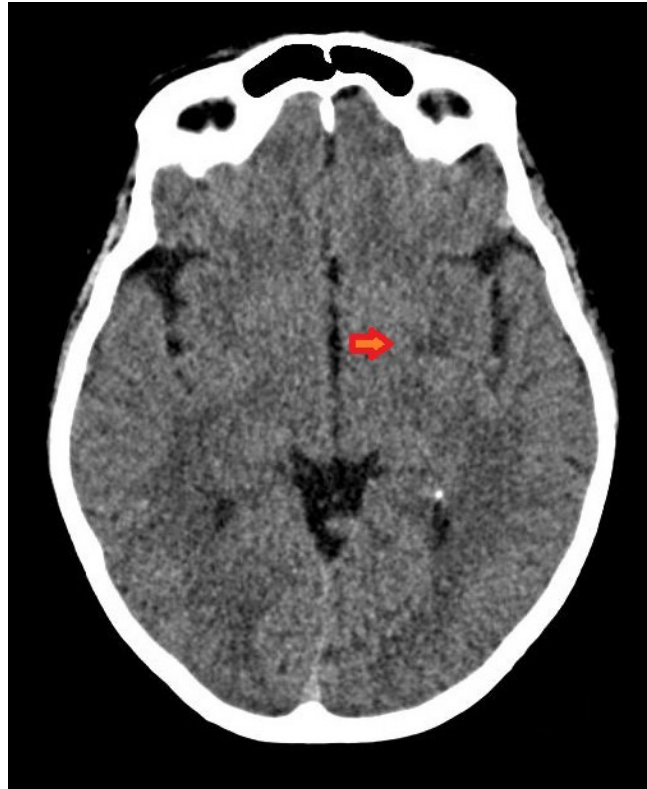


Figure 2. CT of the head on admission - hypodense lesion in the left hemisphere suspicious for acute ischemic stroke

or vascular abnormalities suggesting vasculitis. Transthoracic echocardiography was performed with no evidence of endocardial involvement, and infective endocarditis was excluded due to lack of any major criteria according to the Duke's classification. Further transesophageal echo was not considered in this case due to the severe general condition of the patient.

Despite the treatment with intravenous antibiotics, the patient remained comatose with no change in her neurological status, and in several days had a lethal outcome. Despite the lack of

infective endocarditis, based on the isolated group B *Streptococcus agalactiae* from the blood culture tests, the diagnosis of GBS meningitis with sepsis and multiple ischemic (septic) infarctions was made.

## DISCUSSION

*Streptococcus agalactiae*, also known as Group B *Streptococcus* (GBS), was first differentiated from others in the 1930s.<sup>7</sup> This streptococcus is found in the vaginal tract of healthy women.

Table 1: Cerebrospinal fluid findings on admission and the third day

Cerebrospinal fluid (CSF) results			
Parameter	Units	On admission	On third day
Pandy reaction	Positive/ Negative	(++) positive	(+) positive
Rivalta reaction	Positive/ Negative	(-) negative	(+) positive
Erythrocytes	Count/ $\mu$ l	4000	13000
Leucocytes	Count/ $\mu$ l	2470	894
Neutrophils	Count / $\mu$ l (%)	2097 (84.9%)	592 (66.3%)
Monocytes	Count / $\mu$ l (%)	373 (15.1%)	302 (33.7%)
Glucose	mmol/l	< 0.6	2.0
Protein	g/L	3.44	1.46

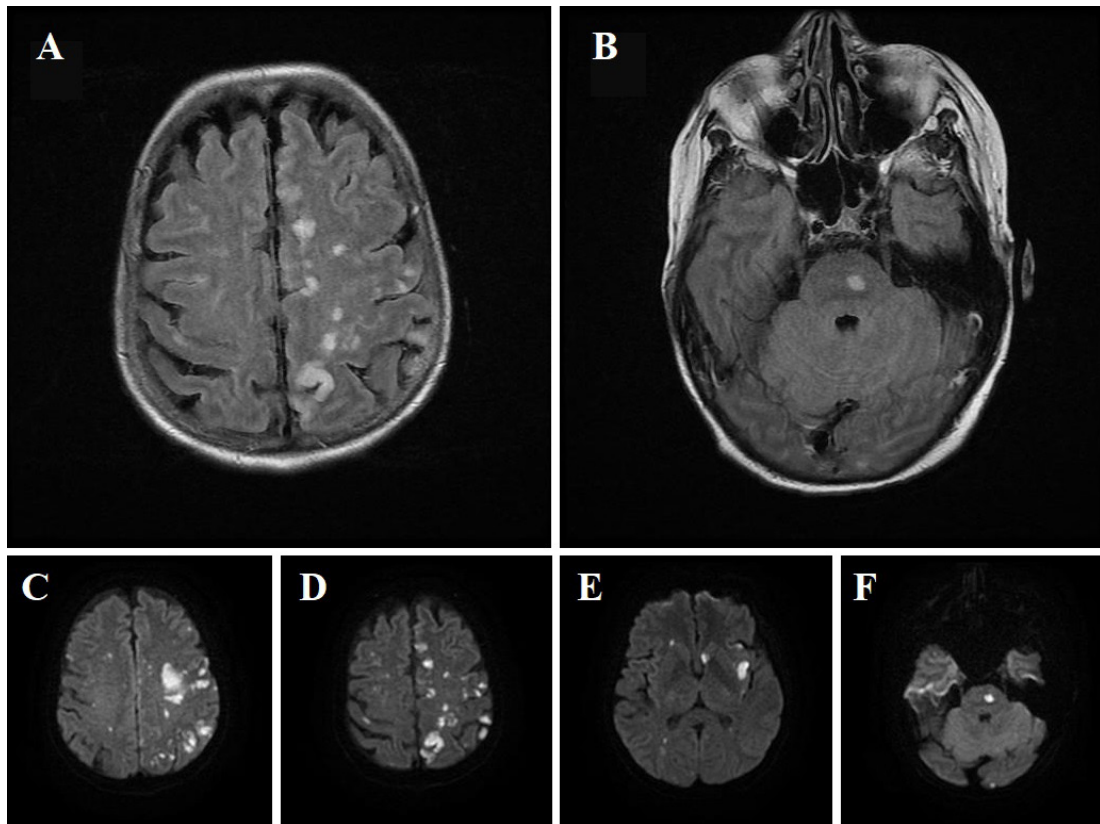


Figure 3. MRI of the head on the fourth day.

A-B: Axial FLAIR images – presenting multiple hyperintense lesions in left hemisphere and brainstem  
 C-F: Axial DWI images – marked hyperintensity in multiple regions characteristic for acute embolic stroke

Its pathogenicity was not described until 1938, when three reports of fatal post-partum infection were published.<sup>8</sup> Invasive GBS disease was rarely identified in humans until the 1960s, when an increasing number of reports of adult and neonatal invasive infections were published.<sup>9</sup>

GBS is a well-known cause for neuroinfection predominating in neonates and children up to 3 years of age and it is generally considered as rare in adult patients less than 1% of all cases.<sup>10</sup> In general, these infections present as bacteremia, and the development of neuroinfections as meningitis is more frequent.<sup>11</sup>

*Streptococcus agalactiae* can cause infection by external inoculation or by spread from contiguous tissues by hematogenous spread. The hematogenous route is predominant allowing seeding of infection. Septic emboli can cause a large area or multiple infarctions and subsequent spread of infection.<sup>12</sup> Septic embolism frequently results from infective endocarditis, but also can be caused by skin, soft-tissue or perivascular infection resulting in septic state.<sup>13</sup> Immune-mediated

vasculitis due to the GBS infection is considered as another mechanism of vascular alteration and cerebral infarction.<sup>14</sup> Nevertheless further work-up and histopathological investigations are required to prove a thrombo-occlusive vasculopathy.<sup>14</sup>

The very first case of an adult with bacterial meningitis caused by *Streptococcus agalactiae* was reported in 1942.<sup>15</sup> Later, M. Edwards *et al.* described the first case of *Streptococcus agalactiae* meningitis presented as acute stroke in 61-year-old male in 1995.<sup>16</sup>

In the following years, several more cases were reported, mainly connected with GBS infectious endocarditis. Sambola *et al.* described 30 patients with infectious endocarditis in 2002. The most common presenting clinical features were fever (8 patients), left-sided heart failure (3 patients), or stroke (3 patients).<sup>17</sup> Another case was of a 75-year-old female with homonymous hemianopsia due to embolic stroke and bacterial endocarditis.<sup>18</sup> Song *et al.* described another case of 26 years of age female who presented with confusion and right-sided weakness due to



cerebral infarction and GBS endocarditis.<sup>19</sup>

Nevertheless, recent studies reported an increased rate of serious GBS disease in adults. Since 2000, more than two-thirds of all cases have occurred in adults as the mean age is about 60 years.<sup>20</sup> Patients with more medical comorbidities and the elderly are at higher risk of having such an infection. The most frequent underlying medical conditions are diabetes mellitus (41%), cardiovascular disease (36%), and malignancy (17%).<sup>21</sup>

There are different manifestations of GBS disease in adults. The most common manifestations are skin and soft tissue infections, bacteremia of uncertain source, urosepsis, pneumonia, meningitis, septic arthritis, and endocarditis.<sup>22</sup> Skin and soft tissue infections and bacteremia with no identified focus are typical findings of infection in elderly adults. Infection of the urinary tract and pneumonia is more often encountered in elderly persons and endocarditis is predominant in young adults. GBS disease affecting the central nervous system is rare in adults and associated with a high rate of disability and mortality.<sup>16</sup>

The clinical presentation of GBS neuroinfection and CSF findings are indistinguishable from other bacterial meningitis, and only the microbiological investigation can prove the diagnosis.<sup>23</sup> After establishing the etiological agent, a proper antibacterial treatment should be administered. GBS is generally less susceptible to penicillin antibiotics than group A streptococci up to 4 to 10 times, but this is still an antibiotic of first choice.<sup>20</sup> Nowadays, a combination of third-generation cephalosporins and aminoglycoside antibiotics or penicillin is broadly used.<sup>23</sup>

Factors associated with a high mortality rate include advanced age, neurological complications such as coma or focal neurological signs, cerebral infarction, and/or extra-neurological complications - shock, acute respiratory failure, acute renal failure, or consumption coagulopathy.<sup>24</sup>

In our case, the patient showed an excellent response to antibiotic therapy, according to the laboratory data. The underlying sepsis and neuroinfection in a patient with severe comorbidity was a predictor of a poor clinical outcome. One feature of the present case was the occurrence of multiple septic cerebral embolisms early in the neuroinfection, which led the patient to a lethal outcome.

In conclusion, GBS infections are a growing problem in older adults and those with chronic medical conditions. Involvements of the central nervous system such as meningitis are less

common but cause severe disease manifestations with high mortality. Cerebral infarction is an adverse effect of neuroinfections leading to an even worse clinical outcome.

Early recognition of the infection, a search for deep-seated infection, and early antimicrobial therapy are vital moments for successful management of the GBS disease.

## DISCLOSURE

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