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Protein S deficiency-induced spermatic vein thrombosis, a rare cause of painful scrotal mass: A case report

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ABSTRACT

A painful scrotal mass requires prompt surgical intervention. Common diagnoses would include testicular torsion, acute epididymo-orchitis, and strangulated inguinal hernia. However, very rarely, it can be diagnosed as a rare clinical disease, including spermatic vein thrombosis (SVT). We present a case of right SVT possibly precipitated by Protein S deficiency, initially presented with a painful right scrotal lump for 2 days. He was treated with Aspirin tablets for 1 week and remained asymptomatic after 3 weeks of initial presentation. At 12 months follow-up, sequelae of right varicocele had developed. SVT is a rare diagnosis with a left-sided prevalence. The etiology of spontaneous SVT remains unclear. In this case, hypercoagulability due to Protein S deficiency could predispose to the formation of venous thrombotic events. Treatment of spontaneous SVT is suggested based on its anatomical location. Complications linked to this disease include varicocele, testicular infarction, pulmonary embolism, and renal vein thrombosis.

Keywords: Painful scrotal mass; Spermatic vein thrombosis; Scrotal Doppler ultrasound; Varicocele; Protein S deficiency.

1. INTRODUCTION

A painful scrotal mass is a surgical emergency that usually requires immediate medical attention. Typically, testicular torsion, acute epididymo-orchitis, and strangulated inguinal hernia are the common differential diagnoses. However, very rarely, acute scrotal pain can present as a rare clinical disease including testicular neoplasm, segmental testicular infarction, testicular vasculitis, SVT, brucellosis as well as from abdominal sources including acute pancreatitis, acute aortic syndrome, retroperitoneal mass, and appendicitis. Currently, there are only 8 cases of spermatic vein/pampiniform plexus thrombosis reported in the recent systematic review (Sieger et al., 2020).

Our case is right SVT complicated with right varicocele as the sequelae, and we will discuss the proposed etiology, therapeutic alternatives, and the related complications.

2. CASE REPORT

A 23-year-old Malay man without an underlying medical/surgical illness presented to a private hospital in Negeri Sembilan, Malaysia with a painful right scrotal lump for 2 days. The lump was about 1.0 x 1.0 cm while the pain was described as dull and non-radiating with a pain score of 4/10. There were no urinary or bowel symptoms and he was not sexually active. Constitutional symptoms were insignificant and there was a negative family history of thrombophilia. History of local trauma was not reported. The gross examination of the scrotum was normal. It did not appear to be swollen or erythematous. A solitary mass was palpable over the right spermatic cord; it was 0.5x 0.5cm, round, smooth surface with a well-defined border, mildly tender but immobile. Palpation of both testes and epididymis was normal.

Initial laboratory investigations showed a normal full blood count, coagulation profile, and liver functions test. A Doppler ultrasound of the scrotum performed revealed a formation of a thrombus measuring approximately 1.6 cm within the right spermatic vein without venous flow. Neighboring arterial structures had normal Doppler flow (Fig. 1 and Fig. 2). These findings complement the diagnosis of SVT and were treated with Aspirin tablets 100mg once daily for 7 days. His symptoms fully resolved after 3 weeks of initial presentation. However, scrotal Doppler ultrasonography after 12 months revealed the formation of the right varicocele without thrombosis (Fig. 3). During the follow-up, a thrombophilia screen was performed, revealing Protein S of 58% (Normal: 63-137%) while both Antithrombin III and Protein C were within the normal range. Consultation with a hematologist recommended another thrombophilia screening in 6 months to reevaluate the level of Protein S deficiency which could have predisposed to SVT.

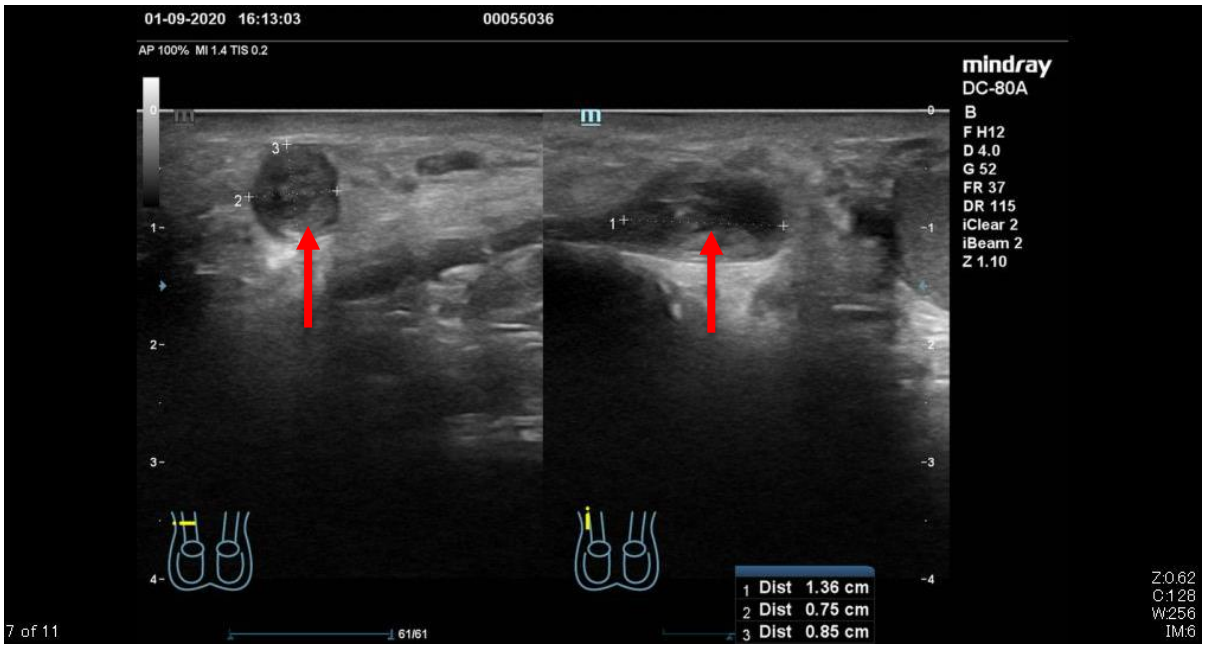

Figure 1 Focal dilatation of right spermatic vein with echogenic thrombus (red arrows) measuring approximately 1.6cm within and was non-compressible.

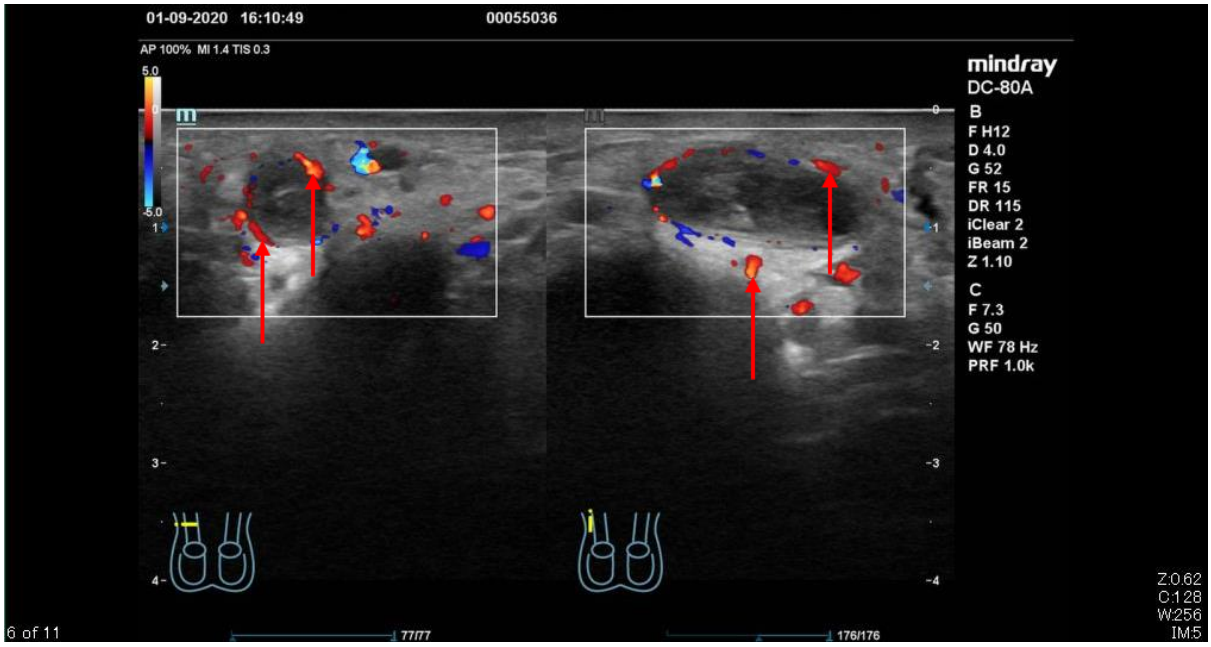

Figure 2 The right spermatic vein lumen with no Doppler color was seen. Doppler flow was normal within the neighboring arterial structures (red arrows).

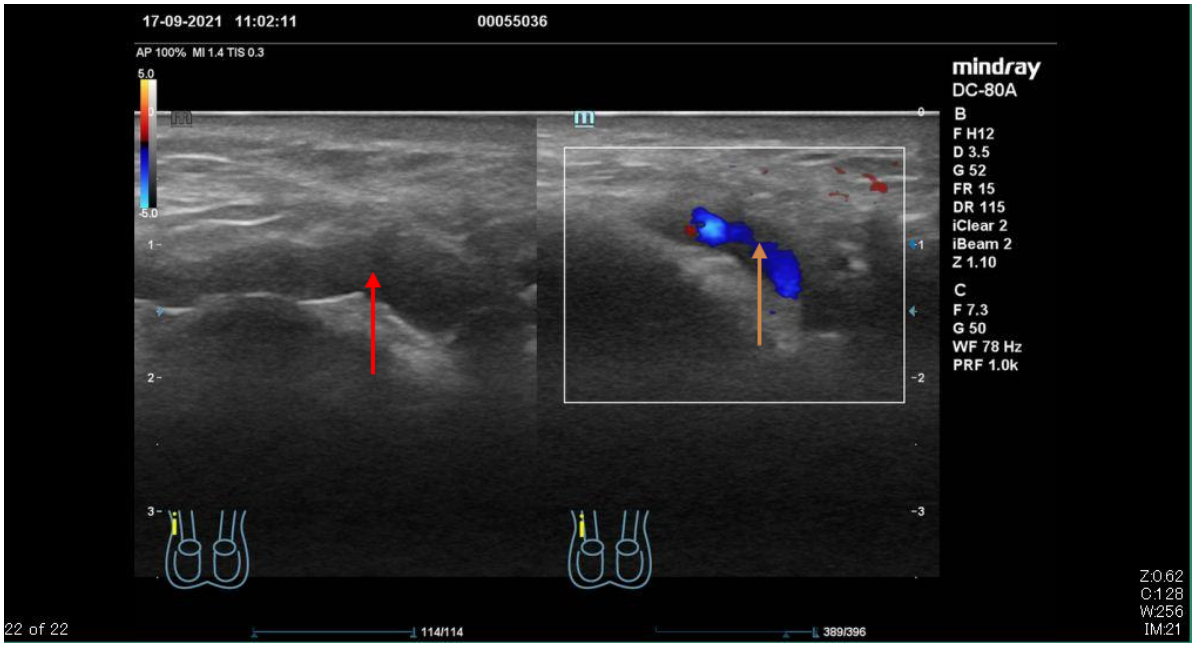

Figure 3 Dilated vein measuring 3.5cm (red arrow) in diameter at right parascrotal region, likely part of the right pampiniform plexus indicating right varicocele. Previously seen focal lesion was absent with no filling defect within (green arrow).

3. DISCUSSION

Virchow's triad: venous stasis, hypercoagulability, and endothelial dysfunction are all known to predispose to the formation of venous thrombosis. However, the cause of spontaneous SVT remains unclear. Considering its rare entity, a comprehensive assessment should be considered, including to rule out thrombophilia disorders. Venous thromboembolism can be due to genetic causes such as Factor V or prothrombin gene mutations (Kleinclauss et al., 2001; Campagnola et al., 1995). Moreover, other predisposing factors for SVT could also be due to continued forceful sexual or sports activities, local trauma, infections, long hours of flights, tumors of the genitourinary tracts, the presence of varicocele, inguinal hernia surgery, drug abuse, and being sedentary

(Sieger et al., 2020; Kayes et al., 2010). These factors relate to venous stasis and vascular endothelial injury. The left renal vein entrapment syndrome, also known as nutcracker syndrome, is a rare anatomical variant in which the aorta and the superior mesenteric artery are compressing the left renal vein in between, predisposing to outflow blockage and venous stasis (Penfold and Lotfollahzadeh, 2021). In our case, none of the risk factors described were present.

A hypercoagulable state, as demonstrated by Protein S deficiency, could potentially be a risk for developing venous thrombosis in this case. Protein S detected in our patient was at 58%, which is slightly lower than the normal range of 63-137%. Hence, a repeat thrombophilia test is recommended in 6 months to confirm the above-mentioned diagnosis. This disorder can be inherited as an autosomal dominant trait or acquired, most commonly due to vitamin K insufficiency, hepatic diseases, or nephrotic syndrome (Gupta et al., 2021). No family history of thrombophilia diseases was noted in this case report. As a result, additional evaluation is necessary to ascertain the cause of this patient's Protein S deficiency. We believe this is the first reported case of spermatic vein thrombosis that was precipitated by Protein S deficiency.

SVT is typically a left-sided pathology with contributing factors that might be associated with the formation of a varicocele. The left spermatic vein drains into the left renal vein at a perpendicular junction, which in turn drains into the inferior vena cava approximately 10cm higher than the right spermatic vein (Fatih, 2021). The other factor is the lack of valves in the left spermatic vein compared to the right spermatic vein (Hashimoto and Vibeto, 2006). Hence, the left venous system is exposed to higher pressure and relatively slower blood flow. Contralaterally, in our case, the presence of the right SVT should prompt further investigations to rule out renal or retroperitoneal tumors (Hutson, 2012).

Therapeutic strategies for spontaneous SVT remain controversial. Conservative therapy with non-steroidal anti-inflammatory drugs (NSAIDs) without anti-coagulant and watchful observation is considered ideal because of satisfactory clinical results and no subsequent episodes of recurrence (Hutson, 2012; Bakshi, 2020). On the other hand, Kyono et al., (2009) proposed a treatment based on its anatomical location. Conservative treatment is preferred if the thrombosis continues beyond the external inguinal ring into the pampiniform plexus, but surgical excision and anticoagulation therapy may be considered to prevent pulmonary embolism in deep-seated thrombus in the external inguinal ring that extends to the nearby renal vein (Kyono et al., 2009).

When taken at a low dose (75 mg daily), Aspirin has an anti-thrombotic effect, whereas at a high dose (1g daily), it has an anti-inflammatory effect (Schrör, 1997). Given the fact that our patient was treated with low-dose Aspirin, which did not comply with the suggested conservative therapy, it is still regarded as superior to placebo, though less effective than anticoagulants for secondary venous thromboembolism prevention (Diep and Garcia, 2020). Furthermore, given the discovery of low Protein S levels after a 12-month follow-up interval, experts would recommend initiating Warfarin medication for the next 6-9 months following the initial venous thrombotic incident. Only if the first thrombotic episode is life threatening or occurs in multiple/abnormal locations such as cerebral veins or mesenteric veins, is lifetime anticoagulant medication suggested (Gupta et al., 2021).

We also believe that this is the first reported case of a thrombosed spermatic vein leading to the formation of a varicocele. The definite pathophysiology of varicoceles remains unknown, but in this case, it was probably due to venous hypertension precipitated by the occlusion of the spermatic veins causing a backup of venous blood flow, hence leading to venous engorgement of the pampiniform plexus (Leslie et al., 2021). This condition predisposes to secondary male subfertility. Other reported complications include testicular infarction, pulmonary embolism due to the direct venous drainage system of the right spermatic vein into the inferior vena cava, and renal vein thrombosis via the left spermatic vein (Hussain et al., 2019; Castillo et al., 2008; Mallat et al., 2014).

4. CONCLUSION

Spontaneous SVT is a rare diagnostic disease with its etiology remains unclear. Hypercoagulability due to Protein S deficiency could be the provoking factor in this patient. Although it has a left-sided predominance, this case presented as a right-sided pathology. Despite the lack of guidelines in the management of the disease, the choice of conservative or surgical and anti-coagulative treatment is suggested to be based on its anatomical location. Complications linked to this disease include varicocele as reported in this case, testicular infarction, pulmonary embolism, and thrombosis in the renal veins.

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Informed consent

Written informed consent was obtained from the patient.

Author contributions

All the authors reviewed the manuscript and approved the final version. Dr. Muhammad Amir Afiq constructed the idea for the case report and prepared the manuscript. Dr. Nur Azidawati is responsible for the analysis of ultrasound and Doppler imaging. Dr. Sherreen Elhariri supervised the manuscript preparation and critically reviewed the article.

Ethical approval

All ethical principles were respected. Publication of the article is approved by KPJ Seremban Specialist Hospital.

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Conflict of interests: The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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