CASE REPORT

Neurogenic pulmonary oedema secondary to vertebral artery dissection while playing tennis

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SUMMARY

We present a case of a patient who developed vertebral artery dissection (VAD) while playing tennis and presented with neurogenic pulmonary oedema. The case highlights two important points: acute pulmonary oedema as an unusual presenting feature of VAD and VAD, an important cause of stroke in young people, as being associated with playing low-impact sports such as tennis. These associations, independent of each other, are under-recognised and can lead to a delay in diagnosis.

BACKGROUND

Neurogenic pulmonary oedema (NPO) association with vertebral artery dissection (VAD) has not been described much in the literature. To our knowledge, it has only been described once in 1999,¹ where a 34-year-old man presented with signs and symptoms of pulmonary oedema preceded by a severe neck and occipital pain without trigger accompanied by dysarthria and right hand paraesthesia. Cerebral angiography and MRI showed dissection of the right vertebral artery with cerebellar and medullary infarction. VAD has been reported to occur with vigorous neck movement and manipulation. However, low-impact sports such as playing tennis has only rarely been reported as a cause.²

CASE PRESENTATION

A 38-year-old female with no previous medical history presented with sudden onset of a headache and neck pain with unsteady gait and dizziness while playing tennis. Physical examination at emergency

department showed evidence of truncal ataxia. Subarachnoid haemorrhage was initially suspected but non-contrast CT head and lumbar puncture were negative (see investigations). She was given analgesia and kept under observation. Three hours later, she started to develop rapidly worsening breathlessness with increasing oxygen requirement from normal oxygen saturation to 90% on 10 L/min within 6 hours. Repeat examination revealed bilateral lung crepitations.

INVESTIGATIONS

Initial chest X-ray showed non-specific mild patchy changes in the left lung. A repeat chest X-ray after she developed breathlessness (figure 1) showed rapidly worsening bilateral lung infiltrates without cardiomegaly. The B-type natriuretic peptide (BNP) level was normal on admission but increased to 358 pmol/L 12 hours later. C-reactive protein was normal but the white cell count was elevated at $20.9 \times 10^9/L$ with neutrophilia.

Brain MRI 3 days later showed a small focus of acute diffusion restriction consistent with an infarct in the posterior right cerebellum in the territory of the posterior inferior cerebral artery (figure 2) with occlusion of the intracranial portion of the right vertebral artery (V4). An MR angiography revealed occlusion of the distal right vertebral artery (figure 3) due to dissection with a flap just distal to the junction between the foramenal (V2) and atlantic (V3) segments (figure 4). There was no evidence of vasculitis or fibromuscular dysplasia.

Investigations for autoimmune disease or infection were negative, confirming the suspicion that the vertebral dissection is likely related to the neck trauma associated with playing tennis. An echocardiogram a week later showed normal systolic function with grade 1 diastolic dysfunction without any valvular pathology.

DIFFERENTIAL DIAGNOSIS

The breathlessness and X-ray changes were thought to represent either pulmonary oedema or bilateral pneumonia. The pulmonary oedema can be neurogenic or secondary to fluid overload, especially if there is a pre-existing cardiac failure. The stroke could have impaired the swallow and lead to aspiration pneumonia. Supporting evidence of NPO is the very brisk development and resolution of symptoms and signs, raised BNP and normal echocardiography.

Figure 1 A chest radiograph showing bilateral lung infiltrates without cardiomegaly.

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Figure 2 A diffusion-weighted MRI showing right cerebellar diffusion restriction consistent with cerebellar infarct.

TREATMENT

She received antibiotics and supportive care through bilevel positive pressure ventilation and high-flow nasal cannula in intensive care unit. A chest X-ray done 24 hours later showed near complete resolution of the infiltrate opacities, consistent with resolving acute pulmonary oedema.

After vertebral dissection was found, she was treated with dual antiplatelet therapy for 3 weeks followed by long-term aspirin. The patient required opioid analgesia and topiramate for the headache.

Figure 3 Non-contrast MR angiography showing occluded intracranial right vertebral artery (red arrow) and patent left one (green arrow).

Figure 4 Fat-suppressed axial T1 MRI images showing the normal flow void in the left vertebral artery (yellow arrow) and lack of flow void with a bright signal surrounding the right vertebral artery (red arrow), indicating a dissection of the right vertebral artery.

OUTCOME AND FOLLOW-UP

She needed a period of inpatient rehabilitation to improve mobility. She made a very good recovery and was discharged to an independent living at home at near baseline function. A follow-up MRI head after 3 months showed resolution of the acute cerebellar infarction changes and the right vertebral artery still entirely occluded with the vertebrobasilar system being supplied exclusively from the left side.

