Hong Kong College of Physicians
Case Report for Interim Assessment
Specialty Board of Advanced Internal Medicine (AIM)

For AIM Training, case reports should be submitted in the prescribed format together with the application form for Interim Assessment at least EIGHT Weeks before the date of Interim Assessment

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Hospital and Unit: RH, M&G	Specialty: GI&Hep and AIM
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Date(s) and place (hospital) of patient encounter: 24-28/06/2021 RH	
Date of report submission:	14/03/2024

Case report

Note: Failure to follow the prescribed format (including the number of words) results in a FAILURE mark (score between 0 and 4) for the Case Report.

Title: An unusual stroke patient with a temperature

Case history:

Mrs. Lo was a 67 years old lady. Her past medical history included impaired fasting glucose and borderline hyperlipidaemia discovered during private body check. She was a nonsmoker and nondrinker. She lived with her family and enjoyed good functional status. She was labelled to have penicillin allergy.

Upon waking up on the day of admission, she was noted to have impaired consciousness, slurring of speech, left sided facial asymmetry and reduced limbs movement over right side. In the preceding few days, she had mild malaise and myalgia. Otherwise, she had no fever, chills, rigors, shortness of breath, chest pain, external wound, back pain or toothache. She remained self-ambulatory at 1AM on the night before admission.

Stroke call was activated at 7AM in the emergency department. The patient was assessed by stroke nurse to have a National Institute of Health Stroke Scale score of 25. She was deemed not a candidate for intravenous thrombolytics in view of the wake-up presentation. She was then sent to the medical ward.

In triage, she was noted to have a low grade fever of 38°C, which spontaneously subsided when she arrived at the medical ward. She had a Glasgow Coma Scale of E2V2M4 on admission. She had anisocoria with the left pupil being 4mm sluggish and the right being 2mm reactive. She had left sided gaze deviation. She had left sided upper motor neuron type facial palsy. She could not obey a formal neurological examination, however there were reduced spontaneous movements over her right limbs.

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Her reflexes were symmetrical and slightly brisk. She had bilateral upgoing plantar reflexes without ankle clonus.

Her first computed tomography of the brain (CTB) showed vague hypodensity sized 1cm over the left thalamus. A computed tomography angiography of the brain was also ordered and showed no large vessel occlusion. Her first electrocardiography showed sinus rhythm.

She was started on aspirin alone for the diagnosis of stroke. On the afternoon of the day of admission, she developed a high fever of 40°C. After septic workup was done, she was started on empirical levofloxacin in view of her history of penicillin allergy.

Her first set of blood tests revealed an elevated white blood cell count of 15 x 10^9/L with left shift, a markedly elevated C-Reactive protein of 385 mg/L, acute kidney injury with a creatinine of 141 umol/L and deranged liver function of mixed pattern. CTB was repeated 14 hours after her presentation. The previous left thalamic hypodensity became more obvious. There were also new hypodensities over right pons and cerebellum. The diagnosis of brainstem stroke was made and disclosed to the family.

Reassessment CTB 34 hours after her presentation showed progressive hypodensities over left thalamus, left midbrain, right pons, right cerebellum and right frontotemporal cerebral hemisphere. The result of the blood culture taken the day before was by then available, and was positive for *Staphylococcus aureus*. Physical examinations were repeated, which found Janeway lesions and cutaneous microembolisms over the patient's hands and feet. There was no Osler's node or Roth's spot. Bedside echocardiogram found a suspected 2cm irregularly shaped hyperechoic vegetation in the left atrium. Two additional blood cultures were ordered, they yielded *S. aureus* as well, which was later found to be methicillin-susceptible. As the patient was labelled to have penicillin allergy, intravenous vancomycin was started for the high suspicion of infective endocarditis with embolic phenomenon, while aspirin and levofloxacin were stopped. Cardiac team was consulted, however by the time of their reassessment, the patient was too unstable to be transferred for formal echocardiogram. Cardiac team colleague performed bedside transthoracic echocardiogram instead, and vegetation was no longer seen in the left atrium by then.

The clinical course was further complicated by multilobar hospital acquired pneumonia. The patient's haemodynamics continued to worsen despite intravenous dopamine infusion. Family understood the grave prognosis, however they still wished for active resuscitation. The patient eventually ran into a pulseless electrical activity arrest. Prolonged cardiopulmonary resuscitation could not achieve any return of spontaneous circulation. Patient finally succumbed on the 28th of June, that was the fifth day of hospitalization. Only a possible, but not a definite diagnosis of infective endocarditis, could be arrived using the Modified Duke Criteria. The case was therefore reported to the coroner.

