CASE REPORT

Successful treatment of extensive splanchnic vein thrombosis in a patient with mycosis fungoides

Nishtha Sanjay Nagral,¹ Vijay Waman Dhakre,² Nirzar Parikh,³ Shaji Marar⁴¹Topiwala National Medical College, Mumbai, Maharashtra, India²Surgical Gastroenterology, Jaslok Hospital and Research Centre, Mumbai, Maharashtra, India³Department of Medical Gastroenterology, Jaslok Hospital and Research Centre, Mumbai, Maharashtra, India⁴Department of Interventional Radiology, Jaslok Hospital and Research Centre, Mumbai, Maharashtra, India

Correspondence to

Dr Vijay Waman Dhakre, vddrvijsd@gmail.com

Accepted 20 January 2018

SUMMARY

A 33-year-old man of a Middle Eastern origin presented to us with abdominal pain and distension secondary to refractory ascites of 1-month duration. The patient had a history of taking oral retinoic acid 25 mg for 4 months for mycosis fungoides. Investigations revealed thrombosis of hepatic veins with extensive thrombosis of the portomesenteric axis. A combination of transjugular intrahepatic portosystemic shunt, balloon angioplasty and thrombolysis with recombinant tissue plasminogen activator was successfully used to treat his condition.

BACKGROUND

A combination of extensive splanchnic vein thrombosis (SVT) along with hepatic vein (HV) thrombosis is rare and challenging to manage. We have used a combination of thrombolysis and transjugular intrahepatic portosystemic shunt (TIPSS), which conventionally has been considered a relative contraindication when Budd-Chiari syndrome (BCS) is associated with portal vein (PV) thrombosis.^{1,2}

CASE PRESENTATION

A 33-year-old man of Middle Eastern origin presented with sudden-onset abdominal pain associated with tense abdominal distension. He subsequently developed jaundice. He had a medical history of mycosis fungoides which was diagnosed on skin biopsy 6 months ago (figure 1). He started to develop abdominal distension and discomfort 4 months after he was started on retinoic acid (25 mg/day), when he was given standard medical treatment and repeated paracentesis. Two months after the onset of symptoms, he developed sudden pain with increased abdominal distension when he first presented to us.

There was no personal or family history of thrombotic tendency or liver disease. His grandmother had a history of mycosis fungoides. He denied alcohol consumption. There was no history of over-the-counter or herbal medicine use.

On examination, he was found to have tense ascites but no pedal oedema. He was haemodynamically stable (blood pressure 120/78 mm Hg, heart rate 80 beats/min) and afebrile. He had been given standard medical treatment for ascites in the form of salt restriction and diuretics but had refractory ascites needing repeated therapeutic paracentesis.

INVESTIGATIONS

On admission, his investigations revealed a total bilirubin 3.9 mg/dL (normal range 0.2–1.3 mg/

dL), direct bilirubin 1.48 (0.1–0.4 mg/dL), aspartate transaminase 290 (5–40 U/L) and alanine transaminase 394 (5–40 U/L). His haemoglobin was 13 g/dL (13–18 g/dL), total leucocyte count $19.380 \times 10^9/L$, platelets $595\,000/mm^3$ ($140\,000$ – $440\,000/mm^3$), serum creatinine 0.7 mg/dL (0.7–1.5 mg/dL) and serum albumin 2.9 g/dL (3.5–5 g/dL). His antinuclear antibody, antismooth muscle antibody and liver kidney microsomal type 1 antibody were negative, and serum ceruloplasmin was normal at 36.40 mg/dL (20–60 mg/dL). HBsAg, HIV, hepatitis A virus IgM, hepatitis E virus IgM antibodies and antihepatitis C virus were non-reactive. Ascitic fluid analysis revealed high serum ascites albumin gradient (ascitic fluid albumin 0.9 g/dL), total cell count of 190, lymphocytes 55%, neutrophils 45%, and fluid culture showed no growth.

On portal venous Doppler there was absence of flow in all the three HVs, main PV, splenic vein (SV) and superior mesenteric vein (SMV).

Thrombophilia workup included factor V Leiden mutation, protein C, protein S, antithrombin III, antiphospholipid tests (lupus anticoagulant, anti-B2-glycoprotein I and anticardiolipin antibody were negative), homocysteine, Janus kinase 2 mutation, MTHFR gene mutation, paroxysmal nocturnal haemoglobinuria (PNH)—PNH CD 55–CD 59, and prothrombin G20210A gene mutation. He was found to be G6PD deficient.

