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Case Report

Double whammy: Delayed cerebral ischemia of a 19-year-old secondary to sinogenic complications from an uncommon bacterial sinusitis, *Arcanobacterium haemolyticum* ☆

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ABSTRACT

Arcanobacterium haemolyticum, found as normal flora in healthy individuals, is an unusual culprit for pharyngitis and sinusitis in young adults, rarely leading to severe infections. Here, we present a singular case involving a 19-year-old immunocompetent male who experienced complications arising from *A haemolyticum* sinusitis, leading to orbital and intracranial sinogenic complications. The patient developed severe cerebral vasospasm with delayed cerebral ischemia, necessitating aggressive management encompassing daily catheter-directed intra-arterial infusions, surgical source control, and maximal medical therapy.

This case explores the challenging diagnostic and management aspects associated with cerebral artery vasospasm secondary to bacterial meningoencephalitis. The abrupt neurological decline in such patients presents a dilemma in recognizing the occurrence of cerebral vasospasm versus the progression of meningoencephalitis. By utilizing computed tomography brain perfusion scans, we were able to identify delayed cerebral ischemia due to cerebral vasospasm, acknowledging that this modality was not used to identify classical territorial stroke infarcts. This decision was made based on the understanding of the potential for bacterial-induced cerebral vasospasm to involve both hemispheres.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Introduction

Arcanobacterium haemolyticum is a species of bacteria classified as a Gram-positive, facultatively anaerobic, beta-haemolytic, bacillus. First described in 1946, it was later reclassified from *Corynebacterium* to "*Arcano-*", translating to "secretive" bacteria due to its previous resemblance [1]. Cultures of *A haemolyticum* can be found as normal skin flora and pharynx of healthy individuals and may often be overlooked as the causative agent of symptoms during an infection [2]. It is a known pathogen to cause pharyngitis or sinusitis among young adults with a prevalence of 0.5%-2.5% of all bacterial pharyngitis according to Mackenzie et al. [2]. Though less common, there are reports of *A haemolyticum* infections causing brain abscess, pneumonia, infective endocarditis, and bacteraemia amongst immunocompromised hosts [2]. In an extensive review encompassing almost four decades of analysis on *A haemolyticum* cases, the evidence of bacteraemia, sepsis and/or associated complications (i.e. abscess, Lemierre's syndrome, end organ failure, etc), revealed a remarkably limited cohort of only 20 documented patients [1,3]. Notably, within this subset, the rates of complications varied, with orbital/periorbital cellulitis, meningitis, and intracranial abscess demonstrating rates of 10%, 25%, and 30%, respectively. 85% of whom were immunocompetent [1].

Case report

A 19-year-old Caucasian male was transferred to our referral hospital with a diagnosis of cerebritis and right orbital subperiosteal abscess. The patient reported a 1-week history of flu-like symptoms and sinus discomfort but initially attributed these to a known history of hay fever. Over the subsequent week, the patient's condition deteriorated, marked by persistent right sided eye tenderness. Upon arrival at the local emergency department, the patient exhibited exacerbated symptoms, including vomiting, headaches, right-sided ophthalmic issues, and intermittent confusion. The patient's past medical history includes seasonal hay fever with no regular medications. The patient otherwise lives with his parents in a rural town and works as a council member. Furthermore, the patient also denies any history of smoking, alcohol consumption, or recreational substance use.

Ophthalmic examination revealed mild proptosis, periorbital oedema, photophobia, and chemosis on the right eye, while visual acuity remained intact. The left eye examined normally. Initial computed tomography of the orbits revealed radiological signs of right orbital cellulitis with severe paranasal sinus mucosal disease involving bilateral maxillary, ethmoidal, and frontal sinuses. Notably, no evidence of an enhancing intracranial collection was observed.