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Post-mortem examination was performed. Over the tricuspid valve, mitral valve and aortic valve, friable yellowish to reddish vegetation was noted, measuring from 0.3cm to 1.5 cm in greatest dimension. Microscopic examination of the vegetations revealed Gram positive cocci. Brain tissue sectioning showed infarction at the left thalamus, left midbrain, right pons and right cerebellum. Besides the central nervous system, infarcts were also noted in the left kidney and both lobes of the liver. In the brain and kidney specimens, septic emboli were noted with Gram positive cocci.

Discussion and literature review

Infective endocarditis (IE) can present with a range of neurological complications. A multicentre retrospective cohort conducted in Spain included 1345 consecutive episodes of left sided IE, among the cases, 14% suffered from ischaemic events, while 4% suffered from intracerebral haemorrhages. Other neurological complications include brain abscess, meningitis, and seizures. [1]

In stroke patients, while the clues to the diagnosis of concurrent IE may not be obvious, in those presenting with unexplained fever, clinicians must bear such possibilities in mind, due to its bearing on the management. Although thrombolytic has been an established treatment for acute ischaemic stroke, it is contraindicated in those with concurrent IE, primarily due to the higher risk of haemorrhagic transformation. A retrospective study was conducted using the USA's Nationwide Inpatient Sample data from the year 2002 to 2010, it compared the clinical outcomes between ischaemic stroke patients with and without concurrent IE. The patients with IE had a significantly higher rate of haemorrhagic transformation after undergoing thrombolysis. The rates were 20% and 6.5% for those with and without IE respectively. [2]

In the unfortunate case presented here, the patient presented with an abrupt history of multifocal neurological deficits, simultaneously affecting both sides, and both anterior and posterior circulation territories. In retrospect, the above was also another clue pointing to the diagnosis of embolic stroke, which further warranted the investigation for the underlying source, cardiac in particular.

Horizontal gaze deviation is not an uncommon presentation in neurological emergencies. The frontal eye fields are responsible for the saccades of horizontal gaze, they innervate the contralateral sixth nerve nucleus and paramedian pontine reticular formation. The contralateral sixth nerve nucleus can then signal the contralateral lateral rectus muscle to contract. Simultaneously by the contralateral sixth nerve nucleus, it innervates the ipsilateral third nerve nucleus via the medial longitudinal fasciculus, thus signaling the ipsilateral medial rectus muscle to contract. Together, both eyes would then look away from the side of the frontal eye fields responsible for the saccade. [3]

Gaze deviation would occur when either side of the signal pathway is unopposed. In destructive lesions

affecting the frontal eye fields, for example in cortical strokes, the eyes would deviate towards the side of the lesions. While in destructive lesions affecting the pons, for example in brainstem strokes, the eyes would deviate away from the side of the lesions. In our patient who presented with left sided gaze deviation, it could be explained by a right sided frontal lesion or a left sided pontine lesion. Subsequent CTB confirmed the involvement of right frontotemporal cortex, which was not apparent in the first scan.

However, the patient's left dilated pupil remained unexplained by the disruption to the horizontal gaze pathway. In the multifocal involvement presented here, notably when left sided midbrain was affected in subsequent scan, it was possible that a mesencephalic syndrome was also present, such as Weber's syndrome. In Weber's syndrome, where the cerebral peduncle and third nerve fascicle are affected, patients would present with contralateral hemiplegia and ipsilateral oculomotor paresis. [4] Therefore, in our case, given the findings of left dilated pupil, it was also possible that the apparent left sided gaze deviation was partially contributed by the "down and out" presentation of a concurrent third nerve palsy.

In cases of suspected infective endocarditis, transthoracic echocardiogram (TTE) is the first line imaging technique, as it is more widely available and less invasive. However, false negative results may occur due to the vegetations being too small or embolized. TTE has a lower sensitivity of around 75% when compared to that of transesophageal echocardiogram (TEE), which can be above 90%. Therefore, in cases of suspected IE with an initial negative TTE, it is reasonable to pursue TEE to improve the diagnostic yield. Even with a positive TTE, TEE is still indicated given its superiority in assessing complications, for example abscess and leaflet perforation. Only in cases with good-quality negative TTE, together with a low level of clinical suspicion, TEE may be considered not mandatory. [5] In our case, it is likely that the vegetation had already been dislodged by the time of cardiologist's assessment. However, she was too unstable to undergo TEE, which further posed obstacle to a definite diagnosis of IE.

