CASE REPORT

Post-thrombotic syndrome

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Post-thrombotic syndrome (PTS) is a potentially disabling complication occurring in up to 67% of adult patients following deep venous thrombosis (DVT). PTS has recently been recognised in children. We present three cases of symptomatic PTS in children, which occurred following the use of central venous lines (CVLs). In two cases, no symptoms of acute thrombosis were noted. The cases highlight the clinical presentation of this syndrome. A review of the literature revealed two reports describing PTS occurring in children following DVT with an estimated incidence of 7–12%. It is concluded that PTS is an important complication of DVT in children. The clinical findings of pain, swelling, and brawny induration are similar to adult patients. The effect on growing limbs is not known. Paediatricians should be aware of the potential of PTS in all children who are at risk of DVT, including patients with malignancy, congenital heart disease, and children who have had previous CVLs, even in the absence of documented acute DVT.

Post-thrombotic syndrome (PTS) is a potentially disabling, chronic complication estimated to occur in 20–67% of adult patients following deep venous thrombosis (DVT).^{1–3} Symptoms vary from mild oedema to chronic pain and ulceration.^{1,2}

The incidence of DVT in children is increasing.⁴ This is a result of improved survival of children with previously incurable conditions and to an increased use of central venous lines (CVLs), which are the most common risk factors for DVT in children.⁵

There is little information on PTS in children in the medical literature. While a few cohort studies have described relative frequencies in children with known DVT, no papers have discussed the clinical impact of this disorder.

We present three cases of symptomatic PTS in children that were not recognised by their primary paediatricians. Two cases occurred in the absence of acute DVT. The third involved PTS of the upper limb. The cases highlight the need for appropriate long term follow up of children who have CVLs.

CASE HISTORIES

Case 1

A 13 year old girl was referred to the thrombophilia service for management of her anticoagulation. The girl described long term symptoms of pain and a pruritic rash on her legs. Her legs were painful and swollen during exercise. She occasionally woke with leg pain and stated that minor cuts and abrasions on her legs took many weeks to heal. The girl was born with complex cyanotic heart disease treated definitively with a Fontan procedure at 2 years of age. Prior to this she had required multiple cardiac catheters via bilateral femoral arteries and veins. Her only medication was warfarin with an international normalised ratio (INR) adjusted to 2.0–2.5. The symptoms of rash and pain had been documented at previous follow up with her primary care paediatricians.

Figure 1 Pigmented rash of severe PTS in a 13 year old girl.

Examination showed a well looking girl with mild central cyanosis. She had a pigmented rash on her legs with markedly distended and tortuous superficial veins. The legs were swollen. The pigmented areas had a dry, roughened texture (see fig 1). Leg lengths were equal.

Doppler ultrasound showed the absence of a deep venous system, from ankle to groin bilaterally. Arterial flow was normal. Management consisted of skin care advice, podiatry referral, fitted graduated stockings, and advice regarding elevation of the legs when symptomatic. One month later the pain in the right leg had reduced. There is slow progression of symptoms after two years.

Case 2

Patient 2 was a 17 year old boy with corrected complex cyanotic heart disease. He presented for elective revision of his stenotic pulmonary valve. The valve revision was complicated by massive intraoperative blood loss requiring a large bore CVL to be inserted into the left brachial vein. The CVL was removed shortly after surgery.

Five days postoperatively the patient complained of a painful swollen left arm. Extensive thrombus in the left subclavian and left internal jugular veins was detected by Doppler ultrasound. The patient was commenced on intravenous standard heparin adjusted to maintain a therapeutic activated partial

Abbreviations: CVL, central venous line; DVT, deep vein thrombosis; INR, international normalised ratio; PTS, post-thrombotic syndrome

Figure 2 Dilated tortuous veins of PTS in the upper limb of a 17 year old boy.

thromboplastin time. The swelling improved and the patient was treated with oral anticoagulation, maintained with an INR of 2.5–3.5 for three months.

Six months later the patient, who is left handed, presented with progressive swelling of the left arm and complained of pain when writing. On examination, the arm was obviously swollen with multiple dilated and tortuous superficial veins on the proximal medial aspect (see fig 2). A venogram showed markedly delayed filling of the left brachial and subclavian veins with a persistent filling defect in the left brachiocephalic vein. Blood returned to the superior vena cava via multiple small collateral vessels in the superior mediastinum.

The patient was advised to elevate the arm whenever possible. He declined to use a fitted compression stocking. The patient continues to experience pain when writing.

