Intravenous leiomyomatosis complicated by Budd–Chiari syndrome

BC Kuenen, PHTJ Slee, CA Seldenrijk, SS Wagenaar

Summary

A 76-year-old woman with intravenous leiomyomatosis complicated by Budd–Chiari syndrome is described.

Keywords: intravenous leiomyomatosis, Budd–Chiari syndrome

Intravenous leiomyomatosis is a rare clinical entity. It is a benign smooth muscle tumour, usually originating in the myometrium of the uterus, with microscopically intrusive growth in uterine, vaginal and ovarian veins, sometimes leading to visible nodular masses on the uterus and/or in veins.[1–8] In more than 10% of cases extension to the inferior vena cava, even to the right atrium, can be found resulting in tricuspid valve dysfunction and/or congestive heart failure.[2,4,5] In the present report an unusual clinical course is described in a patient with intravenous leiomyomatosis who developed an acute Budd–Chiari syndrome.

Case history

A 76-year-old woman, gravida 1, para 1, was admitted because of a swollen left leg, which she had noticed one month earlier. She had undergone an abdominal subtotal hysterectomy 47 years earlier for unknown reasons. Four years ago she underwent a laparotomy, whereby a large tumour with a diameter of 10 cm connected to the cervix remnant was removed. The tumour had caused left-sided hydronephrosis and thrombosis of the left iliac vein. Histological examination showed a multinodular, mostly intravascular, highly vascular tumour composed of elongated cells arranged in bundles with variable amounts of zones of fibrosis. The diagnosis of intravascular leiomyomatosis was made. Two years later she returned with a clinical picture of venous obstruction of the left leg. Computed tomography showed an intravascular mass in the inferior vena cava which extended as far as the renal veins. No intra-abdominal masses were seen. The clinical picture was interpreted as a large deep venous thrombosis and she was treated with heparin and phenprocoumon. Six months before the present admission she had melaena and large haemorrhages due to overdosing with phenprocoumon, which was stopped at that time.

On the present admission, ultrasound examination showed obstruction of the left common iliac vein, while the large saphenous and popliteal veins were open. The patient was treated with intravenous heparin and oral anticoagulants.

In the third week following admission her condition deteriorated. On physical examination she was apathetic and slightly dehydrated. Blood pressure and central venous pressure were normal; pulse was 100 beats/min, temperature 38.4°C. The abdomen was slightly swollen without shifting dullness. For the first time the liver was palpable with 2 cm below the costal margin. A trace of pitting oedema was noticed on both legs.

Laboratory examination showed progressive elevation of creatinine, aspartate transaminase, alanine transaminase, lactate dehydrogenase and bilirubin (see table). The next day the patient was more apathetic and had developed hypotension and tachycardia. Septic shock or the development of a Budd–Chiari syndrome were considered. Her condition deteriorated and severe oedema of both legs developed. The patient died two days after this dramatic change in her condition. Blood cultures remained negative. *Post mortem* disclosed a mass originating in the left common iliac vein, which extended into the inferior vena cava up to the right atrium (figure). Microscopically this mass was composed of intravascular locations of the previously diagnosed leiomyomatosis. Adjacent to and in continuity with the tumour, fresh, partially organised thrombi were present within the inferior vena cava. Dislodgement of these thrombi explained the recent multiple pulmonary thromboemboli;

Intravenous leiomyomatosis

- a benign smooth muscle tumour, mostly originating in the myometrium of the uterus and growing into uterine, vaginal and ovarian veins, sometimes leading to visible nodular masses on the uterus and/or in veins
- in more than 10% of cases, extension to the inferior vena cava, or even to the right atrium, results in tricuspid valve dysfunction and/or congestive heart failure

Budd–Chiari syndrome: characteristics

- abdominal pain, ascites and hepatomegaly
- pedal oedema due to inferior vena cava occlusion

St Antonius Ziekenhuis, PO Box 2500, 3430 EM Nieuwegein The Netherlands
Department of Internal Medicine
BC Kuenen
PHTJ Slee
Department of Pathology
CA Seldenrijk
SS Wagenaar