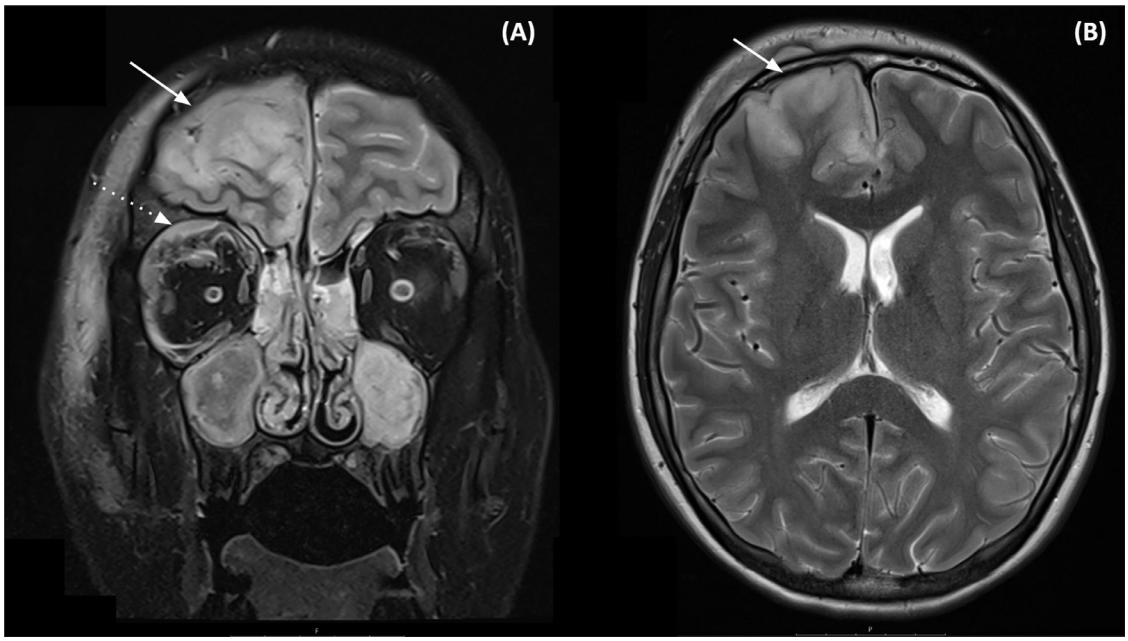

Fig. 1 – Initial MRI Brain with (A) T2 DIXON coronal plane showing areas of subperiosteal collection of the right orbit (Dotted white arrow) and corresponding areas of right frontal lobe cerebritis (Solid white arrow). Note of bilateral diffuse sinusitis with extensive opacification and mucosal enhancement. (B) T2 Axial plane with areas of right frontal cortical and subcortical T2 hyperintense area with mass effect and vasogenic oedema (Solid white arrow).

Table 1 – Final pathology results of bedside lumbar puncture performed in the patient's local emergency department.

CSF analysis	Results	Reference Range
Colour	**Slightly Turbid**	N/A
Total Leucocytes	**4800 x 10^6 /L**	N/A
Total Erythrocytes	**120 x 10^6 /L**	N/A
Polymorphs	**2496 x 10^6 /L**	N/A
Mononuclear	**2304 x 10^6 /L**	N/A
Gram Stain + Culture	**Negative**	N/A
Glucose	**2.00**	2.2-3.9 mmol/L
Protein	**1.72**	0.15-0.45 g/L
CSF Nucleic Acid Detection (PCR)	**Results**	
16S DNA (Bacteria DNA)	**Negative**	
Haemophilous Influenza DNA	**Negative**	
Neisseria Meningitidis DNA	**Negative**	
Streptococcus Pneumoniae DNA	**Negative**	
Literia Monocytogenes DNA	**Negative**	
Herpes simplex virus DNA	**Negative**	
Parechovirus RNA	**Negative**	
Varicella-zolster virus DNA	**Negative**	
Enterovirus RNA	**Negative**	

Subsequent MRI of the brain with gadolinium contrast, conducted 24 hours later, revealed a right orbital abscess with a subperiosteal collection. Additionally, there was evidence of right frontal lobe cerebritis adjacent to the orbital abscess, accompanied by areas of meningitis at the corresponding region which also extended onto the left contralateral side of the brain (Fig. 1).

Lumbar puncture undertaken at patient's bedside revealed a turbid CSF with elevated leukocytes. Subsequent blood cultures were otherwise unremarkable (Table 1). Due to established radiological and clinical signs of meningitis and right orbital abscess, the patient's antibiotic coverage was subsequently broadened and transferred to our hospital for urgent surgical intervention.

Upon transfer (Day 3 of admission), the patient underwent incision and drainage of the right supraorbital abscess, with tissue microbiology and culture identifying *A haemolyticum* as the only causative agent. Progress MRI brain showed reassuring findings with intracranial phlegmon and cerebritis, which remained relatively unchanged in size. Neurosurgical and ENT (ear, nose, and throat) team opted for monitoring at this stage, incorporating serial neurological examinations, and intravenous antibiotics.

On Day 5 of admission, the patient exhibited progressive neurological deterioration consisting of left hand and lower limb paraesthesia, with associated reduction in power of the left upper limb myotomes (Grade 3 manual muscle testing [MMT] score). The following day, the patient had a witnessed left sided facial seizure like episode lasting 6 minutes which terminated with Midazolam and anti-epileptic medication was initiated. Progress MRI revealed cerebritis that was unchanged as the underlying cause.

