Vascular Ehlers–Danlos syndrome undiagnosed during life

M Jarmulowicz FRCPath
W G Phillips FRCP DipRCPath[1]

J R Soc Med 2001;**94**:28–30

Vascular Ehlers–Danlos syndrome causes severe fragility of connective tissue in arteries, veins, skin and other organs. It is of particular importance to surgeons, obstetricians and radiologists since it can present acutely with arterial and gastrointestinal rupture, obstetric catastrophe or complications of surgical and radiological interventions.

CASE HISTORY

A woman aged 33 was seen at another hospital after sudden onset of intense headache while washing her car. On admission she was fully conscious. Lumbar puncture yielded bloodstained cerebrospinal fluid and the provisional diagnosis was subarachnoid haemorrhage. Within four hours she deteriorated to a Glasgow coma score of 9/15; a computerized tomographic (CT) scan revealed no abnormality. On arrival at the neurosurgical unit she was hypertensive and tachycardic with upgoing plantar reflexes and could communicate only by downward conjugate eye movements. A repeat CT scan showed fresh blood within the pons, mesencephalon and fourth ventricle. She was diagnosed as having brainstem infarction with haemorrhage, possibly secondary to a basilar artery thrombosis. Despite sedation and ventilation she deteriorated further and died thirty hours after initial presentation.

At necropsy there was marked subconjunctival haemorrhage and mild proptosis. Extensive fresh bruising was present on the thorax with older bruises on the legs. Multiple scars of previous surgery were noted on both calves. In addition to brainstem haemorrhage there was retroperitoneal haemorrhage and cardiac tamponade secondary to intracardiac and pericardial bleeding. The right carotid artery was occluded, with signs of previous partial rupture (Figure 1).

Histological examination of the skin revealed an abnormal arrangement of dermal collagen (Figure 2) and rupture of a small artery. On the basis of these findings vascular Ehlers–Danlos syndrome was considered likely and further clinical history was sought from her family and physicians.

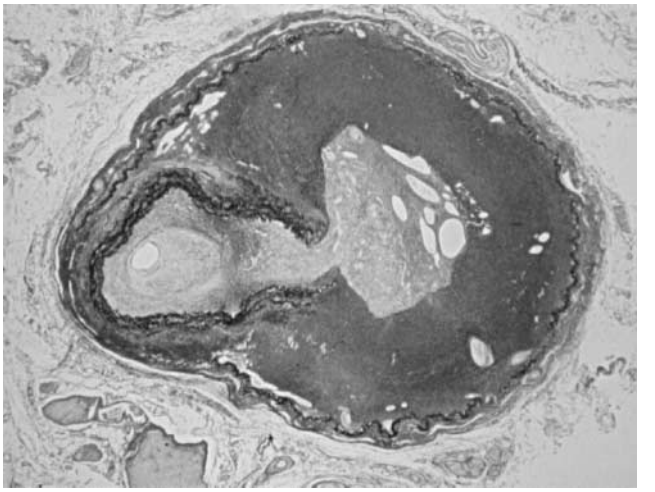

Figure 1 **Carotid artery showing previous contained rupture with subsequent organization.** Elastic van Gieson, ×15

Throughout her life she had bruised on the slightest trauma. Her skin—particularly on the feet—was unusually thin with the veins clearly visible. On four occasions in her

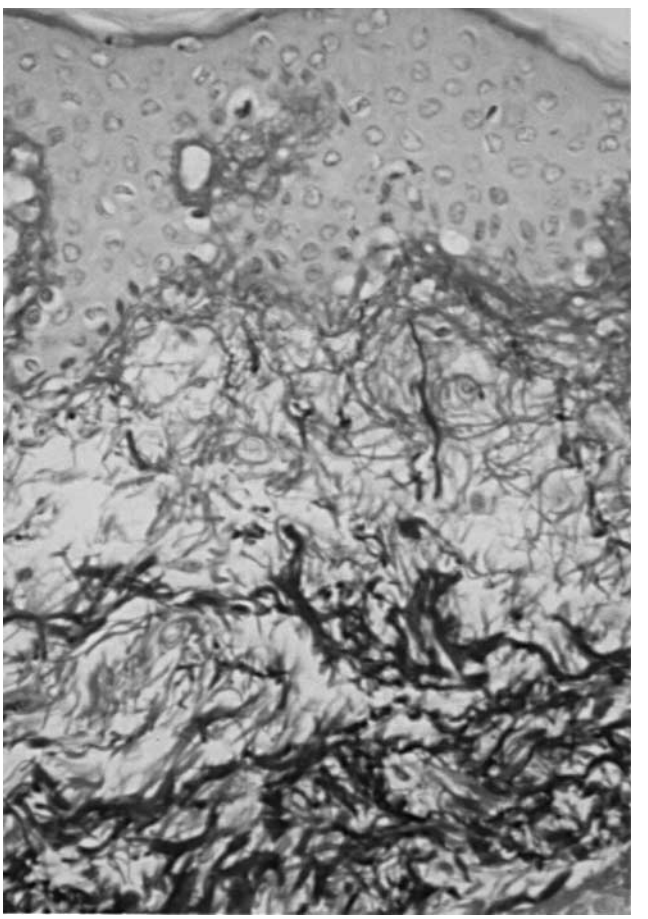

Figure 2 **Skin showing abnormally fine collagen fibres, and relative increase in elastic fibres in the superficial dermis.** Elastic van Gieson, ×380

Department of Histopathology and [1]Dermatology, Royal Free Hospital NHS Trust, London NW3 2QG, UK

Correspondence to: Dr M Jarmulowicz

20s she had spontaneously bled into her calves, with tibial compartmental compression requiring fasciotomy. On the last occasion, rupture of the posterior tibial artery had been documented. The fasciotomy wounds healed very slowly, leading to an erroneous diagnosis of dermatitis artefacta[1]. At the age of 30 she gave birth to a son, and during the delivery she suffered severe vaginal and perineal tearing. Healing was complex and for a long time manual evacuation of faeces was necessary.

