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Congenital abnormalities of the inferior vena cava presenting clinically in adolescent males

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ABSTRACT

Introduction: Congenital anatomic abnormality of the inferior vena cava (IVC) is an important risk factor for the development of spontaneous proximal lower extremity deep vein thrombosis (DVT) in young adults. The incidence of DVT associated with congenital IVC anomalies in paediatric populations has not been described, and the implications of IVC anomalies for treatment and outcomes of DVT are unknown.
Methods: This study reports a series of five adolescent males with spontaneous lower extremity DVTs and underlying congenital IVC abnormalities. Cases were identified by searching the institutional database of patients treated with anticoagulation for venous thromboembolism at a tertiary children's hospital.
Results: The demographics, clinical presentations, imaging findings, treatment courses, and outcomes are described. All cases occurred in males, and accounted for approximately twenty percent of adolescent males presenting with DVT.
Conclusions: IVC abnormality is likely an under-recognized risk factor for DVT in this age group, and detailed vascular imaging should be pursued in adolescents with spontaneous proximal lower extremity DVT when initial ultrasonography does not delineate the proximal clot extent. Management requires individual risk-benefit assessment in the context of providing developmentally appropriate care. Further research is required to establish long-term outcomes and determine optimal treatment strategies.

Introduction

Congenital anatomic abnormality of the inferior vena cava (IVC) is an important risk factor for the development of spontaneous venous thrombosis in young adults. A number of congenital IVC anomalies have been described [1], and the prevalence of IVC anomalies in the general population has been estimated to be between 0.07 and 8.7% [6]. These abnormalities are often asymptomatic, and identified incidentally in patients undergoing imaging investigations for other reasons [8]. It is likely that many, if not most, cases of congenital IVC abnormalities remain undiagnosed and of little or no consequence to affected individuals. However, there is a subset of patients with congenital IVC anomalies who present with clinically significant deep vein thrombosis (DVT). Because the mainstay of diagnosis of DVT is ultrasound with venous Doppler, which does not readily identify IVC anomalies, these anomalies may be underdiagnosed in patients presenting with spontaneous DVTs.

Previous estimates of the prevalence of IVC anomalies among young adult patients with DVTs have been in the range of 5% in patients under 30 years of age, [3,7]. Although there are reported cases occurring in adolescent patients [3,4,7,13], the incidence of DVT associated with congenital IVC anomalies has not been described in paediatric populations. Implications of IVC anomalies for treatment and long-term outcomes of DVT are also unknown.

We report a series of five adolescents who presented with spontaneous DVTs of the proximal lower extremities and have been found to have underlying congenital abnormalities of their IVCs. We describe the demographics, clinical presentations, imaging findings, treatment courses, and outcomes of these patients. To our knowledge, this is the first report of IVC anomalies presenting with venous thrombosis in the paediatric age group that have been managed at a tertiary children's hospital.

Methods

We searched our institutional database of patients who have been treated with anticoagulation for venous thromboembolism between 1999 and 2012 within the department of Clinical Haematology at the Royal Children's Hospital, a tertiary children's hospital in Melbourne, Australia. The database includes all patients requiring anticoagulation for more than 3 months. Therefore, there is the potential to have missed patients with lower limb venous thromboembolism if they were

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anticoagulated for a shorter period. We identified the patients who were found to have underlying congenital anatomic IVC abnormalities and conducted detailed chart reviews on this subset of patients.

Cases

A total of five patients with DVTs who were diagnosed with underlying congenital anatomic IVC abnormalities were identified. An additional two children had IVC anomalies that were acquired as a result of other medical conditions (one secondary to central line placement during neonatal gastroschisis repair, one secondary to multiple vascular catheterizations for dialysis). These patients were not included in this case series. There was a total of 49 adolescent patients (ages 12 – 18 years); 25 male and 24 female, who were treated at our institution for venous thromboembolism between 1999 and 2012. This includes patients with both spontaneous and provoked DVTs.

Of the five patients with DVTs and congenital IVC abnormalities, one (Case 4) presented directly to our children's hospital. The other four patients initially presented to community hospitals or family physician offices and were referred to us. All of the patients were previously healthy and developmentally normal, with unremarkable perinatal histories and no prior vascular catheterizations. Three of the patients (Cases 2, 3, and 5) described symptoms occurring with physical exertion in the weeks prior to their presentations. There were no other provoking factors identified, including immobilization, trauma, or surgery. None of the patients had symptoms suggestive of pulmonary embolism.

The clinical presentations, imaging results, complications, and outcomes of these cases are summarized in Table 1.

Additional information includes that patients 1 and 2 are brothers, who presented one year apart. There is no other known family history of thrombosis or symptomatic IVC abnormalities. Patients 2 and 4 both presented with non-specific signs of systemic illness and inflammation as their main clinical features. Patients 1 – 4 presented with proximal DVTs and were subsequently found to have anatomic abnormalities in their IVCs. Conversely, patient 5 was found to have a congenital abnormality of his IVC prior to the occurrence of his DVT, upon investigation for exercise-induced hypertension and headache. The IVC anomaly was seen on ultrasound and confirmed on magnetic resonance venography (MRV). He then presented one month later with his symptomatic DVT. Patient 5 has a twin brother who is normal with normal abdominal ultrasound.