The patient's neurological status continued to deteriorate, leading to a dense left-sided hemiplegia with facial droop (Grade 0 MMT score), and paraesthesia in the upper and lower limbs by day 10 post admission. Due to escalating concerns, a stroke protocol was initiated, comprising CT brain angiogram, CT perfusion (CTP) studies, and MRI-B. MRI-B revealed a notable progression of delayed cerebral ischemia, presenting as a substantial area of diffusion restriction within the right cerebral hemisphere. This affected the perirolandic, parietotemporal, insular cortex, caudate nucleus (head and body), and putamen, as indicated by corresponding high T2 FLAIR signals in these regions (Fig. 2). Additionally, both MRI-B and CT-brain angiogram identified asymmetric narrowing in the distal right internal carotid artery (ICA), right middle cerebral artery (M1) and left ICA, within the superior cavernous segment (Fig. 3). In the context of ongoing infection, radiological findings favored delayed cerebral ischemia secondary to infection-related cerebral vasospasm. RAPID automated CTP reviled time-to-maximum (Tmax) >6.0 second of 265 mL on both cerebral hemispheres, predominantly on the left, with a mismatch ratio of 4.7 (Fig. 4).

Within 24 hours of these radiological findings, the patient underwent functional endoscopic sinus surgery (FESS) for source control along with Interventional Neuroradiology (INR) intervention for cerebral vasospasm. The patient was also managed with maximal medical therapy, including intravenous Milrinone infusion, Nimodipine infusion, and blood pressure control.

Over the subsequent 8 days (Day 11-18 of admission), the patient underwent digital subtraction angiography (DSA) with catheter-directed intra-arterial verapamil and/or milrinone infusions. Detailed treatment and findings are provided in Table 2 with some resolution in cerebral vasospasm as shown in Figs. 5 and 6.

Three weeks after the patient's last catheter-directed DSA intervention (Day 40 post-admission), functional improvement in the left upper and lower limbs was documented, as outlined in Table 3. Serial MRI Brain scans showed progression of phlegmon into a cerebral collection which was subsequently managed conservatively with antibiotics. (Figs. 7 and 8). On Day 40 post-admission, the patient was transitioned to oral antibiotics. Subsequently, on Day 55, the patient en-