COMMENT

Ehlers–Danlos syndrome combines groups of genetic disorders characterized by articular hypermobility, skin extensibility and tissue fragility. A revised classification has been proposed following elucidation of the biochemical and molecular basis[2]. About 1 in 5000 people have Ehlers–Danlos syndrome, but only a small proportion of these are diagnosed. Vascular Ehlers–Danlos syndrome (previously called type IV)—its true incidence is not known—is particularly important as this is the only form associated with an increased risk of early death. Delay in diagnosis is common even when the clinical features are typical, and the condition often goes unrecognized until necropsy. The clinical features are summarized in Table 1.

Table 1 **Features of vascular Ehlers–Danlos syndrome**

*Major diagnostic criteria**	*Minor diagnostic criteria*
Thin translucent skin	Early onset varicose veins
Arterial rupture (medium sized often in age 20–40)	Hypermobile small joints
Intestinal rupture	Tendon and muscle rupture
Uterine rupture during pregnancy and labour	Carotid-cavernous sinus fistula
Easy bruising	Talipes equinovarus
Facial appearance	Pneumothorax
	Family history of sudden death due to any of the above
	Acrogeria

*The presence of two major criteria is highly suggestive of the diagnosis; the presence of one major criterion and one or more minor criteria should lead to suspicion and further investigation.

The earliest clinical features of vascular Ehlers–Danlos tend to be cutaneous. The patient bruises easily despite normal coagulation studies, and in the young this can lead to allegations of child abuse. The skin is translucent with prominent venous markings. The characteristic facial appearance includes a pinched nose, thin lips, prominent staring eyes and lobeless ears. Vascular complications, which tend to arise at age 20–40, include spontaneous rupture or aneurysms of medium sized and large arteries. Carotid-cavernous fistula, mitral valve prolapse and arterial dissection are well-recognized features, and angiography is a hazardous procedure with a reported incidence of 22% major complications and 5% fatality[3]. Gastroenterological presentations include gastrointestinal haemorrhage and perforation of the bowel, either spontaneous or during endoscopy. In this syndrome, acute abdominal and flank pain should be investigated immediately with non-invasive diagnostic procedures. A patient who experiences a second spontaneous colonic rupture should have prophylactic colectomy.

The diagnosis of vascular Ehlers–Danlos syndrome is confirmed by demonstration that cultured fibroblasts synthesize abnormal type III procollagen. Although all patients have a mutation in the COL3A1 gene, the number of mutations identified is very large[3,4]. Genetic counselling is important. Since this is a dominant disorder, there is a 50% risk that any child of an affected parent will also be affected. Patients also need to consider the greatly increased risk that they will die while their children are young, and be aware of a 77% perinatal maternal mortality[3]. Support groups enable patients and families to learn more about the disease and to contribute to research; several such groups have their own Internet websites[5,6].

Modern information technology ought to render a missed diagnosis such as happened in our patient a thing of the past. Internet search engines and specialist medical databases are readily available online. By entering 'arterial+rupture+bruising' into the non-medical Google search engine[7] we obtained 121 web pages of which 9 of the first 10 pages were about Ehlers–Danlos syndrome. McKusick's *Mendelian Inheritance in Man* is now available online[8] and has over 10 000 entries and an easy search facility. By entering 'arterial rupture bruising' as the keywords we found six entries of which five related to Ehlers–Danlos syndrome and one to a fibrinogen disorder. Our patient saw many doctors yet none made the diagnosis that would have provided her with the advice, care and support she needed during her lifetime.

Acknowledgments We thank Professor Michael Pope, Institute of Medical Genetics, University of Wales College of Medicine, Cardiff and Dr Eduardo Colanje, Director of Diagnostic Dermatology, St John's Dermatology Centre, St Thomas's Hospital, London, for their help in confirming the diagnosis.

REFERENCES

1 Eskander MBF, MacDonald R. Acute tibial compartment syndrome secondary to psychosomatic disorder. *J R Med Corps* 1994;**140**:97–8

2 Beighton P, De Paepe A, Steinmann B, Tsipouras P, Wenstrup RJ. Ehlers–Danlos syndromes: revised nosology, Villefranche, 1997. Ehlers–Danlos National Foundation (USA) and Ehlers–Danlos Support Group (UK). *Am J Med Genet* 1998;**77**:31–7

3 Freeman RK, Swegle J, Sise MJ. The surgical complications of Ehlers–Danlos syndrome. *Am Surg* 1996;**62**:869–73

4 Pepin M, Schwarze U, Superti-Furga A, Byers PH. Clinical and genetic features of Ehlers–Danlos syndrome type IV, the vascular type. *N Engl J Med* 2000;**342**:673–80

5 Ehlers Danlos syndrome UK Support Group. [http://www.atv.ndirect.co.uk]

6 Office of Rare Diseases, National Institutes for Health, Bethesda, Maryland [http://rarediseases.info.nih/gov/org]

7 Google search engine. [http://www.google.com]

8 *Online Mendelian Inheritance in Man, OMIM*, Center for Medical Genetics, Johns Hopkins University and National Center for Biotechnology Information, National Library of Medicine [http://www.ncbi.nlm.nih.gov/Omim/]

Acute abdomen after cardiac surgery: three cases, one fatal

S R Waspe MB ChB N K Agrawal FRCS[1]
T J Spyt MD FRCS(CTh)

J R Soc Med 2001;**94**:30–31

When abdominal complications arise after cardiac surgery they are commonly fatal. Prompt action can avert disaster.