Case 3

The patient is an 11 year old boy with chronic renal failure. Following failure of peritoneal dialysis, he commenced haemodialysis. He had a right femoral vein CVL for 12 months prior to creation of a Dacron arteriovenous fistula connecting the right femoral artery to femoral vein.

Two years after insertion of the initial right femoral CVL, the patient developed a pruritic rash over the anterior aspect of both shins. Examination showed a dry, pigmented rash extending from mid shin to ankle (see fig 3). A dermatology referral resulted in a biopsy of the rash. Histopathology showed areas of extravascular clot formation with haemosiderin deposits in the subcutaneous tissue.

The patient was referred to the haematology unit. Examination was consistent with severe PTS and chronic venous obstruction, with brawny, indurated skin and patchy brown discolouration. There were multiple grossly dilated veins on the back and lower abdomen. The biopsy site over the right shin showed no signs of healing.

Venography showed complete occlusion of the inferior vena cava at the level of the confluence of the common inguinal veins, with blood from the Dacron arteriovenous fistula returning to the thorax via multiple subcutaneous and spinal veins (see fig 4).

Management consisted of fitted graduated compression stockings, podiatry referral, and advice regarding the care of legs and feet. Elevation of the legs was encouraged whenever possible. Over the next two years there were multiple acute exacerbations of pain, swelling, or erythema that settled with rest and elevation. Overall there has been a gradual deterioration in the legs.

LITERATURE REVIEW

An electronic search of the English literature was performed using the following key words: children or paediatrics and

Figure 3 Brawny, indurated rash of severe PTS in an 11 year old boy.

Figure 4 Venogram showing thrombosis of distal IVC with dilated tortuous spinal collateral veins.

“post thrombotic syndrome”, “postphlebotic syndrome”, “chronic venous insufficiency”, or “chronic venous obstruction”. Two papers were identified that described PTS in children.

Monagle *et al* described the follow up of patients with thrombosis prospectively enrolled in the Canadian Childhood Thrombophilia registry. The registry included patients from 1 month to 18 years of age. Only patients with limb thrombotic complications were included in the analysis.⁶ Data on follow up was available for 356 of 405 (88%) patients with a mean duration of follow up of 2.86 years. PTS was diagnosed clinically by the haematologist, based on the symptoms of pain and signs of swelling and brawny discolouration of the affected limb. Fifty patients (12.4%) had evidence of PTS. The majority of these patients developed PTS following lower venous system thrombosis. No comment was made on the severity of symptoms or impact on patient lifestyle.

Gorenstein *et al* described the follow up of 85 children prospectively identified with non-iatrogenic DVT.⁷ Six cases (7.0%) developed symptoms suggestive of PTS. No other information regarding the long term follow up of these patients was given.

DISCUSSION

PTS is a term used to describe the changes that occur in a limb following venous thrombosis. PTS is commonly diagnosed in adults but is rarely diagnosed in children.^{1-3 6 7} We present three cases of PTS in children. The cases show that symptoms and examination findings of PTS in children are similar to those in adult patients. Failure to consider PTS as a diagnosis in children can lead to delays in appropriate supportive management.

The pathophysiology and clinical features of PTS in adults are well described. Venous hypertension occurs when thrombus destroys deep venous valves and hydrostatic pressure is directly transmitted to the skin and subcutaneous tissues.⁸ Residual obstruction at the site of proximal DVT may also lead to valvular dysfunction and venous hypertension.⁹ Venous hypertension results in widening of endothelial cellular junctions and extravasation of red cells, fibrinogen, and inflammatory mediators,⁹ leading to painful, discoloured skin and brawny induration of the subcutaneous tissue.^{8 10} Risk factors for the development of PTS in adults include recurrent, proximal thrombosis and obesity.¹¹ Symptoms of PTS may develop months to decades following DVT.^{1-3 12} Prevention of PTS following DVT with anticoagulation, by using graduated compression stockings, or by early removal of thrombosis by thrombolysis or thrombectomy is controversial.^{13 14} Management of established PTS is unrewarding. Rest, elevation, and graduated compression stockings remain the mainstays of management. Surgical therapy is often disappointing.¹⁵

PTS is most commonly associated with lower limb DVT but has been described in patients following upper limb DVT. Symptoms of PTS have been found in up to 60% of patients following spontaneous DVT of subclavian veins in adult patients.^{16 17} Elevation and the use of compression stockings may not be appropriate in the management of upper limb PTS.

