CASE REPORT

Subclavian vein thrombosis in an otherwise healthy 9-year-old boy

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SUMMARY

We report a previously well 9-year-old boy who presented with an acutely swollen left arm after horse riding. Left subclavian vein thrombosis was demonstrated by MR venography but there was no evidence of an underlying anatomical abnormality. The child was successfully treated with catheter directed thrombolysis and anticoagulation with intravenous unfractionated heparin and warfarin. We have identified 75 previously published case reports of effort-induced upper extremity deep vein thrombosis (UEDVT) and surveyed patient characteristics and precipitating activities. In this case and literature review, we demonstrate that individuals with effort-induced UEDVT show demographic characteristics and presenting features that are distinct from other patient groups with venous thromboembolic disease. We also highlight the difficulties in counselling affected individuals about modifying occupational and recreational activities to minimise the risk of recurrent thrombosis.

BACKGROUND

Effort-induced upper extremity deep vein thrombosis (UEDVT) is a rare thrombotic disorder that may be associated with significant long-term sequelae. Management strategies for effort-induced UEDVT have been discussed in several recent systematic reviews.^{1–5} However, the spectrum of precipitating activities has been documented poorly. Knowledge of the aetiology of effort-induced UEDVT in individual patients is essential to provide appropriate advice about modifying activities to avoid recurrent thrombosis.

CASE PRESENTATION

A 9-year-old boy presented to his local accident and emergency department with swelling of his left arm that developed over an interval of less than 2 h. The child was a keen horse rider and in the week preceding presentation he had been riding considerably more than was usual for him. There were no other identifiable precipitants for unilateral upper extremity swelling, nor any significant comorbid disorders. The child had no personal or family history of venous thromboembolic disease.

On examination, the child's upper left arm was 5.3 cm greater in diameter than the right and was warm to touch, but non-tender. He had prominent dilated superficial veins over his upper left chest and arm. The left arm was well perfused, with normal pulses that were synchronous with the right side. On examination, there were no demonstrable

anatomical abnormalities of the left axilla or thoracic wall.

INVESTIGATIONS

Blood tests at presentation demonstrated raised plasma D-dimer concentration (>10 000 ng/mL; normal <500), but otherwise normal blood count, renal and liver function tests. A MR venogram (figure 1) demonstrated reduced flow in the left subclavian vein, indicating UEDVT. There was no evidence of external compression of the subclavian vein. A plain chest radiograph showed no thoracic or upper limb bony abnormality. Ultrasound of the left axilla and neck identified no soft tissue abnormalities.

DIFFERENTIAL DIAGNOSIS

The diagnosis of UEDVT by imaging investigations was unambiguous. However, determining the underlying aetiology required careful clinical evaluation. Excluding recent surgery or trauma to the upper limb, or recent central venous catheter placement was straightforward from the clinical history. However, exclusion of important underlying inflammatory or even malignant disorders required careful clinical evaluation. The diagnosis of effort-induced UEDVT was reached after exclusion of other precipitants for UEDVT and identification of a physical activity associated with recurrent mechanical impingement of the upper limb venous system.

Figure 1 MR venogram at presentation in the index case. Demonstrates absent flow in the left subclavian and axillary veins.

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TREATMENT

Management comprised catheter-directed thrombolysis with recombinant t-PA (Alteplase), infused via a peripherally inserted central catheter (2 mg/h for 24 h increased to 4 mg/h for 48 h) inserted into the median cubital vein. Unfractionated heparin (20 u/kg/h) was infused continuously for the duration of thrombolysis and was continued for a further 4 days. Oral anticoagulation with warfarin (target International Normalised Ratio 2.0–3.0) was initiated on the day thrombolysis stopped and was continued for 3 months.