CASE HISTORIES

Case 1

A woman aged 75 with severe left ventricular dysfunction, unstable angina, mitral regurgitation and recurrent episodes of ventricular tachycardia underwent urgent coronary bypass grafting combined with mitral valve repair, subendocardial resection and left ventricular aneurysmectomy. An intra-aortic balloon pump (IABP) was inserted to wean her off cardiopulmonary bypass. Initially she required inotropic support, but this was withdrawn, along with the IABP, on the day after surgery.

On the fourth postoperative day the patient reported nausea and vague abdominal pain and had clinical signs of an acute abdomen. She was mildly pyrexial but haemodynamically stable, with a slight leucocytosis, normal amylase and good renal function. Chest and abdominal X-rays were unremarkable. On clinical suspicion of bowel ischaemia, and without further investigation, the general surgeons did an emergency laparotomy. The right colon was found to be ischaemic, so a right hemicolectomy with primary bowel anastomosis was performed. Histological examination confirmed non-occlusive ischaemia of the right colon and part of the transverse colon. Postoperative recovery was slow but the patient was well when discharged home four weeks later.

Case 2

A man aged 73 with unstable angina and pulmonary oedema due to left ventricular dysfunction and mitral regurgitation was referred for urgent cardiac surgery. After seven days with an IABP *in situ*, coronary bypass grafting was performed with mitral valve repair. His initial postoperative recovery was satisfactory and the IABP was removed the following day, inotropes being reduced substantially. On the second postoperative day the patient complained of nausea and abdominal pain. The abdomen was distended, with signs of peritonitis. He was apyrexial and haemodynamically stable but there was a leucocytosis and renal function was deteriorating. Serum amylase was normal and the chest and abdominal X-ray showed nothing of note. Blood gas analysis indicated hypoxia but no acidosis. The general surgeons promptly diagnosed ischaemic bowel, and at emergency laparotomy the caecum and right colon were grossly distended and ischaemic. These were resected and an ileostomy was fashioned. Histological examination confirmed non-occlusive ischaemia of the caecum and ascending colon.

After this operation, haemofiltration was required for two days because of anuric renal failure, but this resolved completely. The patient was discharged home six weeks after surgery, and the ileostomy is to be reversed in the near future.

Case 3

A man aged 74 with severe coronary artery disease and mild renal impairment underwent elective coronary bypass grafting. Inotropes were required in high dosage in the early postoperative period but these were withdrawn the day after surgery. However, his renal function gradually worsened and on the fifth postoperative day he became oliguric and was returned to the intensive care unit. During the night he began to complain of vague abdominal pain but was otherwise well. The following morning his abdomen was found to be grossly distended and generally tender,

Departments of Cardiac Surgery and [1]General Surgery, Glenfield Hospital, Groby Road, Leicester LE3 9QP, UK

Correspondence to: Mr T J Spyt

though without signs of peritonitis. He was haemodynamically stable and apyrexial but the renal function had not improved and there was a pronounced leucocytosis. He was becoming acidotic and hypoxic. The chest X-ray was unremarkable but the abdominal film showed gaseous and distended bowel. The general surgeons, seeing the patient 8 hours after symptom onset, requested further investigations, and abdominal ultrasound showed gross dilatation of the caecum but no free fluid. By mid-morning the patient began to decompensate haemodynamically, requiring increasing doses of inotropes. A colonoscopy was conducted under general anaesthesia at midday to decompress the large bowel, which showed some patchy mucosal change. By this time the patient was hypotensive despite maximum inotropic therapy and had irreversible acidosis; therefore further intervention was not pursued. He died within a few hours. Necropsy showed ischaemia of the large bowel.

COMMENT

The incidence of abdominal complications after cardiac surgery has been reported between 0.12% and 2.9%[1–3], and the causes include peptic ulcer disease, acute pancreatitis, cholecystitis, prolonged ileus, bowel obstruction, liver failure and often most dramatically, ischaemic bowel[1–3]. Mesenteric ischaemia, reported in 0.06–0.1% of patients having such operations[3–5], carries a mortality of between 43% and 91%[3–5]. This high case fatality may be due partly to late diagnosis[1–4]. One reason for delayed diagnosis is that the patient may still be on a ventilator; but another is that ischaemic bowel can present with insidious symptoms such as nausea and constipation.

Analyses of post-cardiac-surgery mesenteric ischaemia have suggested several factors that can alert surgeons to a high risk. These include emergency surgery, failed percutaneous coronary angioplasty requiring emergency surgery, IABPs, a long time on cardiopulmonary bypass, dependence on high doses of inotropes, advanced age and history of previous abdominal disorders[1–5]. Opinions differ on whether valve surgery and long aortic cross-clamp times present an increased risk[2–4]. In the first two cases reported here, several important risk factors were evident, but the third patient was not such an obvious candidate for the development of mesenteric ischaemia.

The most crucial event, in the two successful cases, was the early involvement of the gastrointestinal surgeons and the speed of their intervention. (We also believe that personal consultant-to-consultant referral was an important factor.) Both laparotomies took place within five hours of symptom onset, while the patients were still haemodynamically stable. Investigations such as abdominal ultrasound, mesenteric angiography and diagnostic laparoscopy, although recommended by some authorities[1,2,4], were not undertaken because of the rapid progression of symptoms, clinical suspicion of the diagnosis and the understanding that without immediate surgical intervention the patients could die. In the third case a delay in involvement of the general surgeons was compounded by their request for further investigations.