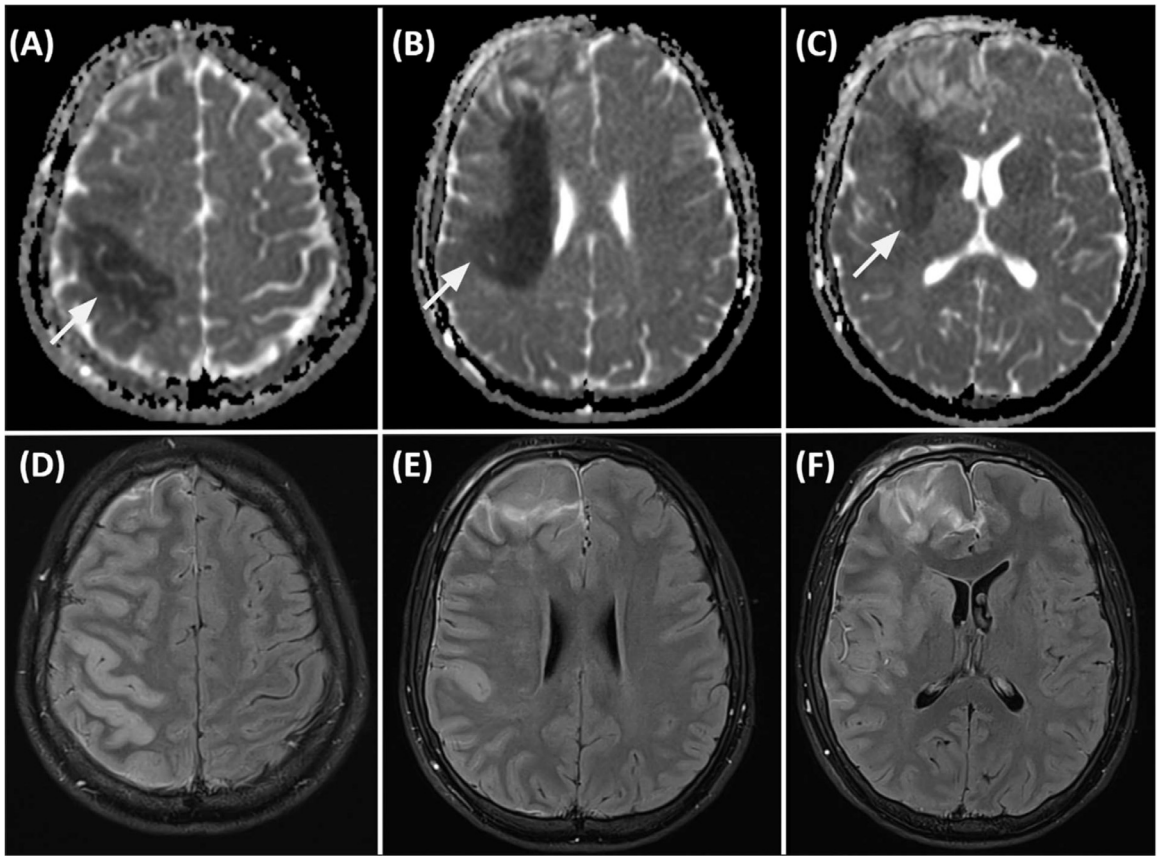

Fig. 2 – (A-C) MRI brain Axial slice with Trace ADC (apparent diffusion coefficient) mapping showing evidence of diffusion restriction (Solid white arrow). (D-F) MRI-B of the corresponding axial slice, FLAIR (fluid attenuated inverse recovery) sequence. Note the subtle hyperintensity of the right hemisphere compared to left.

Table 2 – Summary of daily intraoperative DSA report findings. The patient underwent daily DSA angiogram with catheter directed treatment to improve cerebral vasospasm.

Day(s) post-admission	Severity of reported vasospasm intraoperative					RICA treatment	LICA treatment
	RICA	RM1	RM2	LICA	PTA		
11	Severe	Severe	Severe	Severe	N/A	5mg milrinone + 20mg verapamil	5mg milrinone + 15mg verapamil
12	Severe	Severe	Severe	Moderate	N/A	5mg milrinone + 20mg verapamil	5mg milrinone + 5mg verapamil
13	Severe	Severe	Severe	Moderate	N/A	5mg milrinone + 20mg verapamil	N/A
14	Severe	Severe	Moderate	Moderate	N/A	5mg milrinone + 20mg verapamil	N/A
15	Severe	Moderate	Mild	Moderate	N/A	5mg milrinone + 20mg verapamil	N/A
16	Severe	Moderate	Normal	Mild	RICA / RM1	5mg milrinone + 15mg verapamil	N/A
17	Moderate	Moderate	Normal	Mild	N/A	5mg milrinone + 10mg verapamil	2.5mg milrinone
18	Mild	Moderate	Normal	Mild	N/A	5mg milrinone + 15mg verapamil	N/A

Note the gradual improvement in spasm observed over the following days. Only one episode of Percutaneous Transluminal Angioplasty (PTA) was done at day 16 of admission once the patient's cerebral vasospasm significantly improved.
LICA, left internal carotid artery; PTA, percutaneous transluminal angioplasty; RICA, right internal carotid artery; RM1, right middle cerebral artery M1 segment; RM2, right middle cerebral artery M2 segment.

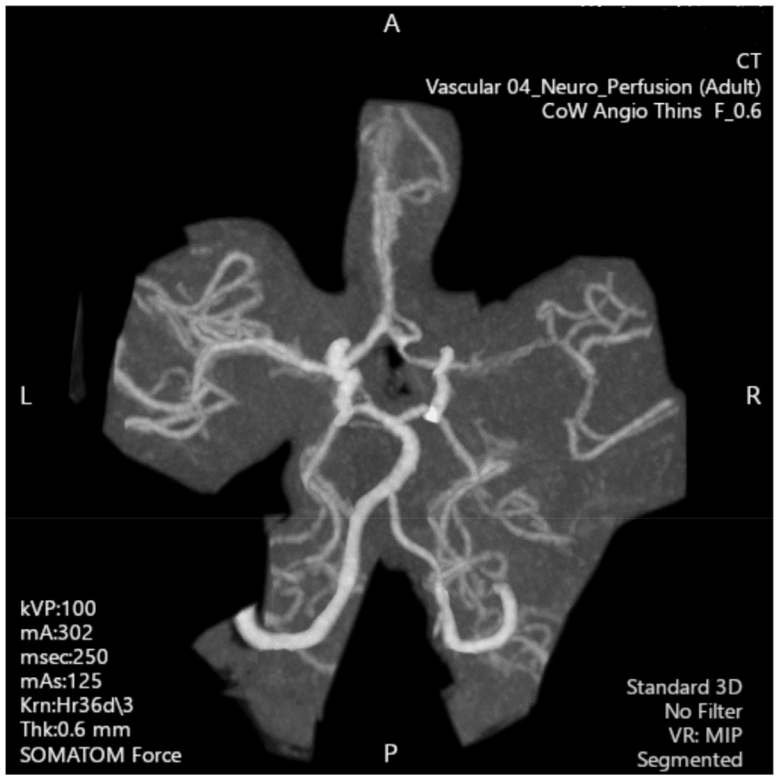

Fig. 3 – CT angiogram virtual reconstruction of circle of Willis using maximum intensity projection. Note the asymmetric narrowing of the right Internal carotid artery and right middle cerebral artery M1 and M2 segments compared to left. Evidence of left sided focal stenosis at the superior cavernous segment of left ICA is not visualized here.