Correspondence to PHTJ Slee

Accepted 12 January 1996

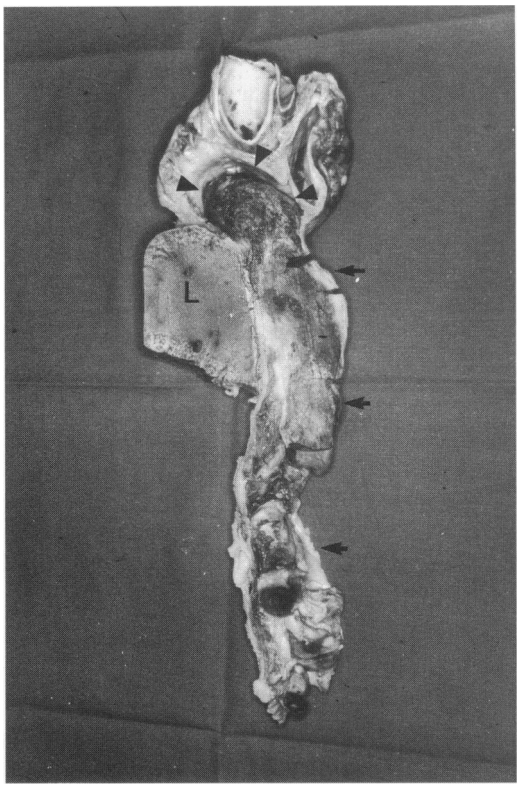

Figure Autopsy specimen showing a tumour in the inferior vena cava extending to the right atrium and a segment of the right lobe of the acute congested liver. Arrow = inferior vena cava; arrowheads = right atrium; L = liver

Table Laboratory data during the last admission

	Day -21	*Day -3*	*Day -2*	*Day -1*
Haemoglobin (g/dl)	8.4	10.5	9.5	9.8
Creatinine (μmol/l)	90	146	203	196
Alkaline phosphatase (IU/l)	110	209	212	245
γ-Glutamyl transferase (IU/l)	46	75	67	82
Bilirubin (μmol/l)	10		62	75
Aspartate transaminase (IU/l)	11	154	330	2.070
Alanine transaminase (IU/l)	18	127	212	1.104
Lactate dehydrogenase (IU/l)	346	1.106	1.448	2.574

focally recanalised thromboemboli, some of which contained small fragments of tumour tissue, so-called tumour emboli, were found in the pulmonary vasculature, indicating recurrent thromboembolism. In the abdomen some ascites was present. Due to thrombotic occlusion of the large hepatic veins the liver was enlarged and extremely congested with extensive confluent centrilobular necrosis of hepatocytes consistent with a Budd–Chiari syndrome, which explains the severe progressive hepatic failure. The portal vein was normal. The left kidney was atrophic, caused by long-standing hydronephrosis and chronic pyelonephritis. No vaginal abnormalities were found.

Discussion

Intravenous leiomyomatosis is a rare neoplasm characterised by nodular masses of histologically benign smooth muscle cells growing within the venous system. The majority of these neoplasms originates in the uterus, although they may arise from the walls of veins in other locations, eg, the inferior vena cava and renal veins.[8] Patients with intravenous leiomyomatosis are 28 to 80 years of age (median 42 years) and may have complaints consistent with uterine leiomyomas.

Two theories concerning the origin of intravenous leiomyomatosis in the uterus have been proposed. One holds that the neoplasm arises from the wall of veins within the myometrium and the second holds that the lesion is the result of intravascular invasion from an intramural leiomyoma. Norris and Palmley reviewed 14 cases and found evidence for both theories of origin.[1] The most important differential diagnosis of intravenous leiomyomatosis is leiomyosarcoma. In intravenous leiomyomatosis, mitotic figures are absent or rare. In the lungs of our patient, thromboemboli containing tumour emboli, were found. Tumour emboli (which differ from metastases) in the lungs of patients with intravenous leiomyomatosis have only been described in four patients.[6] The most remarkable feature in our patient, however, was the development of liver failure and necrosis, due to occlusion of the hepatic veins by thrombosis (Budd–Chiari syndrome), which was the cause of death. In spite of adequate anticoagulation, large quantities of thrombosis were present. A clear explanation is lacking. Possibly the altered haemodynamic situation in the inferior vena cava contributed to the formation of thrombus. To our knowledge, only one other paper has described a case of liver necrosis and failure due to intravenous leiomyomatosis and that case was only diagnosed at autopsy.[8]

At laparotomy the tumour is not always recognised as growing intravascularly.[1,3,6,7] Furthermore, because of the highly variable histological appearance, even within the same tumour, intravenous leiomyomatosis is often overlooked.[3,6–8] Although the histological diagnosis was made in our patient four years earlier, insufficient attention was given to this diagnosis, probably because of unfamiliarity. A diagnosis of intravenous leiomyomatosis should be considered in patients with a mass in the vena cava, right ventricle, or a presentation of a 'deep venous thrombosis' and a history of hysterectomy (because of leiomyoma).