OUTCOME AND FOLLOW-UP

Repeat MR venogram at 1 month after presentation demonstrated thrombus resolution. After the completion of 3 months of oral anticoagulation the child was well and had returned to normal activities, however some residual arm swelling remained. At the end of anticoagulation treatment, levels of antithrombin, protein C and free protein S activities were within laboratory reference interval. The child did not harbour the Factor V Leiden or prothrombin G20210A polymorphisms.

DISCUSSION

UEDVT accounts for 4–11% of all presentations of venous thromboembolic disease,^{6–8} and has an estimated annual incidence of 0.4 to 1 case/10 000 people.⁹ Case series of adults indicate that 80% of UEDVT are associated with indwelling

central venous catheters, pacemakers or defibrillator leads placed in the upper limb venous system or with other secondary causes such as malignant disease, surgery or trauma to the upper limb, pregnancy, the use of oral contraceptives or ovarian hyperstimulation syndrome.⁹ The remaining 20% of UEDVT in adults (primary UEDVT) may be spontaneous in patients with an anatomical abnormality of the thoracic outlet causing external compression of the subclavian or axillary veins (venous thoracic outlet syndrome). UEDVT may also be precipitated by mechanical exertion involving the upper limb (effort-induced UEDVT or Paget-Schroetter syndrome), even in the absence of a demonstrable anatomical abnormality. In children, UEDVT is more frequently associated with the placement of upper limb venous catheters and is very rarely effort-induced.^{10 11}

In order to improve understanding of the aetiology of effort-induced UEDVT we reviewed previous descriptions of precipitants, risk factors and presenting features in the MEDLINE and Embase databases using key words and a systematic inclusion criteria (figure 2). Participant age and gender, precipitating activity, other risk factors and presenting clinical features, were identified in each article and were recorded using a standardised pro forma.

The search and filtering strategy identified 75 cases of effort-induced UEDVT that were presented in 53 individual case reports and 10 case series. The patient group comprised 58 (77%) males and had median age 23 years (range 14–76). In the

Figure 2 PRISMA flow diagram. Studies included in the systematic review. MEDLINE and Embase were searched on 25th July 2013 using the terms 'effort induced', and 'Paget Schroetter' or 'subclavian vein thrombosis' or 'upper extremity deep vein thrombosis'. Duplicate records identified in more than one search and non-English language articles were excluded from further analysis. In order to improve identification of case reports and series which documented the presenting feature and aetiology of effort-induced upper extremity deep vein thrombosis (UEDVT), the search was restricted to the article type 'case reports'. The abstracts, and if necessary, the full text of unique retrieved articles were screened to include all reports of a first acute presentation (within 2 weeks of the start of symptoms) of UEDVT associated with antecedent mechanical activity of the upper limbs. Articles in which there was no documented mechanical precipitant, or without an acute presentation were excluded.

71 cases in which laterality was documented, UEDVT occurred in the right upper limb in 45 (63%). In the 28 cases in which limb dominance was recorded, the dominant arm was affected in 19 (68%). The median time interval from the identified precipitating activity to the development of symptoms was 1 day (reported in 29 cases; range 0.5–14). The presenting symptoms were reported in 74 cases and comprised swelling in 68 (92%), pain in 46 (62%), and paraesthesia in 6 (8%) cases. No patients presented with symptoms suggestive of pulmonary embolus or venous thromboembolic disease at other sites. The findings of clinical examination were reported in 71 cases and comprised swelling or oedema of the affected arm in 51 (72%), discolouration in 37 (52%) and dilation of superficial veins in 27 (38%) cases.

A potential mechanical precipitant was documented in all 75 cases (table 1).

External compression or other abnormality of the subclavian vein was reported in 15 (20%) cases. The presence or absence of underlying risk factors of thrombosis were reported in 57 (76%) cases. The results of a venous thrombophilia screen were documented in 30 (40%) cases, eight of these (27%) contained at least one abnormal result. Of the 30 cases in which a family history of venous thromboembolic disease was documented, 26 (87%) cases had a negative and four (13%) cases had a positive

family history. Of the 40 cases in which a previous personal history of venous thromboembolic disease was documented, 39 (98%) cases had a negative previous personal history and one had a positive history. In six cases, the affected individuals had recent exposure to the combined oral contraceptive pill.