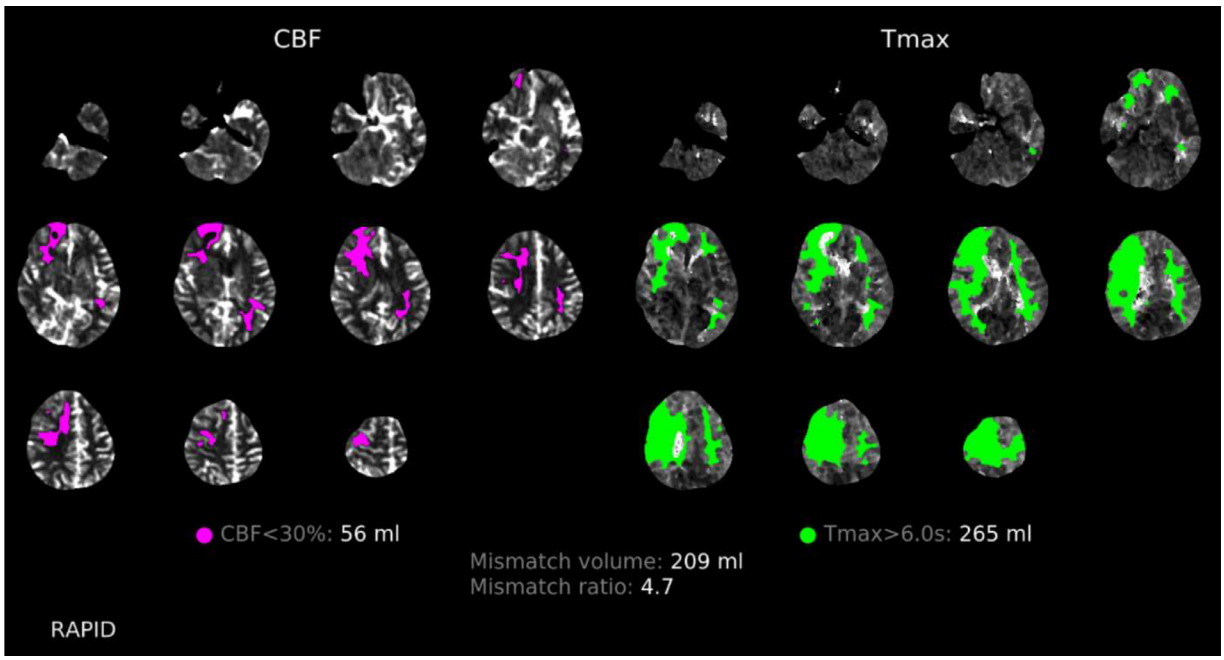

Fig. 4 – Computer tomography perfusion scan using RAPID program to assess cerebral blood flow and time-to-maximum (T-Max) perfusion parameter. Note areas of reduced CBF and prolonged T-max on both cerebral hemispheres not corresponding to a classical vascular territory that would be expected on a classical stroke series.