Some gastrointestinal surgeons are reluctant to operate in the early phase after cardiac surgery because of the supposed instability of the patient's cardiovascular system[1,4]. In reality, most patients will have gained better cardiac function after open-heart surgery but will be unable to compensate much further for the considerable demands of severe abdominal complications. Our first two cases illustrate that even patients with severely compromised cardiac function are able to withstand major abdominal intervention after their heart surgery. Conversely, those with less severe cardiac dysfunction preoperatively, if they develop acute abdominal complications, will decompensate quickly without early operation. A policy of early intervention will lead to the occasional negative laparotomy, but this does not seem to upset recovery of cardiac patients; in the absence of a life-threatening abdominal disorder, the additional trauma is not great.

REFERENCES

1 Sakorafas GH, Tsiotos GG. Intra-abdominal complications after cardiac surgery. *Eur J Surg* 1999;**165**:820–7

2 Christenson JT, Schmuziger M, Maurice J, *et al*. Postoperative visceral hypotension the common cause for gastrointestinal complications after cardiac surgery. *Thorac Cardiovasc Surg* 1994;**42**:152–7

3 Tsiotos GG, Mullany CJ, Zietlows S, *et al*. Abdominal complications following cardiac surgery. *Am J Surg* 1994;**167**:553–7

4 Allen KB, Salam AA, Lumsden AB. Acute mesenteric ischemia after cardiopulmonary bypass. *J Vasc Surg* 1992;**16**:391–5

5 Klempnauer J, Grothues F, Bektas H, *et al*. Acute mesenteric ischemia following cardiac surgery. *J Cardiovasc Surg* 1997;**38**:639–43

Remission of precapillary pulmonary hypertension in systemic lupus erythematosus

João M Ribeiro MD Margarida Lucas MD
Rui M M Victorino MD PhD

J R Soc Med 2001;**94**:32–33

When pulmonary hypertension develops in systemic lupus erythematosus (SLE) the usual cause is chronic thromboembolism or interstitial lung disease[1–4]. Very occasionally, however, it has the features of the primary form of pulmonary hypertension[1].

CASE HISTORY

A Caucasian woman aged 42 was admitted with a two-month history of severe fatigue and progressive exertional dyspnoea (New York Heart Association class III). She also reported polyarthralgia, Raynaud's phenomenon and low-grade fever for the past year. On admission, temperature was 38.5 °C, blood pressure 110/68 mmHg and pulse 100 per minute; she was mildly tachypnoeic. Lung fields were clear but there were signs of right ventricular failure—raised jugular pressure and lower-limb oedema. Haemoglobin was 9.0 g/dL, leucocytes 4.1×10^9/L with absolute lymphopenia (0.3×10^9/L), platelet count normal, erythrocyte sedimentation rate 133 mm/h, C-reactive protein 2.5 mg/dL, C3 and C4 complement depressed, and gamma-globulin high at 29 g/L. Liver and renal function tests were normal and HIV-1 and HIV-2 serology was negative. Antinuclear antibodies (titre $>1/256$) and double-stranded anti-DNA 1130 U/L were detected; direct Coombs test was positive with IgG and C3 specificities; she had proteinuria of 760 mg/day. Systemic lupus erythematosus was diagnosed but the right heart failure demanded further investigation. Chest X-ray showed clear lung fields, and enlargement of both pulmonary arteries was seen clearly on magnetic resonance imaging (Figure 1); transoesophageal doppler echocardiography disclosed a high pulmonary artery systolic pressure (PASP) of 45 mmHg at rest with peak values of 78 mmHg on exertion; myocardial, pericardial and valvular heart disease were excluded. On pulmonary function testing, CO diffusing capacity (D_LCO) was very low at 42%; and restrictive lung diseases were ruled out, as was thromboembolism, by repeated arterial blood gases and normal ventilation–perfusion lung scanning. Antiphospholipid antibodies were persistently negative and computed tomography did not show interstitial lung disease. On cardiac catheterization the severe pulmonary hypertension was confirmed (PASP 42 mmHg); pulmonary vascular resistance was high at 352 dyne.s.cm^{-5} and capillary wedge pressure was normal (15 mmHg). Methylprednisone 500 mg twice daily was prescribed for three days, followed by prednisone 1 mg/kg and azathioprine 2.5 mg/kg per day, maintained for two years. In the next few months the patient's functional status improved with progressive lessening of exertional dyspnoea and reduction of PASP on repeated doppler echocardiography. By the twelfth month of follow-up PSAP was 30 mmHg and D_LCO was 82%. Three years after diagnosis and one year after stopping azathioprine and prednisone, the patient is symptom-free.