In the four patients whose IVC anomalies were identified only after presenting with DVT (cases 1 – 4), ultrasonography with venous Doppler demonstrated the thrombosis but did not specifically identify IVC anomalies. The anomalies were seen on subsequent imaging with computerized tomography (CT) scans or MRV scans, which were done to further delineate the extent of proximal clot seen on ultrasound. Three of the patients had additional indications for further imaging including acute severe abdominal pain (case 2), and neurogenic back pain with pelvic masses on ultrasound (cases 3 and 4). The pelvic masses proved to be large thrombosed varices in both cases.

Three of the patients (cases 1, 2 and 3) underwent laboratory testing for inherited thrombophilic conditions. Antithrombin, protein C, protein S, and homocysteine levels were all within the normal ranges. Activated protein C resistance was negative, therefore Factor V Leiden was not tested. Prothrombin gene mutational analysis was tested only in cases 1 and 2 and was negative. Routine formal Lupus Anticoagulant testing was not undertaken in this series of patients given their underlying structural vascular abnormalities.

All patients were initially treated for DVT with either unfractionated heparin or subcutaneous low molecular weight heparin, and were then transitioned to warfarin with a target INR range of 2 – 3. Compliance with compression stockings was variable. Decisions regarding duration of anticoagulation were individualized and made in discussion with the patients and their families. The option of ceasing anticoagulation was discussed with each patient after the initial 12 months of therapy, and all patients elected to cease anticoagulation over the next six months after detailed explanations of the risk benefit ratio for this decision. Patient 4 remains on anticoagulation indefinitely because of DVT recurrence after stopping warfarin.

All patients had improvement in their clinical signs and symptoms of thrombosis and associated partial resolution on follow-up imaging. However, there were significant effects of their illnesses on quality of life. In particular, all of these patients are physically active and had to limit their involvement in sport because of their thrombotic symptoms and because of the recommended precautions while on anticoagulation. Two of the patients (cases 3 and 4) were referred to Adolescent Medicine specialists for help coping with their functional impairments. Patients 1 and 5 declined a referral, despite having symptoms consistent with depressed mood. Additionally, Patient 2 required referral to psychiatry for depressed mood and suicidal ideation, which subsequently resolved. This was not felt to be related to his hematologic issues, however did occur while still on anticoagulation therapy. These factors were of consequence in the patients' decisions to cease anticoagulation.

Discussion

Congenital anomalies of the IVC are known to be a risk factor for the development of venous thrombosis in young adults, however the prevalence of these anomalies among paediatric patients with spontaneous DVT has not been studied. We report 5 consecutive cases which presented during adolescence. The cases only occurred in males, and accounted for approximately twenty percent of all adolescent males presenting with DVT at our institution. Comprehensive imaging and consideration of congential IVC abnormalities is important in teenagers who present with spontaneous lower limb thrombosis.

The results of this case series suggest that the presence of IVC abnormalities as a risk factor for DVT has been under-recognized in this age group. Our finding that five out of twenty five adolescent males with spontaneous DVTs had underlying IVC anomalies may be a conservative estimate of the true incidence in our cohort, as there may have been other patients with IVC abnormalities that were not recognized on routine imaging. Additionally, if cases of provoked DVT (for example DVT associated with central access devices or other systemic illness) were excluded from the total number of cases to include only adolescent male patients with spontaneous DVTs, then the incidence of IVC abnormalities among this subset of patients is even higher.

The etiology of venous thromboembolism (VTE) in children is vastly different from adults. Most VTE in children occurs in the setting of severe illness, and the most common precipitating factor is the presence of a central venous catheter [2]. Inherited prothrombotic states have been shown to contribute to the risk of VTE in children [15], however their role relative to other risk factors remains controversial. Within the paediatric population, adolescents with spontaneous VTE have a higher likelihood of having an abnormal result on thrombophilia testing, and therefore testing in this group is often undertaken [11]. The cases reported in this series suggest anatomic IVC anomalies as another important congenital risk factor in this age group, and highlight the importance of pursuing more detailed imaging in adolescents with spontaneous DVT of the proximal vessels of the lower extremities.

Within our pediatric population, all of the cases of IVC abnormalities we identified occurred in adolescence. Previous reports have described similar presentations in the young adult age group of under 40 years of age [3,4,7,9,13]. In the absence of an acquired vascular injury IVC anomalies are presumed to be congenital, however they do not seem to present clinically until at least the second decade of life. This suggests that for the anomaly to manifest as DVT a second "hit" is required. Venous collaterals may be able to compensate for the lack of a normal IVC to a degree, and then fail once the demands for venous drainage exceed the capacity of the collateral veins. DVT presumably then occurs via a primary mechanism of stasis. Potential factors contributing to clinical presentation in adolescents and young adults may include reasons for increased demand