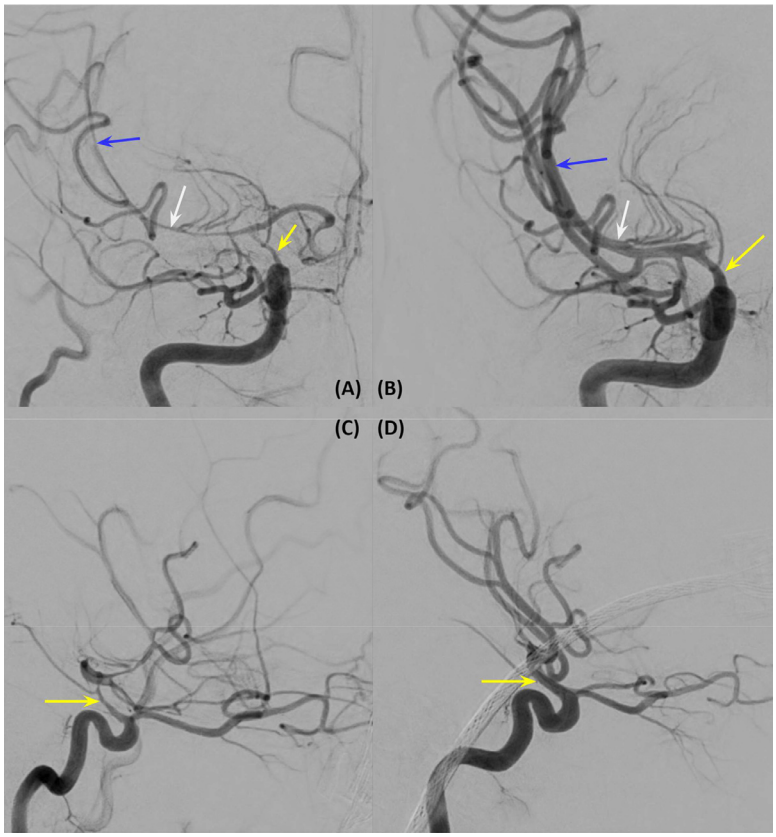

Fig. 5 – Catheter dirrected DSA of the right internal carotid artery (R-ICA). (A) Anteriorposterior (AP) view of Initial DSA pre-procedure with correspinding lateral view (C). Note findings of severe narrowing in the C7 communicating segment (Yellow arrow), middle cerebral artery (MCA) M1 Segment (White arrow) and MCA M2 Segment (Blue arrow) on initial DSA run. Image (B) and (D) corresponding radiologic finding 8 days post intervention with significant improvements on vasospasm.

Table 3 – Summarized Manual Muscle Testing score of the patients left upper and lower limb recorded on the day of, day after final DSA treatment, and 22 days after final DSA treatment. Patients Right upper and lower limb was otherwise unremarkable.

Day(s) post final DSA	Pre- procedure	1	22
Day(s) post admission	11	19	40
	Manual Muscle Testing Score		
Left Upper Limb			
Shoulder Shrug	0	0	2
Shoulder Forward Flexion	0	0	2
Shoulder Extension	0	0	1
Elbow Flexion	0	0	0
Elbow Extension	0	0	0
Finger Flexion	0	0	2
Finger Extension	0	0	0
Left Lower Limb			
Hip Flexion	1	2	3
Hip Extension	0	2	3
Ankle Plantar Flex	0	2	2
Ankle Dorsi Flex	0	0	2

tered a step-down program under rehabilitation medicine. Despite ongoing outpatient rehabilitation and multidisciplinary involvement, the patient continues to experience persistent left-sided hemiparesis with no recurrence of complications.

Discussion

Comprehension of cerebral vasospasm is crucial in this context. Described as the local or diffuse persistent spastic contraction of the smooth muscle within the vascular walls of cerebral arteries, it manifests as a dynamic reduction of intraluminal diameter. This constriction, in turn, results in reduction of cerebral blood flow [4]. Whilst exact pathophysiology is not fully understood, common agreement exist that cerebral inflammation is the primary driving factor for both bacterial meningoencephalitis and subarachnoid hemorrhage. Often involving the direct effect of oxyhemoglobin on the vascular wall, breakdown of red blood cell products, and imbalance of vasoactive agents [4]. From extensive knowledge of cerebral vasospasm secondary to subarachnoid hemorrhage, cerebral vasospasm appears around 72 hours, reaching its peak at 7 to 10 days, and resolving spontaneously after 21 days [4,5].