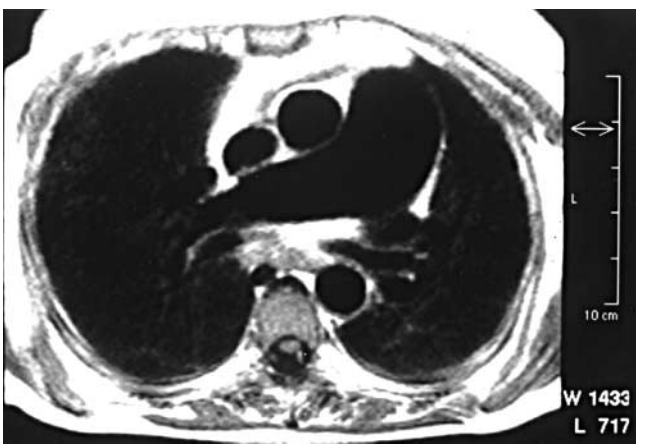

Figure 1 **Magnetic resonance scan showing dilatation of pulmonary artery.**

COMMENT

In a series of 24 patients with pulmonary hypertension and SLE, Asherson *et al.*[1] identified antiphospholipid antibodies in 16. These antibodies are associated with microthrombosis in the alveolar capillaries[3,4]. But in addition to the thrombotic mechanism[3,4] it has been proposed that antiendothelial antibodies can lead to release of interleukin-6 by endothelial cells in alveolar capillaries, so increasing in another way pulmonary vascular resistance[5].The usual view is that this pulmonary hypertension resembling the 'primary' form of the disease will be resistant to treatment[6]; however, we are not the first to contest this view. Before us, Goupille[7] and Groen[8] and their co-workers reported reductions in pulmonary hypertension

Medicine Department 2, University Hospital of Santa Maria, Lisbon, Portugal

Correspondence to: Professor Rui M M Victorino, Faculdade de Medicina de Lisboa, Serviço de Medicina 2, Hospital Universitário de Santa Maria, Av. Prof. Egas Moniz, 1600 Lisboa, Portugal
E-mail: rvict@fml.fm.ul.pt

when treating two patients with corticosteroids and cyclophosphamide. Our patient differs from theirs in having gone into a complete remission which was sustained a year after stopping azathioprine and prednisone. We conclude that, in a patient with this rare and usually fatal manifestation of SLE, aggressive immunosuppressive therapy is warranted.

REFERENCES

1 Asherson RA, Higenbottam TW, Xuan ATD, Khamashta MA, Hughes GRV. Pulmonary hypertension in a lupus clinic. Experience with twenty-four patients. *J Rheumatol* 1990;**17**:1792–8

2 Orens JB, Martinez FJ, Lynch JP. Pleuropulmonary manifestations of systemic lupus erythematosus. *Rheum Dis Clin N Am* 1994;**20**:159–93

3 Brucato A, Baudo F, Barberis M, *et al.* Pulmonary hypertension secondary to thrombosis of the pulmonary vessels in a patient with the primary antiphospholipid syndrome. *J Rheumatol* 1994;**21**:942–4

4 Asherson RA, Cervera R. Antiphospholipid antibodies and the lung. *J Rheumatol* 1995;**22**:62–6

5 Yoshio T, Masuyama JI, Kohda N, *et al.* Association of interleukin 6 release from endothelial cells and pulmonary hypertension in systemic lupus erythematosus. *J Rheumatol* 1997;**24**:489–95

6 Gaine SP, Rubin LJ. Primary pulmonary hypertension. *Lancet* 1998;**352**: 719–25

7 Goupille P, Fauchier L, Babuty D, Fauchier JP, Valat JP. Precapillary pulmonary hypertension dramatically improved with high doses of corticosteroids during systemic lupus erythematosus. *J Rheumatol* 1994;**21**:1976–7

8 Groen H, Bootsma H, Postma DS, Kallenberg CG. Primary pulmonary hypertension in a patient with systemic lupus erythematosus: partial improvement with cyclophosphamide. *J Rheumatol* 1993;**20**:1055–7

Sarcomatoid renal cell carcinoma metastatic to right ventricle

K H H Lim FRCS M Brett FRCPath[2]
J Pitts-Crick FRCP G D Angelini FRCS
R Persad FRCS(Urol)[1]

J R Soc Med 2001;**94**:33–35

When sarcomatoid renal cell carcinoma is found in ventricular myocardium, it has usually extended along the inferior vena cava.

CASE HISTORY

A woman aged 50 with right loin pain, microscopic haematuria, weight loss and raised erythrocyte sedimentation rate (ESR) was found to have a localized right renal mass without vena caval involvement on ultrasound or computed tomographic imaging. A radical nephrectomy was performed and the specimen, weighing 350 g and measuring 15 × 8 × 5 cm, had a large pale firm mass in the upper two-thirds. Microscopically, the tumour diffusely invaded the stroma and renal tubules but did not breach the capsule. It consisted predominantly of large spindle cells, mixed in some areas with large squamoid cells. Morular (whorl-like) aggregates were seen with the squamoid cells (Figure 1). Although some areas contained cells with translucent cytoplasm, typical clear-cell carcinoma was not seen. No cartilaginous or osteoid differentiation was identified. Frequent mitoses, extensive patchy necrosis and microvascular invasion were observed. There was no evidence of localized tumour developing in the collecting ducts, and the pelvic urothelium was normal. No tumour was found in the renal vein at the hilum. On immunostaining the tumour cells were strongly positive for vimentin and cytokeratin (AE1/AE3) but negative for epithelial membrane antigen (EMA), CD68 (macrophage

Bristol Heart Institute and [1]Department of Urology, Bristol Royal Infirmary, Bristol BS2 8HW; [2]Department of Cellular Pathology, Southmead Hospital, Bristol BS10 5NB, UK