CT venogram revealed non-visualisation of all the HVs with only a small stump in the region of right HV (figure 2). Retrohepatic inferior vena cava (IVC) was narrow in calibre; however, there was no thrombus inside it. The entire porto-splenic-superior mesenteric vein axis was not well opacified with contrast suggesting a thrombus inside (figure 3). He had hepatomegaly with heterogeneous enhancement, splenomegaly and ascites with bilateral pleural effusion. Upper gastrointestinal endoscopy showed large oesophageal varices and portal hypertensive gastropathy. The patient underwent digital subtraction angiography (DSA) which revealed complete thrombosis of the portal, splenic and superior mesenteric veins.

TREATMENT

Initially our patient was started on heparin infusion of 80 units/kg bolus dose followed by 18 units/kg/hour for over 24 hours to which he did not respond as was evident from the increasing nature of pain suggesting an extension of the thrombus. Therefore,

To cite: Nagral NS, Dhakre VW, Parikh N, *et al.* *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222710

Figure 1 Cutaneous T cell lymphoma manifesting as skin erythroderma.

mechanical and pharmacological thrombolysis approach was initiated.

Using the transjugular route, the PV was cannulated (figure 4). This was followed by thromboaspiration of large amount of dark clots (figure 5). Partial recanalisation of the PV was achieved. The patient then underwent TIPSS placement (1 cm×10 cm) and local thrombolysis was started using recombinant tissue plasminogen activator in the form of 10 mg alteplase bolus through fountain catheter which was placed through TIPSS into SMV. After procedure, the patient was continued on injection of alteplase 1 mg/hour for 48 hours through the fountain catheter. Heparin 500 IU/hour was started as an intravenous infusion to keep the activated partial thromboplastin time ratio 1.5 times the normal value and was monitored every 6 hours.

TIPSS Doppler done on the next day revealed relative increase in velocities (IVC end 22.7 cm/s, mid-TIPSS 44.7 cm/s and portal end 34.6 cm/s), patchy flow in extrahepatic PV with thrombosed right and left branches of PV and SV near the porto-splenic confluence. Follow-up venogram done 2 days later revealed near complete recanalisation of SV and the TIPSS. Follow-up Doppler done 3 days later showed patent portal, splenic and superior mesenteric veins and good flow within the TIPSS stent. The patient was then switched to low molecular weight heparin (LMWH) after stopping unfractionated heparin and alteplase. Also, after procedure, there was complete resolution of ascites and the patient was discharged on low-dose aspirin (75 mg) and LMWH (enoxaparin) (60 mg subcutaneously twice daily).

Figure 2 All hepatic veins, splenic vein and inferior mesenteric vein occluded with veno-venous collaterals (red arrow).

Figure 3 Portal vein, splenic vein and superior mesenteric vein occluded (red arrows).

Two months later, ultrasonography Doppler revealed high velocities at the portal venous end of the TIPSS suggestive of stenosis. Repeat TIPSS venogram confirmed the stenosis with pressure gradient of 10 mm Hg. A self-expanding metallic stent was placed from the main PV to the mid-part of TIPSS whose dilatation was done by 10 mm angioplasty balloon. The gradient reduced to 3 mm Hg after the dilatation.

A positron emission tomography (PET)-CT scan did not reveal any metastatic disease. An oncology opinion was sought for the mycosis fungoides and it was opined that the patient did not merit any specific treatment as he had stage 1 of the disease.

OUTCOME AND FOLLOW-UP

The patient was followed up for 12 months after the procedure and remains well without recurrence of ascites and patent portal venous axis and TIPSS. The aspirin has been omitted and he continues to be on LMWH.

DISCUSSION

SVT is a rare life-threatening event in which involvement of two or more sites of thrombotic segments of PV, MV, SV or supra-HVs (ie, BCS) is described.¹ Very little is known of the

Figure 4 Transjugular access of portal vein, splenic vein and superior mesenteric vein.

Recanalisation after TIPSS placement, thrombo aspiration and local catheter directed thrombolysis

Figure 5 Recanalisation after transjugular intrahepatic portosystemic shunt (TIPSS) placement, thromboaspiration and local catheter-directed thrombolysis.

natural history of SVT and mild non-specific symptoms of SVT can be missed in initial stages of the disease.¹⁻³

The overall risk of SVT is approximately 1% in general population. Patients with cirrhosis have a prevalence of SVT in the range of 0.6%–25%.⁴ The annual rate of SVT is about 10% and in those with hepatocellular carcinoma, SVT incidence is 44%.