DISCUSSION

This case highlights two important points: acute pulmonary oedema as an unusual presenting feature of VAD and also illustrates how VAD, an important cause of stroke in young people, could be associated with playing low-impact sports such as tennis. These associations are under-recognised and can lead to a delay in diagnosis. Our patient is unfortunate to develop two rare associations.

Despite the fact that NPO has been known about for more than a century, it is still underappreciated, probably partly due to its heterogeneous causes, unpredictable occurrence, lack of clear diagnostic criteria and definitive treatment modalities.³ NPO, a relatively uncommon condition, is associated with many neurological insults, most commonly subarachnoid haemorrhage,⁴ traumatic brain injury⁵ and seizures (especially status epilepticus).⁶ A common theme in most case descriptions of NPO is the severity and acuity of the precipitating neurological injury.³ Neurological insults to the brainstem can lead to NPO. Aneurysmal subarachnoid haemorrhage originating from the vertebral artery is associated with higher risk of NPO.⁷ Other conditions that can give rise to NPO include medullary and cerebellar haemorrhage.⁸

NPO typically develops within minutes to hours following the neurological injury with an impressively abrupt respiratory distress, as seen in our case report. Typical features are acute dyspnoea, tachycardia and hypoxia with bilateral crackles on lung auscultation. Fever and leucocytosis can occur, and this was observed in our case. A chest radiograph typically reveals acute

bilateral infiltrates which resolve swiftly within 24–48 hours as symptoms abate.³

The mechanism by which NPO develops is not completely understood but is likely related to excessive sympathetic activation through increased intracranial pressure, medulla oblongata and hypothalamus injury.³ VAD leading to brainstem ischaemia could give rise to these NPO triggers. Abrupt high intracranial pressure is common with brainstem injury and correlates with higher likelihood of NPO through neuronal compression and ischaemia which leads to intense sympathetic outflow.^{7,9} Medulla oblongata is also key in NPO development, and studies have shown medullary injuries can cause NPO.⁷ These central triggers cause pulmonary oedema through increased hydrostatic pressure in lung capillaries. Increased capillary permeability has also been implicated based on the exudative properties of some of the pulmonary fluid in NPO possibly due to barotrauma-related structural damage to lung capillary endothelium leading to vascular leak.³ Although it is 'non-cardiogenic', there is evidence that NPO can cause, in some patients, transient cardiomyopathy as evidenced by findings on myocardial biopsies and wall motion abnormalities on echocardiography.¹⁰ However, this is not always found, and in our patient, the echocardiography showed normal systolic function with no wall motion abnormalities. Elevated BNP can also occur in conditions such as subarachnoid haemorrhage where it is associated with cardiac dysfunction and development of NPO.¹¹

VAD has an overall incidence of approximately 1–1.5 per 100 000 people.^{12–14} The average age of patients is 40 years,¹⁵ with only 7% of patients aged ≥ 60 years.¹⁶ Men are affected more than women.¹⁷ Spontaneous dissections of the carotid and vertebral artery account for only about 2 per cent of all ischaemic strokes,¹² but they constitute up to 25% of ischaemic strokes in patients younger than 45 years old.¹⁸

VAD can be spontaneous or secondary to trauma. Acute hypertension has been implicated as a risk factor in spontaneous VAD.^{19,20} Causative link with vascular risk factors, such as chronic hypertension and hypercholesterolaemia, is less established because atherosclerosis, which affects older population, appears to be less common in patients with carotid and VAD.²¹ The trauma trigger does not have to be major neck trauma. Although sport activities have been associated with VA, playing tennis has only rarely been reported to cause VAD.² Other minor trauma includes chiropractic manipulation, abrupt head turning, massage, falls, bending over, positioning for surgery or riding a roller coaster. Sports identified as possible risk factors are jogging, horseback riding, skiing and surfing. Other risk factors are smoking and connective tissue disorders, including fibromuscular dysplasia. This is in addition to major trauma, such as motor vehicle accidents.^{22,23} Some other activities include neck hyperextension or rotation such as practising yoga, painting a ceiling or the receipt of anaesthesia.²¹

VAD can arise through an intimal flap with extravasation of blood into the vessel wall or through haemorrhage of the vasa vasorum within the media layer due to trauma. The dissection can expand to intracranial vessels and rupture leading to subarachnoid haemorrhage. However, this occurs less commonly in VAD compared with carotid dissection.²⁴ The MR angiography finding of intimal flap probably supports the former in our case. This has led to complete occlusion of the distal vertebral artery either due to expanding haematoma or thrombosis due to the thrombogenic intimal disruption. VAD commonly presents with headache and neck pain and can lead to brainstem and cerebellar ischaemia. Cerebellar ischaemia has been reported in up to 33% of patients with VAD in a case series.²⁵ In a series of

195 patients with VAD,²⁶ the most common presenting symptom (in 88%) was head and neck pain. 77% of patients had transient ischaemic attack (TIA) or stroke, while only 1.5% had subarachnoid haemorrhage with or without stroke. The most common locations for VAD were pars transversaria segment (V2) and the atlas loop segment (V3). Our patient had the dissection in this common location, and this led to cerebellar infarction manifesting as truncal ataxia. In our patient, an MRI should have probably preceded the lumbar puncture given the focal neurological sign of ataxia.

