Case Report

Ischaemic stroke caused by Group B Streptococcus associated meningoencephalitis in young, immunocompetent adults – a case series and systematic review of literature

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Teaching point

- These cases highlight the association of stroke with bacterial meningoencephalitis. Clinicians should have high index of suspicion for investigation and a low threshold for initiating empirical antibiotic treatment in patients presenting with this atypical form of stroke.

1st Case History

A 51-year-old man presented with mild headache followed by sudden onset of right sided weakness and dysarthria on the background of one week history of right sided sciatica and malaise. He was apparently immunocompetent with only past medical history being hypertension. There was no consumption of tobacco or excess alcohol and he previously had normal liver and renal function.

In the emergency department, his observations were within normal limits and lactate was normal on a venous blood gas. On examination, he had right hemiparesis, hemianopia and visual/sensory neglect (National Institute of Health Stroke scale, NIHSS 15). Systemic examination revealed no abnormal findings, notably no heart murmurs. He was thrombolysed for a suspected left middle cerebral artery territory stroke following a normal CT brain/CT angiogram. 90 minutes later, he developed 30sec of right facial twitching followed by right hemiplegia and right gaze palsy (NIHSS 23). His Glasgow Coma Score (GCS) was 10/15 with poorly reactive and dilated left pupil. He was treated for possible focal seizure with levetiracetam and lorazepam. Repeat CT brain did not show any intracranial haemorrhage but showed possible early cerebral oedema. He was transferred to ITU where he was intubated and ventilated. Blood tests showed a CRP of 296, deranged renal/liver function tests but normal white cell count and HbA1c. HIV testing was not completed. He was treated for aspiration pneumonia with intravenous amoxicillin-clavulanate.

Within 8 hours, he deteriorated further with both pupils becoming fixed and dilated. A third CT brain showed diffuse oedema resulting in effacement of cortical sulci and gyri, compression of CSF spaces and mild tonsillar herniation. He was given IV mannitol without benefit. MRI brain showed restricted diffusion changes in the left parietal lobe and severe bilateral cortical oedema with 2cm of cerebellar herniation (Figure 1). Brainstem death was confirmed 48 hours after admission. One set of blood cultures taken on admission was subsequently positive for *Streptococcus agalactiae* Serotype III. This rapid deterioration and death meant further investigations for systemic infection such as an echocardiogram or spinal imaging were not performed.

2nd Case History

A 40-year-old man presented with a four-day history of fever, headache, photophobia, myalgia and confusion. He was previously well with no past medical history. On admission, he was tachycardic, hypotensive and pyrexial at 38.5^{0}C. Examination showed GCS 12/15 with a positive Kernig's sign but no focal neurology. Baseline HbA1c, liver and renal function tests were normal, and HIV test was negative. He had raised inflammatory markers and CT brain was normal.

He was treated empirically with IV ceftriaxone, gentamicin, acyclovir and dexamethasone. Cerebrospinal fluid (CSF) revealed pleocytosis (230 white cells; 60% lymphocytes, 40% neutrophils), raised CSF protein (2.5 g/L), but normal CSF:serum glucose ratio. The CSF cultures and CSF PCR for *Mycobacterium tuberculosis* were negative.

He developed dense left hemiparesis with left sided neglect 9 hours after admission. A repeat CT head