Various aetiological factors have now been identified in relation to SVT. These are intra-abdominal malignancy, myeloproliferative disorders, leukaemia/lymphoma, inflammatory bowel disease, pancreatitis, oral contraceptive pills, hormonal replacement therapy, liver cirrhosis, postoperative (postliver transplant, postsplenectomy), sepsis, connective tissue disorders, various thrombophilic disorders and pregnancy.^{1-3,5} These factors play a major role in selecting treatment strategy and in determining prognosis, rate of recurrence and long-term outcomes. The most common aetiology includes malignancy 27% and cirrhosis 24%.⁵ Clinically, patients may present with abdominal pain (55%), ascites (10.4%) or gastrointestinal bleeding in 8.7% of cases.¹ Abdominal pain and ascites without any evidence of gastrointestinal bleed were the presenting symptoms in our case. Contrast enhanced CT (CECT) with portogram is the investigation of choice with sensitivity reaching 90%. CECT will also give us a global picture of abdomen, status of intestine in terms of intestinal ischaemia, collaterals, liver and vascular anatomy, and possibly may also help in clenching aetiological factor(s). DSA is the gold standard and has a diagnostic and therapeutic value.⁶

All patients with SVT should initially receive anticoagulation therapy after ruling out active bleeding. In case active bleeding is evident, start of anticoagulation should be withheld until source of bleeding is controlled. LMWH is preferably used especially in malignancy-related hypercoagulation. In patients with thrombocytopenia or cirrhosis, a lower or half dose of LMWH is advisable, which should be preceded by screening for gastro-oesophageal varices and prophylactic banding in case of patients with cirrhosis. If invasive procedure or surgery is inevitable in near future, unfractionated heparin is the drug of choice.⁷

Thrombolytic agents should be reserved for patients not responding to anticoagulation or showing signs of increasing pain or intestinal ischaemia.⁷ In our patient, we had to step up to mechanical and pharmacological thrombolysis as he needed repeated paracentesis every 15 days and had evidence of extensive thrombosis. Alteplase was used (1mg/hour infusion) for catheter-directed thrombolysis.

There are various routes of endovascular/interventional therapy for mechanical thrombolysis of the portal venous system, namely TIPSS, percutaneous transhepatic or transplenic route, direct catheterisation intraoperatively and thrombolysis via superior mesenteric artery (SMA) route. TIPSS and direct transhepatic route with or without combination of other routes are the commonly used routes.^{2,6} These routes can be employed to quickly recanalise blood flow, and rapidly reduce thrombus load thereby reducing total thrombolytic dose, balloon dilatation or angioplasty and stent placement if required.^{4,5}

The SMA route is technically most easy and sometimes referred to as the indirect thrombolysis technique where a catheter is placed in SMA and thrombolytic agent is instilled leading to thrombolysis in capillaries and venules. Besides, papaverine can be delivered to reduce the spasm of the blood vessel.⁶

The TIPSS route seems to be the safest route in those with or without cirrhosis, those with altered portal anatomy, portal cavernoma or marked liver atrophy. Hence, when compared with pharmacological thrombolysis, mechanical thrombolysis allows rapid reduction of thrombus load, and reduces incidence of intestinal infarction and overall mortality.⁴ Very few cases of combined BCS with spleno-mesenteric-portal vein thrombosis are mentioned in the literature, where the TIPSS route was used with favourable clinical outcome.^{8,9} Leebeek *et al*, in their case of BCS with thrombosed PV and SMV, used this route to thrombolysis.¹⁰

Our case possessed a similar challenge with extensively blocked hepatic and portal venous axis. Also, the presence of a cutaneous T cell lymphoma—mycosis fungoides, a malignancy—could have triggered the extensive thrombosis, although this has not been described in literature. One more trigger in our patient may have been the use of all-trans retinoic acid (ATRA) which has been shown to cause extensive venous thrombosis especially in patients who are undergoing treatment for acute promyelocytic leukaemia, where ATRA reduces the thrombotic tendency of the leukaemia but does not correct the diffuse intravascular coagulation-like syndrome leading to persistent procoagulant state.¹¹⁻¹³

We report a case of extensive SVT and HV thrombosis where therapy with TIPSS and aggressive endovascular mechanical and catheter-guided pharmacological thrombolysis was

Patient's perspective

Doctors in India have helped me so much. At one point I had lost hope...I feel patients with complicated problems like mine need to keep the doctors informed of all the symptoms they develop however minor they may seem.