The most common risk factor for DVT in children is the presence of a CVL.⁵ CVLs are important in the management of an increasing number of life threatening conditions and are usually inserted into the deep veins of the upper limb. Clinical detection of DVT complicating CVL insertion is unreliable. Many CVL related DVTs remain subclinical, but prospective studies show that venography proven DVT can occur in up to 66% following CVL insertion.¹⁸ The incidence of long term complications and PTS following subclinical CVL related DVT is not known. Early diagnosis and treatment of CVL related DVT will reduce the incidence of PTS. Carefully designed, prospective studies are required to determine if primary prevention of CVL related DVT is possible with prophylactic long term anticoagulation.

In the three children we present, symptoms of PTS are having a major impact on quality of life. Disease progression of PTS in children is difficult to predict and the effect on growing

limbs can only be speculated. Symptomatic relief with fitted graduated compression stockings, positioning, and advice regarding skin care is important but of limited effectiveness. Children who require CVLs should have long term follow up to monitor for the development of PTS even in the absence of acute symptoms of DVT.

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REFERENCES

- 1 **Immelman E**, Jeffery P. The post phlebotic syndrome. *Clin Chest Med* 1984;**5**:537-50.
- 2 **Prandoni P**, Lensing A, Prins M. The natural history of deep vein thrombosis. *Semin Thromb Hemost* 1997;**23**:185-8.
- 3 **Strandness D**, Langlois Y, Crmer M, et al. Long term sequelae of acute venous thrombosis. *JAMA* 1983;**250**:1289-92.
- 4 **Andrew M**, Monagle P, Brooker L. Epidemiology of venous thromboembolic events. In: *Thromboembolic complications of childhood*. Hamilton: BC Decker, 2000.
- 5 **Andrew M**, David M, Adams M, et al. Venous thrombotic complications (VTE) in children; first analysis of the Canadian registry of VTE. *Blood* 1994;**83**:1251-7.
- 6 **Monagle P**, Adams M, Maloney M, et al. Outcome of pediatric thrombophilic disease: a report from the Canadian Childhood Thrombophilia Registry. *Pediatr Res* 2000;**47**:763-6.
- 7 **Gorenstein A**, Katz S, Levy P, Schiller M. Non-iatrogenic deep vein thrombosis of lower extremities in children. *Zeitschrift für Kinderchirurgie* 1986;**41**:375-8.
- 8 **Labropoulos N**, Leon M, Nicolaides A, et al. Venous reflux in patients with previous deep venous thrombus; correlation with ulceration and other symptoms. *J Vasc Surg* 1994;**20**:20-6.
- 9 **Rutherford R**. Pathogenesis and pathophysiology of the post thrombotic syndrome; clinical implications. *Semin Vasc Surg* 1996;**9**:21-5.
- 10 **Browne N**, Burnand K. The cause of venous ulceration. *Lancet* 31 July 1892.
- 11 **Biguzzi E**, Mozzi E, Alatri A, et al. The post thrombotic syndrome in young women: retrospective evaluation of prognostic factors. *Thromb Haemost* 1998;**80**:575-7.
- 12 **Piovella F**, Barone M. Long term management of deep vein thrombosis. *Blood Coagul Fibrinolysis* 1999;**10**(suppl 2):S117-22.
- 13 **Comerata AJ**, Aldridge SC. Thrombolytic therapy for deep venous thrombosis: a clinical review. *Can J Surg* 1993;**36**:359-64.
- 14 **Plate G**, Akesson H, Einarsson E, et al. Long-term results of venous thrombectomy combined with a temporary arteriovenous fistula. *Eur J Vasc Surg* 1990;**4**:483.
- 15 **Ackroyd JS**, Browne NL. The investigation and surgery of the post thrombotic syndrome. *J Cardiovasc Surg* 1986;**27**:5-16.
- 16 **Swinton NW**, Edgett JW, Hall RJ. Primary subclavian-axillary vein thrombosis. *Circulation* 1968;**38**:737.
- 17 **Lindblad B**, Bormyr S, Kulledndorff B, Bergqvist D. Venous haemodynamics of the upper limb after subclavian thrombosis. *Vasa* 1990;**19**:218-22.
- 18 **Andrew MM**, V Pencharz, P. A cross sectional survey study of catheter related thrombosis in children receiving total parenteral nutrition at home. *J Pediatr* 1995;**126**:358-63.