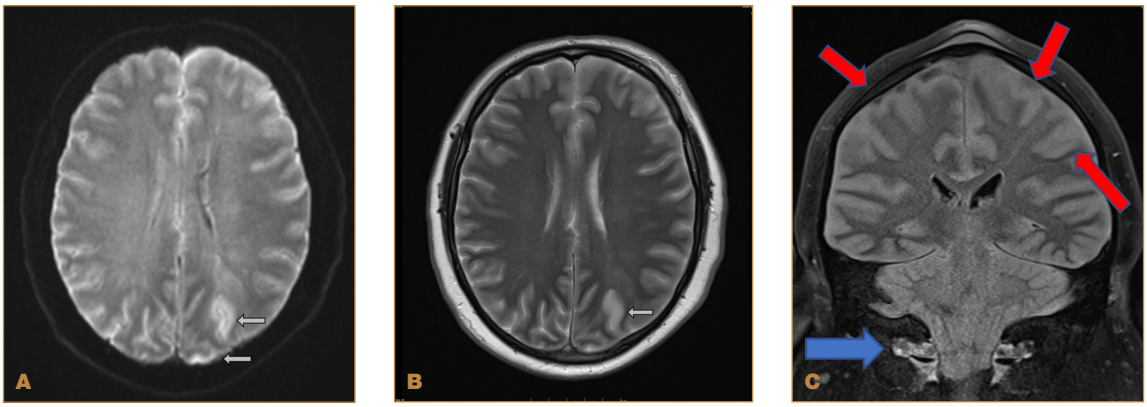

Figure 1. MR imaging of 1st patient
Diffusion B1000 (a) and T2 (b) axial images through midbrain showing areas of restricted diffusion and oedema of the left parietal lobe (white arrow). Coronal Flair image (c) at the foramen magnum, showing more diffuse cerebral oedema (red arrows) and tonsillar herniation (blue arrow).

showed hypodense changes in the right superior frontal gyrus. His MRI brain/time of flight angiography (Figure 2) showed an acute right frontal lobe infarct but there was no intracranial stenosis or beading.

Further investigations were performed to rule out other causes of stroke. Autoimmune screen looking for connective tissue and thrombophilia disorders was negative. Carotid doppler, transthoracic echocardiogram, chest X-ray and CT abdomen/pelvis were normal. One set of blood cultures from admission was positive for *Streptococcus agalactiae* Serotype III.

During his 14 day admission, he completed a 10 day course of 2gram BD IV ceftriaxone. His hemiparesis resolved within 2 days of antibiotic treatment. He was reviewed in clinic 10 weeks post-discharge, and had made a complete recovery and returned to work and driving.

Discussion

These cases are notable as *Streptococcus agalactiae*/Group B streptococcus (GBS) is a rare cause of meningoencephalitis, especially in healthy, non-parturient adults.[1]

GBS is a gram positive, catalase negative cocci.[1] It was first discovered by the French vet and microbiologist, Nocard, in 1887 as a cause of bovine mastitis.[2] It was differentiated from other forms of haemolytic streptococcus by Lancefield in 1930s.[3] In the 1960s, increasing reports of more serious sequelae emerged, notably in neonates and the elderly.[4] A screening programme in North America to identify asymptomatic mothers in pregnancy and treat infection prior to delivery has reduced the prevalence in neonates from 1990s onwards. This contrasts to recent UK studies indicating a two-to fourfold increase in incidence of GBS meningitis over

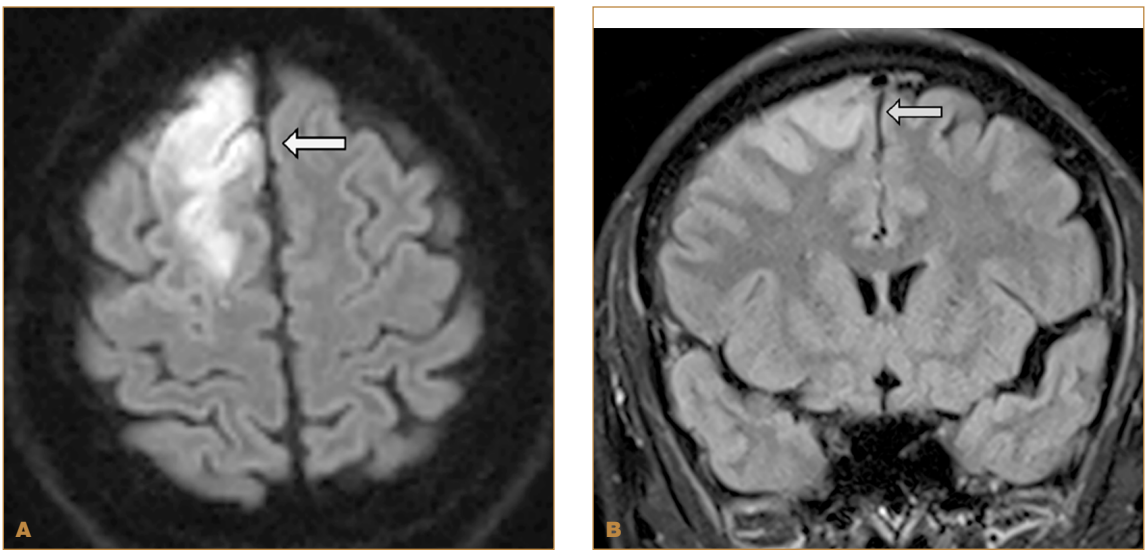

Figure 2. MR imaging of 2nd patient
Diffusion B1000 images (a) and Coronal flair (b) through the frontal lobes showing a discrete area of restricted diffusion and oedema.