Although intravascular and pelvic extensions or recurrence of the tumour may be amenable to surgical excision and the prognosis may be favourable, it is better to prevent fatal complications.[2,4,5] Management should include complete removal of the tumour and internal genitals as well as routine follow-up, including ultrasound examination of the inferior vena cava, iliac and femoral veins. Avoidance of oestrogens is recommended.[5–8]

Summary/learning points

Obstruction of the leg veins may be due to thrombus formation, but also to growing tissue in the veins, eg, intravenous leiomyomatosis of the uterus

1 Norris HJ, Parmley T. Mesenchymal tumors of the uterus. V. Intravenous leiomyomatosis. A clinical and pathological study of 14 cases. *Cancer* 1975; **36:** 2164–78.
2 Cooper MM, Guillem J, Dalton J, *et al.* Recurrent intravenous leiomyomatosis with cardiac extension. *Ann Thorac Surg* 1992; **53:** 139–41.
3 Mulvany NJ, Slavin JL, Ostor AG, Fortune DW. Intravenous leiomyomatosis of the uterus: a clinicopathologic study of 22 cases. *Int J Gynecol Pathol* 1994; **13:** 1–9.
4 Timmis AD, Smallpiece C, Davies AC, Macarthur AM, Gishen P, Jackson G. Intracardiac spread of intravenous leiomyomatosis with successful surgical excision. *N Engl J Med* 1980; **303:** 1043–4.
5 Mazzola A, Gregorini R, Procaccini B, *et al.* Intracaval and intracardiac leiomyomatosis of uterine origin. *Ann Vasc Surg* 1986; **1:** 134–8.
6 Clement PB. Intravenous leiomyomatosis of the uterus. *Pathol Annu* 1988; **23:** 153–83.
7 Clement PB, Young RH, Scully RE. Intravenous leiomyomatosis of the uterus. A clinicopathological analysis of 16 cases with unusual histologic features. *Am J Surg Pathol* 1988; **12:** 932–45.
8 Bahary CM, Gorodeski IG, Nilly M, *et al.* Intravascular leiomyomatosis. *Obstet Gynecol* 1983; **59:** 73s.

Treatment of hyperemesis gravidarum with the 5-HT_3 antagonist ondansetron (Zofran)

DG Tincello, MJ Johnstone

Summary
Ondansetron is a 5-hydroxytryptamine receptor antagonist which is known to be a highly effective anti-emetic drug for chemotherapy-associated nausea and vomiting and for postoperative nausea. We report here a case where ondansetron was used in severe hyperemesis gravidarum to avoid parenteral nutrition. The drug was used intermittently in every trimester with no apparent adverse effects on mother or infant.

Keywords: hyperemesis gravidarum, ondansetron, 5-hydroxytryptamine receptor

A 29-year-old woman presented at eight weeks gestation in her first pregnancy with nausea and vomiting and a weight loss of 3.5 kg. On admission she was clinically dehydrated and tachycardic, although there was no ketonuria. Intravenous fluid replacement was commenced together with intramuscular promethazine (Phenergan) for nausea. An ultrasound scan confirmed a singleton pregnancy of the same gestation. Two days after admission the vomiting was unrelieved and so intramuscular prochlorperazine (Stemetil) was added to the regime. (Rectal therapy was refused by the patient.) This combination did not relieve her symptoms and she remained on intravenous fluids, unable to tolerate any oral intake. Potassium chloride supplementation was required to correct hypokalaemia of 2.9 mmol/l. On the 14th day of admission intramuscular metoclopramide (Maxalon) was added with gradual relief of her symptoms over the following seven days. She was then discharged on oral metoclopramide.

At 12 weeks gestation the patient was readmitted with worsening recurrent nausea and vomiting which failed to respond to any of the drugs previously used. She was again dehydrated and tachycardiac on admission and urinalysis revealed moderate ketonuria (2+ on ward dipstick testing). She had lost 10 kg in weight (20% of the pre-pregnancy weight). Intravenous fluid replacement was recommenced. The patient and her partner were unwilling to consider termination of pregnancy or parenteral nutrition. After 14 days with no relief from vomiting, ondansetron (Zofran) 8 mg intravenously twice daily was commenced resulting in dramatic cessation of vomiting after a single dose although the nausea persisted. She was able to tolerate a light diet and oral therapy two days later and was well enough to be discharged 14 days after admission, taking ondansetron 4 mg tid orally.

At formal antenatal booking two weeks later she was still nauseated. The vomiting was controlled on an oral dose of ondansetron

Ondansetron (Zofran)

Uses
- management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy
- prevention and treatment of postoperative nausea and vomiting

Mode of action
- highly selective 5-HT_3-receptor antagonist
- precise mode of action not known, but 5-HT_3 receptors are present in vagal afferents from the small intestine and in the floor of the fourth ventricle
- mode of action probably by antagonism of the receptors in both central and peripheral sites

Side-effects
- constipation, headaches, flushing/sensation of warmth of the head and epigastrium
- transient disturbances of liver aminotransferases
- rarely, hypersensitivity reactions, visual disturbances, chest pain, cardiac arrhythmias

Department of Obstetrics and Gynaecology, Fazakerley Hospital, Aintree Hospitals NHS Trust, Liverpool L9 4AL, UK
DG Tincello
MJ Johnstone

Correspondence to
Dr DG Tincello, Liverpool Women's Hospital, Crown Street, Liverpool L8 7SS, UK

Accepted 12 January 1996