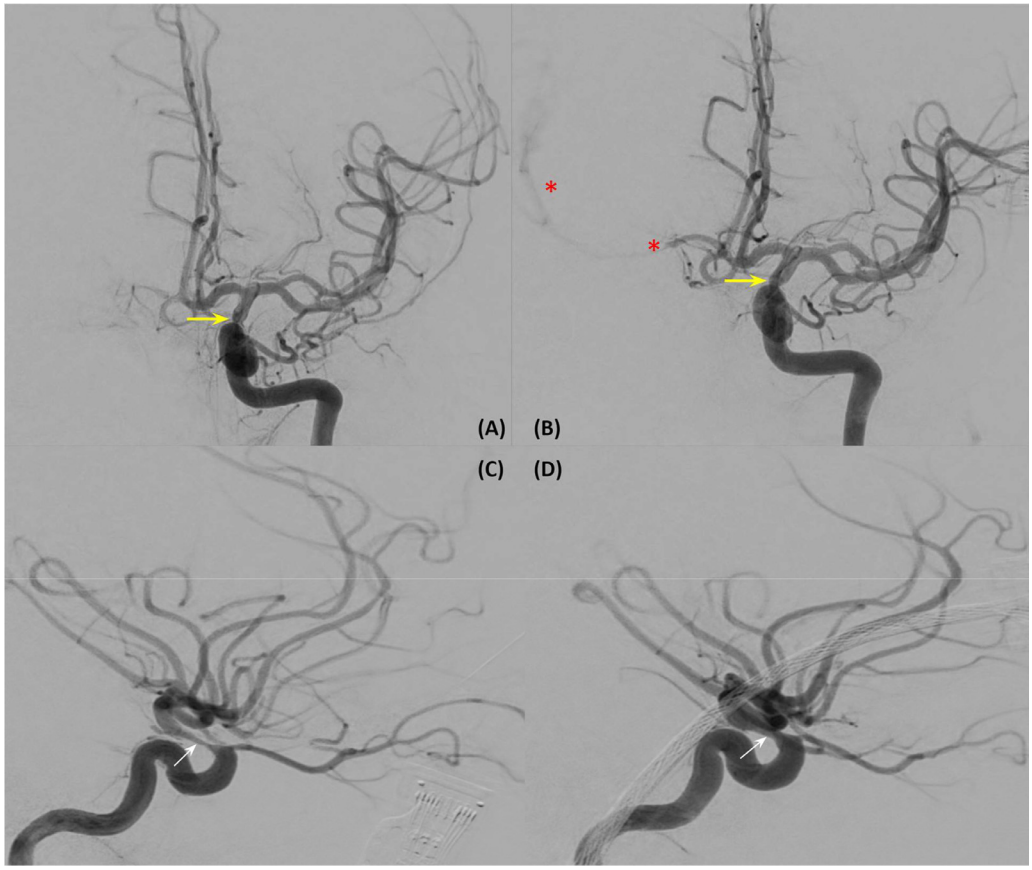

Fig. 6 – Catheter dirrected DSA of the left internal carotid artery (L-ICA). (A) Anteriorposterior (AP) view of Initial DSA pre-procedure with corresponding lateral view (C) with severe narrowing in the C7 communicating segment. Image (B) and (D) shows corresponding radiologic findings, 8 days post intervention with significant improvements on vasospasm. Note in image (B) the collateral supply given off to the contralateral R-MCA (Red astrix).

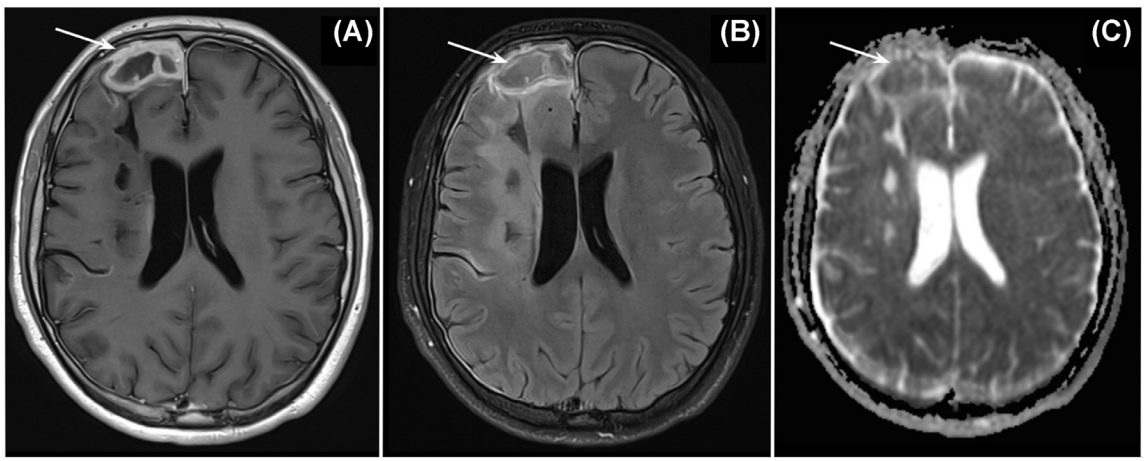

Fig. 7 – About 2 months post progress brain MRI with right frontal lobe thick-walled rim enhancing collection as seen on (A) T1 contrast enhance axial slice. Corresponding axial slice (B) FLAIR sequence with no hyperintensity and (C) Apparent diffusion coefficient (ADC) with no convincing central diffusion restriction to suggest persistent infection. Patient was managed non operatively and stepped down to oral antibiotics.