Learning points

- ▶ In patients with a combined hepatic and portal vein thrombosis, transjugular intrahepatic portosystemic shunt placement is technically possible and should no longer be considered a contraindication.
- ▶ Combination of pharmacological thrombolysis and mechanical thromboaspiration is a treatment of choice in acute extensive splanchnic vein thrombosis.
- ▶ Patients with high-risk or multiple-risk factors of thrombosis/hypercoagulable states need long-term anticoagulation therapy.

used. Low-dose alteplase (1mg/hour infusion) was used as mid-doses (1–1.5 mg/hour) and high doses (>1.5 mg/hour) are associated with higher risk of complications.¹⁴ This resulted in resolution of refractory ascites and contributed to improving the liver functions. This extensive thrombosis may have been caused by the mycosis fungoides itself or its treatment with retinoic acid. Recurrence of thrombosis and long-term prognosis will depend on the cutaneous lymphoma and his thrombophilic status.

Contributors NSN and NP constructed the case presentation and contributed in formulating the discussion. VWD gathered the investigation, designed the discussion and prepared the images. SM did the proofreading and finalised the complete case report.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Ageno W, Riva N, Schulman S, *et al.* Long-term clinical outcomes of splanchnic vein thrombosis: Results of an international registry. *JAMA Intern Med* 2015;175:1474–80.
- 2 Guglielmi A, Fior F, Halmos O, *et al.* Transhepatic fibrinolysis of mesenteric and portal vein thrombosis in a patient with ulcerative colitis: a case report. *World J Gastroenterol* 2005;11:2035–8.
- 3 European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu. EASL Clinical Practice Guidelines: Vascular diseases of the liver. *J Hepatol* 2016;64:179–202.
- 4 Midia M, Razavi MK. Splanchnic venous thrombosis: Challenges and opportunities. *Endovascular Today* 2014;56–60.
- 5 Thatipelli MR, McBane RD, Hodge DO, *et al.* Survival and recurrence in patients with splanchnic vein thromboses. *Clin Gastroenterol Hepatol* 2010;8:200–5.
- 6 Yang S, Wu X, Li J. Transcatheter thrombolysis centered stepwise management strategy for acute superior mesenteric venous thrombosis. *Int J Surg* 2014;12:442–51.
- 7 Ageno W, Beyer-Westendorf J, Garcia DA, *et al.* Guidance for the management of venous thrombosis in unusual sites. *J Thromb Thrombolysis* 2016;41:129–43.
- 8 Pfammatter T, Benoit C, Cathomas G, *et al.* Budd-Chiari syndrome with spleno-mesenteric-portal thrombosis: treatment with extended TIPS. *J Vasc Interv Radiol* 2000;11:781–4.
- 9 Mancuso A, Watkinson A, Tibballs J, *et al.* Budd-Chiari syndrome with portal, splenic, and superior mesenteric vein thrombosis treated with TIPS: who dares wins. *Gut* 2003;52:438.
- 10 Leebeek FW, Lameris JS, van Buuren HR, *et al.* Budd-Chiari syndrome, portal vein and mesenteric vein thrombosis in a patient homozygous for factor V Leiden mutation treated by TIPS and thrombolysis. *Br J Haematol* 1998;102:929–31.
- 11 Song LX, Lu HY, Chang CK, *et al.* Cerebral venous and sinus thrombosis in a patient with acute promyelocytic leukemia during all-trans retinoic acid induction treatment. *Blood Coagul Fibrinolysis* 2014;25:773–6.
- 12 Goldschmidt N, Gural A, Ben Yehuda D. Extensive splenic infarction, deep vein thrombosis and pulmonary emboli complicating induction therapy with all-trans-retinoic acid (ATRA) for acute promyelocytic leukemia. *Leuk Lymphoma* 2003;44:1433–7.
- 13 Falanga A, Marchetti M, Barbui T. All-trans-retinoic acid and bleeding/thrombosis. *Pathophysiol Haemost Thromb* 2003;33 Suppl 1(Suppl 1):19–21.
- 14 Chan J, Rees CR, Song AK, *et al.* Usefulness of catheter-directed thrombolysis using alteplase in peripheral vascular occlusion. *Proc* 2001;14:3–7.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow