New disease

Multi-territory ischaemic strokes and subacute bacterial endocarditis

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Summary

We describe an elderly patient presenting with cardio-embolic stroke who was found to have infective endocarditis (IE) affecting the mitral valve. Penicillin-resistant *Facklamia hominis* was identified as the causative pathogen. Despite initiation of aggressive antibiotic treatment, the patient suffered a fatal myocardial infarction 2 days post-diagnosis of IE.

Facklamia spp. have not been previously reported to be associated with IE. Here, we discuss the link between IE and cardio-embolic stroke along with a discussion of various causative pathogens.

BACKGROUND

Causes of embolic stroke can be broadly divided into three categories: atherosclerotic emboli, cardiac emboli and trauma-associated emboli. Up to a quarter of ischaemic strokes are due to cardio-embolism, and atrial fibrillation and infective endocarditis (IE) are two of the commonest causes of cardio-embolic strokes. Ischaemic stroke is the commonest neurological complication of IE.

CASE PRESENTATION

An elderly patient presented with fever and sudden onset left arm weakness. The patient had presented 3 months previously with expressive dysphasia and right hemiparesis with MRI of the brain (figure 1) showing a right internal capsule lacunar infarct and left cortical parietal infarct with fragmentation indicative of embolic aetiology. The patient had been discharged 6 weeks later on aspirin and dipyridamole with the sequelae of mild expressive dysphasia. No apparent causative factor had been found despite various investigations, including trans-thoracic echocardiogram (TTE).

Examination showed a pyrexia of 39.2°C, blood pressure of 118/62 mm Hg and heart rate of 82 bpm, normal heart sounds with no murmurs, tachypnoea and right basal crepitations. Neurologically, there was global dysphasia, a right homonymous hemianopia and power 3/5 in the left upper limb. The power of lower limbs had remained unchanged.

INVESTIGATIONS

ECG showed a normal sinus rhythm. Blood results of note showed Hb 8.8g/dl, C reactive protein (CRP) 58.2 mg/l (rising to 159.8 mg/l during admission), erythrocyte sedimentation rate 87 mm/h, white cell count $10.0 \times 10^9/l$ and normal renal function. A chest x-ray showed evidence of right basal consolidation and CT brain scan showed acute left occipital lobe and right parietal lobe infarcts with evidence of his previous left middle cerebral artery stroke.

In view of multiple territory infarction, a cardio-embolic source was suspected. Aspirin and dipyridamole were discontinued in favour of clopidogrel. Oral augmentin was started for suspected community acquired pneumonia.

Subsequent blood culture showed penicillin-resistant non-haemolytic cocci resembling *Streptococcus viridans* prompting investigations for IE. Gentamicin and vancomycin were started.

TTE (figure 2) showed thickened mitral valve leaflets with mitral regurgitation. The full blood culture grew *F hominis*.

DIFFERENTIAL DIAGNOSIS

Based on the Duke criteria for the diagnosis of IE,¹ the patient met one major criteria (echocardiographic evidence of endocardial involvement) and three minor (pyrexia, embolic stroke as vascular phenomenon, positive blood culture that did not meet the major criteria).

OUTCOME AND FOLLOW-UP

Unfortunately, despite aggressive intravenous antibiotic treatment, the patient suffered a fatal myocardial infarction 2 days later. At that stage, there had been no response to antibiotic treatment with persistently rising inflammatory markers. Following a brief discussion with family regarding autopsy, the medical team decided that an autopsy was not essential for provision of death certificate and cause of death was recorded as stroke secondary to infective endocarditis.

DISCUSSION

Cerebrovascular complications occur in up to 40% of patients with IE.² Research has shown that initiation of antibiotic treatment can reduce the rate of neurological complications from 25% to only 6–6.3%,³ which further highlights the need for rapid diagnosis and treatment of IE.

F hominis is a Gram-positive, alpha-haemolytic, catalase-negative coccus and was the first of the *Facklamia* spp.

Figure 1 MRI brain, DWI image of a man with expressive and receptive dysphasia as well as left arm weakness.

Figure 2 Trans-thoracic echocardiogram on second hospital admission.

described in 1997.⁴ *Facklamia* spp. resemble viridans streptococci on 5% sheep blood agar and are thought to have previously been wrongly identified as part of this group of organisms.

Of the human clinical specimens that *Facklamia* spp. have been isolated from, including blood cultures and cerebral spinal fluid, only one has been reported as from a male. It has been postulated that the female genital tract is the natural habitat of *Facklamia* spp., in contrast to *S viridans* whose natural habitat is the oropharynx.⁵ *Facklamia* spp. have not previously been associated with IE. While some strains have shown resistance to penicillin, none has demonstrated resistance to vancomycin.

It is interesting to speculate whether this patient had developed the IE earlier at presentation of the first two multi-territory strokes. The previous ECG was re-examined with no evidence of vegetations. One study⁶ found a median incubation period for IE of 10 days with the longest period being 2 months. However, the median time to diagnosis was 6 weeks.

Delay in diagnosis was thought to be due to mild and non-specific early manifestations and antibiotic use. During the initial admission, the patient had spiked a temperature and a rising CRP with some coinciding loose stools. It was thought this was due to a viral infection and the CRP did appear to improve. No blood cultures were sent at the time.

But what further complicates the case in retrospect is that there are reports of cases where traditional microbiological methods for microbial identification had incorrectly identified *Facklamia* spp. as the causative organism in endocarditis only for 16S rRNA gene sequencing to identify the isolate as *Enterococcus faecalis*.⁷ This raises the possibility that, in the present case, erroneous microbiological identification may have occurred; thereby, influencing the antibacterial treatment. However, whether this would have had an effect on patient prognosis is doubtful, in view of the severe sepsis and co-morbidities.

Nevertheless, this highlights the need for using 16S rRNA gene sequencing and other genetic tools when traditional microbiological identification methods identify pathogens not typically associated with serious infections, such as endocarditis, where misidentification of pathogens has the potential detrimental effect on patient prognosis. However one also has to bear in mind that the genetic tools have their

own drawback, such as their cost, which is much greater compared to the traditional methods.

Learning points

- ▶ IE is an important cause of ischaemic stroke and a high degree of suspicion is required for its timely diagnosis, as its early detection and subsequent initiation of treatment can have a positive impact on the prognosis.
- ▶ The finding of IE caused by *F hominis* in a male patient and the aggressive way in which the patient was affected highlights the need for further study of the *Facklamia* spp.
- ▶ Alpha-haemolytic streptococci isolated from blood cultures are frequently discarded as contaminants; therefore, it also draws to attention the need to consider the addition of *Facklamia* spp. to commercial rapid identification kits for Gram positive cocci.
- ▶ Consider using rRNA gene sequencing and other genetic tools when traditional microbiological identification methods identify pathogens not typically associated with serious infections, such as endocarditis.

Competing interests None.

Patient consent Not obtained.

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