This patient is unique in that severe orthostatic hypotension is the isolated feature of this paraneoplastic neuropathy. To the authors' knowledge this has not yet been described in the literature. The largest report of CRMP-5 paraneoplastic syndromes comes from an analysis of 116 CRMP-5 seropositive patients [3]. In this retrospective study, 31% were found to have autonomic manifestations, and of these, one-third had multiple autonomic features and two-thirds had isolated gastro pseudo-obstruction.

In patients with CRMP-5 seropositivity, 9% will be without a clinical syndrome [5]. In our patient, we were satisfied that hypovolaemia, adrenal insufficiency and diabetes were excluded. Our patient was also not on any regular medications associated with postural hypotension.

We felt chemotherapy-induced neuropathy to be the most important differential [2]. Peripheral neurotoxic effects of chemotherapy can manifest immediately, shortly after, or even with a long delay following cessation of therapy, and autonomic dysfunction is frequently present [6,7]. Neuronal damage is typically dose dependent. While the first cycle of carboplatin would be of adequate dose to cause neurotoxicity, orthostatic hypotension is rarely documented and importantly, the delay between last treatment and hypotension makes it an unlikely culprit. The neurotoxic dose of vincristine is greater than 4 mg and more than 33% of patients develop autonomic neuropathy, including orthostatic hypotension [7]. However, our patient's symptoms commenced if not before, then at the time of, the first cycle of vincristine (cumulative dose 2 mg). It is quite possible, however, that our patient's paraneoplastic neuropathy was worsened with neurotoxic chemotherapy. It is well recognised that these dual neuro-pathologies can frequently be at play in the setting of malignancy [7].

Paraneoplastic autonomic dysfunction is unfortunately a poor prognostic finding. The Paraneoplastic Neurologic Syndrome Euronetwork Database found these patients did not improve with immunotherapy after tumour treatment and had the highest incidence of paraneoplastic syndrome related death [8]. As in this patient, for both prognostication and advanced planning, it is therefore very beneficial to accurately diagnose the cause of an autonomic neuropathy occurring on a background of malignancy.

## Conflicts of interest/disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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# Thromboembolic stroke associated with thoracic outlet syndrome

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ABSTRACT

Thoracic outlet syndrome occurs due to compression of the neurovascular structures as they exit the thorax. Subclavian arterial compression is usually due to a cervical rib, and is rarely associated with thromboembolic stroke. The mechanism of cerebral embolisation associated with the thoracic outlet syndrome is poorly understood, but may be due to retrograde propagation of thrombus or transient retrograde flow within the subclavian artery exacerbated by arm abduction. We report an illustrative patient and review the clinical features, imaging findings and management of stroke associated with thoracic outlet syndrome.



## 1. Introduction

Thoracic outlet syndrome (TOS) occurs due to compression of the neurovascular structures as they exit the thorax between the scalene muscles, the clavicle and the first rib, and can present with neurological, arterial or venous occlusive symptoms [1,2]. Subclavian arterial compression is commonly attributed to a cervical rib. This abnormality is present in around 1% of the population, is bilateral in 50% of patients, and is twice as common in women [1].

Subclavian arterial compression leads to claudication, weak pulse and reduced blood pressure in the affected arm, all of which become more pronounced with arm abduction [1,2]. A subclavian bruit or a pulsatile supraclavicular mass may be present if there is a stenosis and associated post-stenotic aneurysm. If thrombus

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forms within the aneurysm, this may embolise to the axillary or brachial arteries leading to acute arterial occlusion. Thromboembolic stroke associated with TOS is a rare event first described by Symonds in 1927 [3], although a patient with obliterative arteritis described by Gould in 1884 and updated in 1887 may also represent the association [4,5]. We report a case of right middle cerebral artery (MCA) territory ischaemic stroke in a teenager with a concurrent diagnosis of cervical rib and subclavian arterial compression.

## 2. Illustrative patient

A 16-year-old girl presented with left hemiparesis. Past history included several months of intermittent digital cyanosis, pain and numbness of the right hand only. She was otherwise healthy with no regular medications, had modest alcohol intake, smoked tobacco occasionally, and denied illicit drug use.

Ten days before admission, the patient had an episode of left-sided weakness, which lasted several hours but completely resolved. On the day of presentation the patient awoke with left-sided weakness and mild right-sided headache. Right brachial blood pressure was unrecordable and brachial, radial and ulnar pulses were absent. Her preferred sleeping posture was right lateral decubitus with extreme right shoulder abduction for head support.

MRI of the brain revealed acute right MCA territory infarction (Fig. 1). A plain radiograph demonstrated bilateral cervical ribs (Fig. 2). Digital subtraction angiography of the head, thoracic outlet, and right upper extremity revealed occlusion of the M1 segment of the right MCA, segmental occlusion of the right proximal brachial artery, and functional occlusion of the right distal subclavian artery (SCA) during shoulder abduction with post-stenotic dilatation (Fig. 3). No thrombus was seen in the dilated portion of the SCA.

Blood cell counts with film and inflammatory markers were normal. Thrombophilia and vasculitis tests were negative. Electrocardiogram showed sinus rhythm with no arrhythmia during 48 hours of telemetry. A trans-thoracic echocardiogram with agitated saline injection and delayed phase imaging did not reveal an interatrial shunt, and trans-oesophageal echocardiogram was normal.

The patient was commenced on warfarin and underwent rehabilitation. She subsequently underwent surgical resection of the right cervical rib via a supraclavicular approach. There was compression of the SCA between a complete cervical rib (which articulated with the first rib) and scalenus anterior (Fig. 4). Anterior scalenotomy was performed, and the first and cervical ribs were resected; SCA reconstruction was not required. The patient recovered without complication.

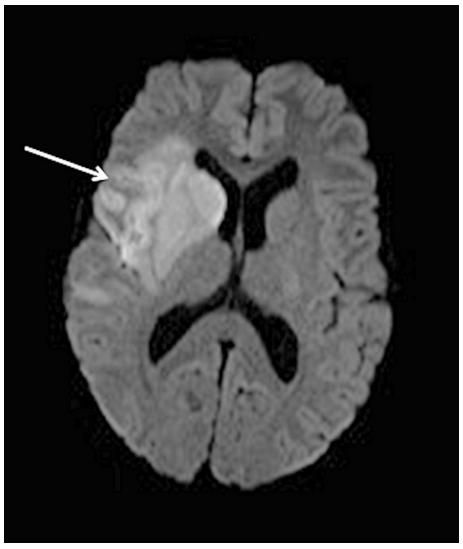

**Fig. 1.** Axial diffusion weighted MRI demonstrating acute right middle cerebral artery infarction.

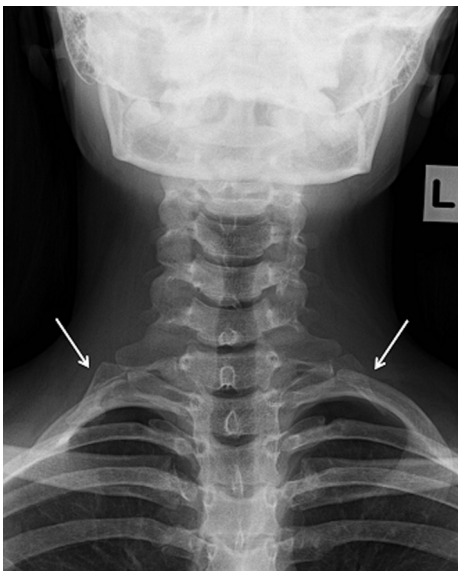


**Fig. 2.** Plain anteroposterior radiograph demonstrating bilateral cervical ribs (arrows).

## 3. Discussion

The mechanism by which TOS-associated cerebral embolisation occurs is poorly understood. Subclavian arterial compression leading to stasis, intimal trauma and thrombus formation is likely the initial event. Retrograde propagation of thrombus to the origin of the vertebral or common carotid arteries may occur next [3]. In some patients with TOS and associated stroke, thrombus extending into the innominate artery has been found on vascular imaging [6,7], and during surgery [8]. An alternative explanation is transient retrograde flow within the SCA. This has been identified using ultrasonography in some patients with TOS associated with stroke [8,9], and experimental studies have demonstrated that retrograde SCA flow can be readily induced [10,11]. In this patient it is proposed that prolonged occlusion of the SCA during sleep with extreme shoulder abduction could have led to stasis and thrombus formation at the SCA origin. The episode of weakness a week prior to presentation is suggestive of a separate episode of embolisation from this source; extensive investigation did not reveal a cardiac abnormality to account for these events.

Including the patient reported here, 33 patients with stroke or transient ischaemic attack associated with SCA disease have been reported in detail, as well as an additional three patients within case series without detailed clinical information [12–14]. Twenty-six of these reported patients were associated with cervical rib [3–9,15–29]. Other reported causes of SCA disease associated with stroke include left first rib anomaly [30], a non-united right clavicular fracture [31], repetitive sporting injury [32], atheroma [8,15], dissection [33], and presumed congenital saccular aneurysm of the axillary artery [34].

Stroke associated with cervical rib is an entity seen in young people; among the 26 reported patients with stroke associated with cervical rib, the median age was 21 years (range, 14–49 years). Thirteen (50%) were male. Twenty-one (81%) patients had preceding symptoms suggestive of TOS for between 3 weeks