Correspondence to: Mr KHH Lim

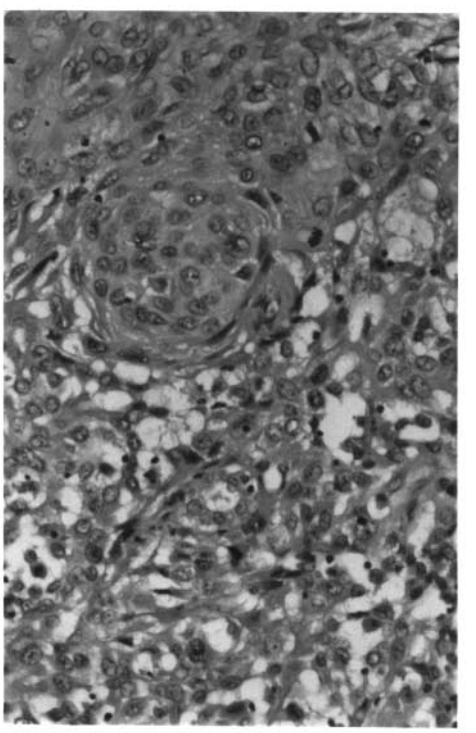

Figure 1 **Sarcomatoid renal cell carcinoma with squamoid differentiation and morule formation (top)** [Haematoxylin and eosin × 250]

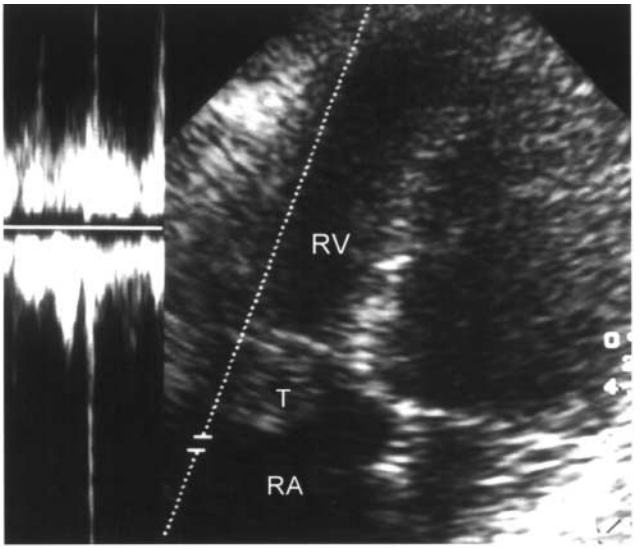

Figure 2 **Echocardiogram showing pedunculated right ventricular lateral wall mass prolapsing through tricuspid valve.** RA=right atrium; RV=right ventricle; T=tumour mass

marker) and acidic-calcium-binding protein S100. Sarcomatoid renal cell carcinoma (SRCC) was diagnosed. Two months after the nephrectomy the woman complained of left loin discomfort and again had microscopic haematuria. An abdominal ultrasound scan did not reveal further abnormalities but her urine grew coliform organisms. Not responding to oral antibiotics, she was readmitted with pyrexia, rigors, tachycardia, dyspnoea and chest discomfort. She also had an episode of syncope with hypotension and bradycardia. A left sternal systolic heart murmur was heard and intravenous antibiotics were immediately started on suspicion of infective endocarditis; however, an echocardiogram showed a large pedunculated right ventricular mass prolapsing through the tricuspid valve in systole (Figure 2). A biopsy taken during diagnostic right heart catheterization was sterile on culture and histological examination revealed metastatic SRCC. With her ensuing rapid clinical deterioration and the aggressive nature of her tumour, palliative heart surgery was not performed; two days later she had a cardiac arrest and died.

COMMENT

Sarcomatoid renal cell carcinoma, which accounts for some 1–13% of all renal carcinomas, is a highly aggressive bimorphic tumour with both sarcomatoid and carcinomatous components. Patients, usually in the sixth decade, tend to present late and their overall median survival after diagnosis is about 6 months[1,2]. Immunohistochemistry is often necessary to distinguish SRCC from a true sarcoma, a transitional cell carcinoma or other unusual tumour[3]. (Squamous and spindle cell differentiation occur in some cases of transitional cell carcinoma.) In SRCC the sarcomatoid cells sometimes bear markers of epithelial cell differentiation, and these should be looked for: membrane surface glycoprotein EMA and cytoplasmic keratin peptides, which are subunits of cytoskeletal intermediate filaments, indicate epithelial differentiation—note, however, that EMA expression can be *low* in SRCC. Intermediate filament component vimentin, although expressed by cells of mesodermal origin and mesenchymal tumours, is also found in renal cell carcinoma. Coexpression of cytokeratin and vimentin supports a diagnosis of renal cell carcinoma, including the SRCC subtype[4]. Furthermore, the lack of pelvic urothelial neoplasia and absence of localized tumour arising within the collecting ducts make a diagnosis of transitional cell carcinoma unlikely. Though first described in neuroendocrine cells, S100 protein is expressed in many cells of non-neuronal tissues, including renal tubular cells; lack of staining for S100 does not rule out renal cell carcinoma but is useful for excluding malignant melanoma. The carcinomatous component in SRCC commonly has features of clear, granular or chromophobe cell types but squamoid differentiation, as seen in this case with formation of aggregates or morules, is very unusual. Furthermore, unlike transitional cell carcinoma, a renal cell carcinoma very seldom invades renal tubules.