Table 1. A summary of previous case reports on immunocompetent adults with GBS-meningoencephalitis related stroke

Author/Yr	Age/Sex	Blood cultures growing GBS?	CSF cultures growing GBS?	CT head showing infarct?	Territory	Dexamethasone given?	Focus of infection identified?	Survived?
Klassen et al 1994[1]	61M	Y	Y	Y	Posterior circulation	Y	N	N
Espinoza Gomez et al 2009[7]	39M	Y	N	Y	Left MCA	N	Native valve endocarditis	Y
Fujita et al 2015[10]	43M	Y	Unknown	Y	Multiple	N	Infective endocarditis	Y
Park et al 2015[11]	60F	Y	Y	Y	Right cerebellar	Y	Soft tissue infection	Y
Wilder-Smith et al[13]	45M	Y	Y	Unknown	N/A	Unknown	Pneumonia	N
Wilder-Smith et al[13]	45F	Y	Y	N	N/A	Unknown	Cellulitis	Y
Wilder-Smith et al[13]	42F	N	Y	N	N/A	Unknown	N	Y
Wilder-Smith et al[13]	63F	Y	Y	N	N/A	Unknown	N	Y
Wilder-Smith et al[13]	38F	Y	N	N	N/A	Unknown	N	Y
Wilder-Smith et al[13]	59F	Y	N	Y	Unknown	Unknown	N	Y
Wilder-Smith et al[13]	62M	Y	Y	N	N/A	Unknown	N	Y
Wilder-Smith et al[13]	59F	Y	Y	Y	Unknown	Unknown	N	Y
Wilder-Smith et al[13]	29M	Y	Y	Y	Unknown	Unknown	N	Y
Wilder-Smith et al[13]	27M	Y	Y	Y	Unknown	Unknown	N	Y
Wilder-Smith et al[13]	24F	Y	Y	N	N/A	Unknown	N	Y
Current case 1	51M	Y	Not done	Y	Left MCA	N	N	N
Current case 2	40M	Y	N	Y	Right frontal	Y	N	Y

the last 20 years, especially over the age of 65, where there is no screening programme.[5] Serotype III is predominant, and more likely to cause meningitis in neonates. Serotypes 1a and 1b are the most common in adults.[6]

GBS typically colonises the gastrointestinal or genitourinary tract and can be found in up to 40% of adults.[5] GBS can lead to a range of clinical symptoms, including soft tissue infections, osteomyelitis, pneumonia or endocarditis.[4] In adults with co-morbidities, especially alcoholism, renal disease, diabetes, HIV, cancer, or obesity, it is more likely to cause invasive disease.[7,8] It infrequently causes primary meningitis in adults, but these cases have a reported mortality rate of 34%.[9,10] Therefore, our cases are unusual given the relatively young age of onset in patients who were apparently immunocompetent.

A literature review in PUBMED and EMBASE identified 11 immunocompetent adults without co-morbidities in articles reporting GBS-meningoencephalitis related stroke (Table 1).[1,7,10-13]

Stroke is often a late complication of meningitis, as it typically results from hypotension, arteritis, vasospasm or venous occlusion secondary to fulminant disease. Therefore, cerebral infarction at presentation in our cases is also unusual. A recent study[12] showed invasive GBS could be secondary to a zoonosis, acquired via consumption of contaminated freshwater fish. Interestingly, majority of the 14 patients studied who developed GBS related meningoencephalitis had asymptomatic brain infarcts on MRI imaging, highlighting the link between this pathology and ischaemic stroke.[12]