Most recommendations on NPO management centre on supportive management through supplemental oxygen or ventilation.²⁷ If non-invasive or mechanical ventilation is required, caution is advised as permissive hypercapnia strategy, commonly employed in acute respiratory distress syndrome, can cause cerebral vasodilation, thereby increasing intracranial blood flow and pressure.²⁷ Diuretics may be used to treat NPO, although there are no trials to definitely support it and it carries a risk of hypovolaemia and compromised cerebral perfusion. Prognosis of NPO depends mainly on the underlying neurological injury rather than the pulmonary oedema, which tends to be transient and well tolerated with supportive treatment.

There are only a few small-size observational studies to guide the optimal management of VAD. The treatment of VAD without subarachnoid haemorrhage has evolved from surgical or endovascular intervention to now mainly antithrombotic medical treatment.^{17,24} Endovascular or surgical treatment may be taken only if there is recurrent ischaemic symptoms or subarachnoid haemorrhage.¹⁷ Endovascular options include angioplasty or stent placement, thereby occluding the false lumen and restoring the true lumen patency.

The optimal antithrombotic choice in arterial dissection is unknown as there are no large randomised trials comparing antiplatelet agents with anticoagulants. The Cervical Artery Dissection in Stroke Study (CARDISS) trial is the only randomised trial that compared patients with extracranial carotid and vertebral dissection on either antiplatelet (aspirin, dipyridamole or clopidogrel alone or in combination) or anticoagulation (warfarin with or without preceding heparin). There was no difference in the rates of ischaemic stroke (antiplatelet 2%, anticoagulation 1%), major bleed (antiplatelet 0%, anticoagulation 0.8%) or death between the two treatments.²⁸ However, the overall rate of stroke among the study population was much smaller than reported in other studies (with a 2% stroke rate within 3 months and no deaths) and diagnosis was not established using standard radiographic criteria in many cases. A retrospective study of 370 patients with carotid and vertebral dissection demonstrated no significant difference in the rate of new or recurrent ischaemic or haemorrhagic events between antiplatelet (used aspirin alone in 32% of cases, clopidogrel alone in 18% and both in 50% of cases), anticoagulation (warfarin with initial heparin) or the combination treatment strategies. There was also no difference between intracranial and extracranial dissections. The rate of unfavourable clinical outcome (Modified Rankin Score 3–6) did not differ between patients on different courses of treatment.²⁹ Multiple meta-analyses of non-randomised studies of carotid and VADs showed no difference in recurrent stroke, complications or mortality comparing anticoagulation with antiplatelet therapy.^{30,31} In a systematic review of 762 patients with cervical dissections, no difference was detected in the risk of TIA and stroke with antiplatelets (7%) and anticoagulants (3.8%).³² In another systematic review of 327 patients, mortality and disability were similar between both treatments (1.8%).³³ There are no studies that examined the use of new oral anticoagulants.

Anticoagulation carries a higher risk of bleeding, and it should be avoided if there is subarachnoid haemorrhage or other risk factors for major bleeding.¹⁷ Evidence suggests that thrombolysis in VAD does not carry any greater risk compared with stroke from other causes.³⁴

Most guidelines suggest treatment with either therapy for 3–6 months.^{35 36} The duration of acute treatment likely reflects the time course of healing of the vessel wall as most arterial disruptions stabilise or resolve by 3–6 months. Initial arterial occlusion reduces the likelihood of complete recanalisation.³⁷ This probably explains why our case had persistent occlusion of the vertebral artery at 3 month follow-up. The guidelines also suggest that for patients with recurrent cerebral ischaemic events despite medical therapy, endovascular therapy (stenting) may be considered.³⁵

The clinical outcomes for VAD are generally good, especially in patients without ischaemic symptoms. Complications, such as subarachnoid haemorrhage recurrent stroke and mortality, are not common,²⁴ with the rates of recurrent ischaemic events estimated to be in the range of 0%–15%.³⁸

Learning points

- Neurogenic pulmonary oedema can occur following many neurological insults and typically develops and resolves rapidly and overall prognosis depends on the underlying neurological injury.
- Vertebral artery dissection can occasionally occur with low-impact sports such as playing tennis.
- Vertebral artery dissection can present atypically with cerebellar infarction and neurogenic pulmonary oedema.

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