This case was unusual not only in presentation and tumour histology; there are only two previous reports of SRCC affecting ventricular myocardium without caval involvement[5,6]. Metastatic lesions to the heart are rare in isolation and usually occur in the setting of disseminated disease. Collectively, renal carcinoma involves the heart in 1–4% of patients through tumour–thrombus extension along the inferior vena cava. Non-contiguous ventricular metastasis is highly unusual[5]. Although 50% of cases of cardiac myxoma may present with fever, raised ESR, malaise and weight loss—features described in this patient—it should be remembered that new cardiac signs appearing in a patient with a background history of malignancy should arouse suspicion of a metastatic lesion to the heart[7]. Furthermore, renal tumours have a protean mask at presentation. Fever, observed in 7%, was not a feature of the primary tumour but was striking in this patient's second presentation. Thus the presence of a heart murmur together with a clinical picture resembling generalized sepsis following a diagnosis of urinary tract infection contributed to the initial diagnostic challenge. This right ventricular lesion prolapsing into the atrium may have caused tricuspid valve obstruction and thus explained her unusual set of cardiovascular symptoms and signs. Although surgery was inappropriate here, one centre that operated on metastatic tumours to the heart, in attempts to restore circulatory haemodynamics, had an operative survival of

68%[8]. Surgery does not greatly alter the prognosis; combined with adjuvant therapy it is said to offer a modest gain in group survival[1,2].

REFERENCES

1 Sella A, Logothetis CJ, Ro JY, Swanson DA, Samuels ML. Sarcomatoid renal cell carcinoma. A treatable entity. *Cancer* 1987;**60**:1313–18

2 Cangiano T, Liao J, Naitoh J, Dorey F, Figlin R, Belldegrun A. Sarcomatoid renal cell carcinoma: biologic behavior, prognosis, and response to combined surgical resection and immunotherapy. *J Clin Oncol* 1999;**17**:523–8

3 DeLong W, Grignon DJ, Eberwein P, Shum DT, Wyatt JK. Sarcomatoid renal cell carcinoma. An immunohistochemical study of 18 cases. *Arch Pathol Lab Med* 1993;**117**:636–40

4 Ordonez NG, Rosai J. Urinary tract. In: Rosai J, ed. *Ackerman's Surgical Pathology* 8th edn. St Louis: Mosby-Year Book, 1996:1149–51

5 Riccioni L, Damiani S, Pasquinelli G, Scarani P. Solitary left ventricle metastasis by renal cell carcinoma with sarcomatoid features. *Tumori* 1996;**82**:266–9

6 Santo-Tomas M, Mahr NC, Robinson MJ, Agatston AS. Metastatic renal cell carcinoma invading right ventricular myocardium without caval involvement. *J Cardiovasc Surg* 1998;**39**:811–12

7 Chitwood WR Jr. Cardiac neoplasms: current diagnosis, pathology, and therapy. *J Cardiovasc Surg* 1998;**3**:119–54

8 Murphy MC, Sweeney MS, Putnam JB, Ott DA, *et al.* Surgical treatment of cardiac tumours—a 25 year experience. *Ann Thorac Surg* 1990;**49**:612–18

Common iliac aneurysm rupture with sinus bradycardia

M Muttalib MSc FRCSI

J R Soc Med 2001;**94**:35–36

The presentation of aneurysm rupture is surprisingly variable. Bradycardia is not to be expected.

CASE HISTORY

A man aged 52, ex-smoker but previously healthy, collapsed at a pub quiz night but was caught by a bystander, who prevented head or other injury. He was free from chest pain or breathlessness and there were no ischaemic changes on the electrocardiogram, but he had a persistent sinus bradycardia of 30–50 beats per minute. Initial blood pressure was 76/50 mm Hg, which improved to 110/70 mm Hg with intravenous colloid infusion. Oxygen saturation remained at 99%. Haemoglobin was 12.0 g/dL and cardiac enzymes were normal.

While in the resuscitation bay, the patient suddenly developed a severe, sharp, constant left-sided abdominal pain radiating to his back. There was no associated nausea or vomiting and the blood pressure and bradycardia were unchanged. He was rigid and tender only in the left side of the abdomen and flank, without any bruising. Bowel sounds were absent. An abdominal aortic aneurysm was not clinically evident and all peripheral pulses were present. The left hemidiaphragm was elevated on the chest X-ray. The only finding on abdominal radiography was displacement of the bowel gas pattern away from the left side.

Spiral computed tomography (CT) of the abdomen and pelvis, performed to look for blunt trauma to the left kidney or spleen from the patient's fall or for a ruptured aneurysm, disclosed an isolated 4 cm diameter left common iliac artery aneurysm (Figure 1) with rupture into the peritoneal cavity (Figure 2). Thereafter the patient was noted to have developed a weakened left femoral pulse and absent left pedal pulses. He was transferred promptly to a vascular unit where the aneurysm was repaired with a synthetic graft.

COMMENT

Most iliac artery aneurysms are found in association with abdominal aortic aneurysms. Isolated iliac artery aneurysms account for under 1% of all vascular aneurysms. The natural history is of gradual enlargement, with rupture the most common clinical presentation.

Patients seen shortly after collapse may be surprisingly well—haemodynamically stable with good peripheral

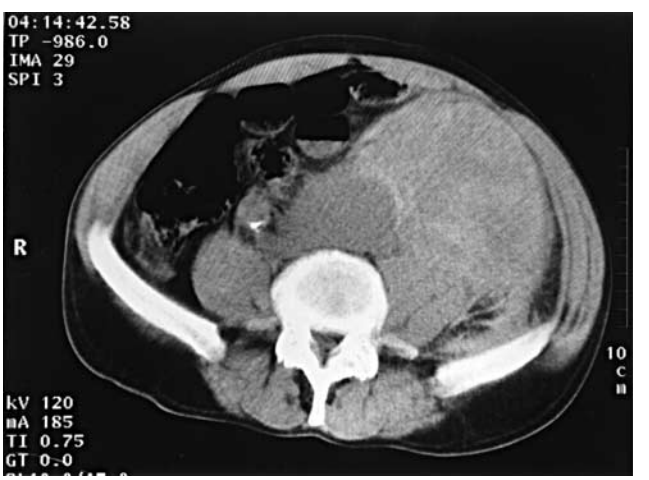

Figure 1 **Computed tomographic scan showing ruptured isolated left common iliac artery aneurysm**