GBS cannot be clinically distinguished from other organisms causing adult bacterial meningitis.[14] Case 1 highlights the rapid and catastrophic deterioration that can occur in patients with acute central nervous system infections. As such, early investigation with blood and CSF cultures and treatment with empirical antimicrobial therapy is paramount. Treatment with ceftriaxone was used in favour of benzylpenicillin as an empirical choice in case 2 to cover a range of organisms responsible for bacterial meningitis before the blood culture result became available. It is also easier to administer in the high doses needed with similar clinical outcomes. From bacteraemia surveillance data from the British Society for Antimicrobial Chemotherapy 2019, 100% of *Streptococcus agalactiae* remain susceptible to penicillin and ceftriaxone in the UK, with MICs between 0.015 and 0.06 for penicillin.[15]

Conclusion

We have described ischaemic stroke secondary to Group B Streptococcus associated meningoencephalitis in two immunocompetent adults. The first case highlights bacterial meningoencephalitis can present atypically and catastrophically. Clinicians should consider it in patients with non-specific prodrome but markedly raised inflammatory markers at the point of stroke presentation. Blood and CSF cultures should be sent and empirical treatment initiated promptly.

Consent

Written assent and consent to publish have been obtained from the 1st patient's spouse and 2nd patient respectively.

Conflicts of interest

There are no conflicts of interest relating to this Case Report's contents or its publication.

References

1. Klassen H, Klassen M, Huncharek M. Group B Streptococcal meningitis presenting as stroke in a non-debilitated man. *Yale Journal of Biology and Medicine*. 1995; **68**:1-6.
2. Nocard, M, and R. Mollereau. Sur une mammite contagieuse des vaches laitieres. *Ann. Inst. Pasteur* 1887; **1**:109.
3. Lancefield RC. A Serological Differentiation of Human and Other Groups of Haemolytic Streptococci. *J Exp Med;* 1933; **57**: 571–595
4. Raabe V, Shane A. Group B Streptococcus (Streptococcus agalactiae) *Microbiol Spectr*. 2019; **7(2)**
5. Holyoak A, Fraser T. Group B Streptococcal meningitis in a middle aged woman. Crit care resus. 2007; **9**: 181-183
6. Van Kassel *et al.* Molecular epidemiology and mortality of group B streptococcal meningitis and infant sepsis in the Netherlands: a 30 year nationwide surveillance study. *Lancet* 2021; **2**: 32-40.
7. Espinoza-Gomez *et al.* Infective Endocarditis Caused by Streptococcus agalactiae in a Native Aortic Valve, Complicated by Meningitis and Cerebral Embolism. *Internal Medicine.* 2009; **48**: 1099-1101.
8. Kjaergaard N, Bodilsen, Justesen U *et al.* Community-acquired meningitis caused by beta-haemolytic streptococci in adults: a nationwide population-based cohort study. *Eur J Clin Microbiol Infect Dis* 2019; **38**: 2305–2310.
9. Khan F. Streptococcus agalactiae Meningitis in Adult Patient: A Case Report and Literature Review. Case Reports in Infectious Diseases. 16: 2016.
10. Fujita H, Nakamura, Tsukimori et al. Severe infective endocarditis in a healthy adult due to Streptococcus agalactiae. *International Journal of Infectious diseases.* 2015; **38**: 43-45.
11. Park D, Lee S, Yoon D, Kim J. A Nonpregnant Woman with Group B Streptococcal Meningitis and Multifocal Embolic Infarctions. *J Clin Neurol*. 2016; **12(4)**: 517-518.
12. Tan K, Wijaya L, Chiew H *et al.* Diffusion-Weighted MRI Abnormalities in an Outbreak of Streptococcus agalactiae Serotype III, Multilocus Sequence Type 283 Meningitis. *J Magn, Reason, Imaging*. 2017; **45**: 507-514.
13. Wilder-Smith *et al.* Group B streptococcal meningitis in adults: recent increase in Southeast Asia. *Aust NZ J Med*. 2000; **30**: 462-465.
14. McGill F, Heyderman R, Michael B *et al.* The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults. *J Infect*. 2016; **72(4)**: 405-38.
15. The British Society of Antimicrobial Chemotherapy. Bacteraemia data. Accessed at: http://www.bsacsurv.org/reports/bacteraemia#results