We have described the youngest reported case of effort-induced UEDVT in the world literature and summarised a series of 75 further cases in which the presenting features, precipitant and risk factors are described. The striking characteristics of this patient cohort are the young age at presentation (median 23 years) and sex bias (3:1 male). This contrasts with data from previous demographic studies of all-cause UEDVT in which the median age of participants was 58 (50% male),⁸ 46 years (29% male)¹² and 54 years (52% male).⁶ In these previous studies, the proportion of patients with UEDVT that was related to a central venous catheter was approximately 50%. However, in subgroup analyses in which central venous catheter patients were excluded, the remaining patients with UEDVT were of older age at presentation and approximately equal gender distribution^{8 12} which contrasts with the demographic profile of effort-induced UEDVT identified in our case series and illustrated by our case report.

Together, these findings suggest that patients with effort-induced UEDVT comprise a demographically distinct group of predominantly young males. One explanation for this association is that this group may be more likely to participate in high-risk activities for this disorder. In support of this, effort-induced UEDVT occurred more frequently in the right/dominant upper limb in affected individuals suggesting a local mechanical effect. The other characteristics of the effort-induced UEDVT such as presenting symptoms and signs, and frequency of thrombophilia and other risk factors were similar to those reported in other demographic studies of all cause UEDVT.^{6 8 12}

It is significant that all of the precipitating activities identified in this case series and in our illustrative case report involve repetitive or strenuous activity of the upper limb, typically including shoulder abduction. The subclavian vein passes through the anterior part of the thoracic outlet, between the junction of the clavicle and the first rib and the costoclavicular ligament at which point it is susceptible to extrinsic compression during abduction of the upper limb. Our findings support the hypothesis that local thrombus formation may be precipitated by endothelial microtrauma as a consequence of venous compression at this site.⁹ This case report and series review also illustrate that in the majority of patients no underlying anatomical abnormality could be demonstrated in the thoracic outlet. Thus, compression significant to cause UEDVT is possible without pre-existing narrowing of the course of the subclavian vein. This is consistent with repetitive or forcible shoulder activity being a key precipitant of effort-induced UEDVT.

Table 1 Antecedent activities of all case reports

Activity category n (%)	Activity	n
Sport 47 (63)	Weightlifting, pushups and/or body building	19 (26%)
	Baseball	4
	Swimming	3
	Volleyball	3
	Basketball	2
	Pool	2
	Clay pigeon shooting	1
	Cycling	1
	Football	1
	Goal keeping	1
	Gymnastics	1
	Handball	1
	Lacrosse	1
	Rowing	1
	Rugby	1
	Skiing	1
	Softball	1
	Squash	1
	Tennis	1
	Wrestling	1
Lifting/carrying objects 11 (14.5)	Heavy lifting	5
	Luggage	2
	Backpack	1
	Carrying a television	1
	Carrying hay poles	1
	Lifting a fridge	1
Manual work 9 (12)	Decorating	3
	Ice cream scooping	1
	Mechanic	1
	Motorcycling	1
	Waiter	1
	Using an electric drill	1
	Washing clothes	1
Dancing 3 (4)	Dancing	3
Musical instrument 2 (2.5)	Guitar	1
	Violin	1
Other 3 (4)	Non-specific strenuous effort	2
	Strain to be braced	1

n, n=75.

Learning points

- ▶ Effort-induced UEDVT is a demographically distinct disorder most commonly affecting young males.
- ▶ Effort-induced UEDVT is typically precipitated by sporting or other activities involving forcible or repetitive upper limb activity.
- ▶ This disorder should be considered in individuals who have participated in such activities who present with pain or swelling or the upper limb.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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