The key components of the management for infective endocarditis include timely institution of appropriate antimicrobials, and valve surgery for selected cases with complications. Two or preferably three sets of blood culture should be obtained before starting the antibiotics, if clinical condition allows. In cases with native valve staphylococcal infective endocarditis, one of the societies' guidelines suggested to commence ampicillin with either ceftriaxone, cloxacillin or gentamicin as empirical treatment. While in those with early prosthetic valve endocarditis, healthcare associated infection or beta lactam allergy, vancomycin can be considered as empirical therapy. Indications of surgery depend on the side of heart valves affected, size of vegetation, resistance of the causative organism, response to medical treatment and presence of heart block, heart failure or paravalvular abscess. [6]

Aside from the neurological complications mentioned in the first paragraph, infective endocarditis is also associated with cardiac complications, metastatic infections and immune mediated complications, such as glomerulonephritis. Adverse outcomes are not uncommon with studies showing 6 months mortality up

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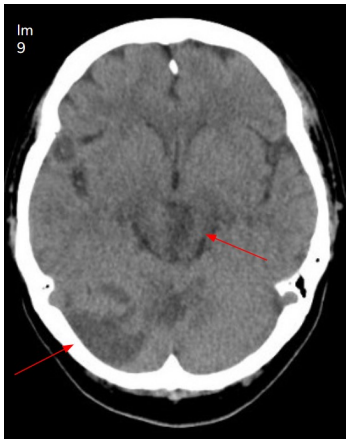
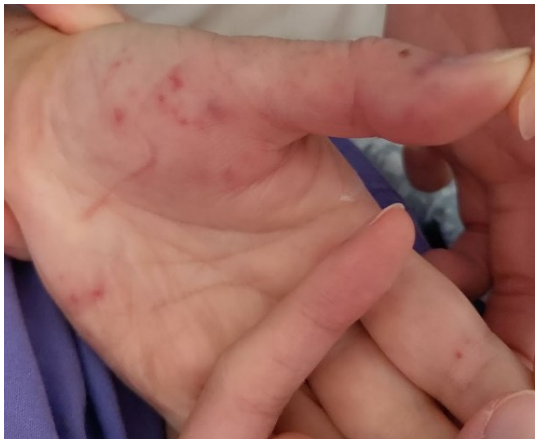
to 27%. [7] Follow up is important to look for relapse, secondary heart failure and need for late valve surgery. Enrolling patients into cardiac rehabilitation programme is also encouraged by international guidelines.

Tables and figures (where applicable) (no more than two figures)

1. 

2. 

1. CTB 34 hours after presentation, showing infarct over left midbrain and right cerebellum.
2. Patient's left hand showing Janeway lesions and cutaneous microembolisms.

Reference (not more than 10)

1. García-Cabrera E, Fernández-Hidalgo N, Almirante B, et al. Neurological complications of infective endocarditis: risk factors, outcome, and impact of cardiac surgery: a multicenter observational study. Circulation. 2013;127(23):2272-2284. doi:10.1161/CIRCULATIONAHA.112.000813
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3. Liu, Galetta, Volpe. Ch.16 Eye Movement Disorders: Conjugate Gaze Abnormalities. In: Liu, Volpe, and Galetta's Neuro-Ophthalmology: Diagnosis and Management. Edinburgh etc.: Elsevier; 2019:549-584.
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6. Delgado V, Ajmone Marsan N, de Waha S, et al. 2023 ESC Guidelines for the management of endocarditis [published correction appears in Eur Heart J. 2023 Sep 20;:] [published correction appears in Eur Heart J. 2024 Jan 1;45(1):56]. Eur Heart J. 2023;44(39):3948-4042. doi:10.1093/eurheartj/ehad193
7. Wallace SM, Walton BI, Kharbanda RK, Hardy R, Wilson AP, Swanton RH. Mortality from infective endocarditis: clinical predictors of outcome. Heart. 2002;88(1):53-60. doi:10.1136/heart.88.1.53

No of words in Case History and Discussion (excluding references): 1686 .

(should be between 1000-2000)

Declaration

I hereby declare that the case report submitted represents my own work and adheres to the prescribed format. I have been in clinical contact with the case selected. The case report has not been submitted to any assessment board or publication and it is NOT related to my second specialty(ies), if any. My consent is hereby given to the College to keep a copy of my case report, in written and/or electronic, at the College Secretariat and allow the public to have free access to the work for reference.

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(signature of Trainee)

Endorsed by Supervisor *

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