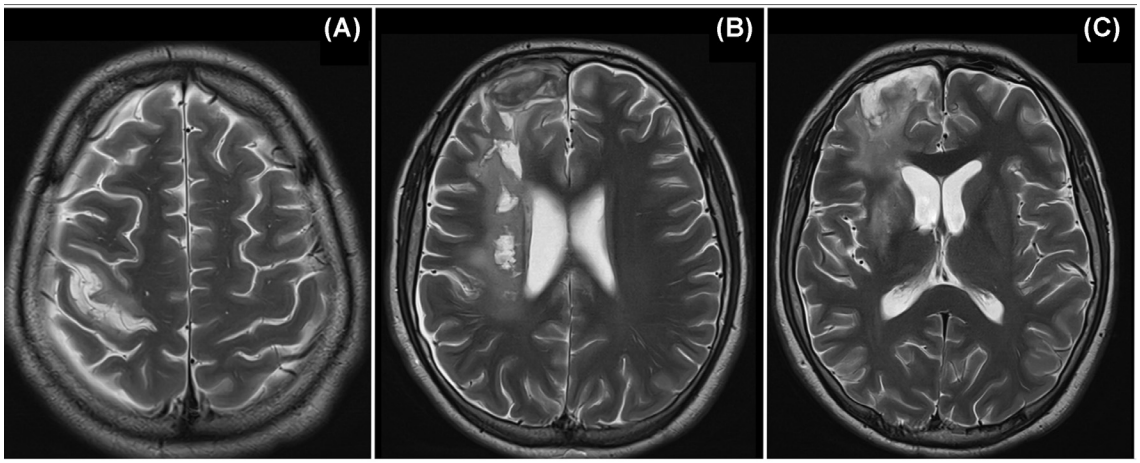

Fig. 8 – About 2 months post progress brain MRI T2 sequence. (A) Cortical enhancement at posterior right frontal lobe/ parietal lobe post cerebral ischemia with gliotic changes. (B and C) Interval progression of right frontal lobe white matter encephalomalacia and surrounding gliotic changes.

Divergent theories exist regarding the pathophysiology of delayed cerebral ischaemia following subarachnoid hemorrhage versus bacterial meningoencephalitis. Some authors recognize that cerebral artery vasospasm secondary to bacterial meningitis encompasses elements of vasospasm, vasculitis, and vasculopathy, underscoring the complex and multifactorial nature of vascular complications in this context [6,7]. *Beuker et al.*, theorized that the temporo-spatial pattern of cerebral vasospasm secondary to bacterial meningitis could distribute among both hemispheres with predisposition to territories of arteries located in vicinity of infection focus [6]. This was present in our case report, with the patients CT perfusion identifying time-to-maximum (T-max) parameter of >6 seconds in both cerebral hemisphere, more so on the affected right frontal with radiological evidence of cerebritis. This played a critical role in interpreting CT perfusion scan as it could be misinterpreted if cerebral vasospasm and delayed cerebral ischemia is not identified as a differential. This acknowledges the theory of various inflammatory mediators within the cerebrospinal fluid compounding this condition [6,7].

Cerebrovascular complications of bacterial meningitis has been reported to reach as high as 30%, consisting of various pathophysiological process such as cerebral hemorrhage, vasculitis, vasospasm, and hypercoagulation [5–8]. Isolated reversible vasospasm following meningitis, however, is notably less common with only isolated case reports documented [5–8]. Unfortunately, preventative and treatment guidelines for bacterial cerebral vasospasm have been extrapolated from the management of subarachnoid hemorrhage. One author even reported aggressive surgical treatment as far as extracranial-intracranial bypass to limit ischemic injury [6–8]. Mechanical balloon angioplasty, an alternative interventional option for cerebral vasospasm, was not immediately utilized until day 6 of daily angioplasty once cerebral vasospasm improved. This cautious approach stems from its associated high mortality rate (8%) due to the risk of stretching target vessel beyond its baseline calibre, predisposing the vessel to injury such as dissection, perforation, and thromboembolism [5].

Conclusion

This case report underscored two critical points. Firstly, it highlights the increasing prevalence of *A haemolyticum*, an unusual source of sinus infection with potential sinogenic complications by contiguous spreading to surrounding structures such as orbits and frontal lobe. The role of radiology has certainly played a significant role in early diagnosis and management due to widespread availability of CT, reducing mortality from 50% to 10% [9].

Secondly, this report advocates for the use of CT brain perfusion scans in identifying cerebral vasospasm and delayed cerebral ischemia, especially in patients with bacterial meningoencephalitis who exhibit worsening neurological symptoms despite appropriate treatment. Unlike typical stroke where signs may be localized to specific territorial infarcts, patients with bacterial meningoencephalitis induced ischemic stroke may present with more diffuse symptoms affecting both hemispheres. Furthermore, the added benefit of a perfusion study would assist radiologist in identifying areas of vasospasm on CT angiography. Therefore, recognizing the possibility of delayed cerebral ischemia in the context of bacterial meningoencephalitis is crucial, which may manifest as symptoms resembling “classical territorial stroke”, regardless of the patient’s age.

Patient consent

Written and verbal informed consent for publication of their details was obtained from the patient and parents.

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