Department of Surgery, Stoke Mandeville Hospital, Aylesbury HP21 8AL, UK

Correspondence to: 16 Ryecroft Road, London SW16 3EG, UK

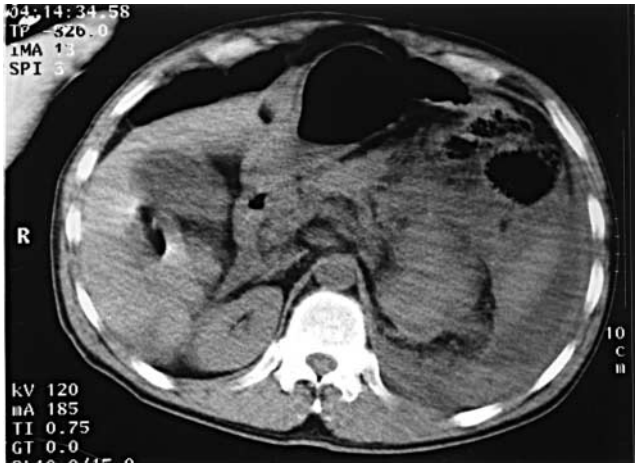

Figure 2 **Computed tomographic scan showing intraperitoneal blood tracking around spleen and left kidney**

pulses. This phase is often referred to as the 'herald bleed'. As rupture ensues, a spectrum of physical signs can develop, sometimes during the course of assessment, as here. The cause of the persistent sinus bradycardia in this patient may have been vagal stimulation by stretching of bowel mesentery from aneurysm rupture.

When elevation of the left hemidiaphragm is associated with a ruptured thoracic aortic aneurysm[1], the mechanism is thought to be compression of the left phrenic nerve. In the present case the likely cause was not paralysis but an upward push from the blood accumulating below, leading to splinting of the abdomen and displacement of bowel to the right.

Aneurysm rupture can present in numerous ways[2–5], and timely surgical intervention depends on clinical alertness. A notable case of ruptured aneurysm was seen in Albert Einstein, who despite having a known abdominal aortic aneurysm, presented with features simulating acute cholecystitis[6]. The correct diagnosis was not made until necropsy, where intraperitoneal blood from the ruptured aneurysm was found to track around the gallbladder. In patients with previously documented aneurysms, abdominal pain must be presumed to be due to aneurysm rupture until proved otherwise—the Einstein sign.

REFERENCES

1 Rabago G, Martin-Trenor A, Lopez-Coronado JL. Chronic aneurysm of the descending thoracic aorta presenting with right pleural effusion and left phrenic paralysis. *Texas Heart Inst J* 1999;**26**:96–8

2 Lederle FA, Parenti CM, Chute EP. Ruptured abdominal aortic aneurysm: the internist as diagnostician. *Am J Med* 1994;**96**:163–7

3 Lodder J, Cheriex E, Oostenbroek R, Soeters P, Vreeling F. Ruptured abdominal aortic aneurysms presenting as radicular compression syndromes. *J Neurol* 1982;**227**:121–4

4 Goff CD, Davidson JT, Teague N, Callis JT. Hematuria from arteriovesical fistula: unusual presentation of ruptured iliac artery aneurysm. *Am Surg* 1999;**65**:421–2

5 Owen ER, Kark AE. Irreducible inguinal hernia as a presentation of ruptured abdominal aortic aneurysm [letter]. *J Roy Coll Surg Edinb* 1990;**35**:399

6 Chandler JJ. The Einstein sign: the clinical picture of acute cholecystitis caused by ruptured abdominal aortic aneurysm [Letter]. *N Engl J Med* 1984;**310**:1538

Subclinical presentation of massive retropharyngeal abscess

Paul Chatrath MRCS Myles Black FRCS
Sean Blaney FRCS

J R Soc Med 2001;**94**:36–37

In young infants and children a retropharyngeal abscess typically shows itself with fever, sore throat, dysphagia and neck swelling. But the presentation can also be insidious.

CASE HISTORY

A 2½-year-old boy was referred to our department with acute airway difficulties following adenoidectomy. The preceding history included recurrent sore throats, intermittent low grade pyrexia and cervical lymphadenopathy over two months. Tonsillitis had been diagnosed and treated with oral antibiotics but subsequently the child had developed increasing stertor and feeding difficulties. These features had been thought due to adenoidal hypertrophy, hence the adenoidectomy. After the procedure, rapid onset of acute upper airway obstruction required emergency intubation and ventilation. Subsequent extubation failed on two occasions. On transfer to our unit, a plain lateral soft tissue neck radiograph showed widening of the prevertebral space (Figure 1) and computed tomographic (CT) scanning revealed a massive bilateral and symmetrical retropharyngeal abscess (Figure 2). The abscess was treated initially by CT-guided needle aspiration but it quickly reaccumulated. It was then incised and drained and the patient had no evidence of recurrent infection when reviewed two months later.

COMMENT

Retropharyngeal abscesses have become uncommon since the advent of antibiotics but presentation remains typically

Department of Otolaryngology, Great Ormond Street Hospital for Children, London, UK
Correspondence to: Mr P Chatrath, 11 Long Acre, Orpington, Kent BR6 7RD, UK

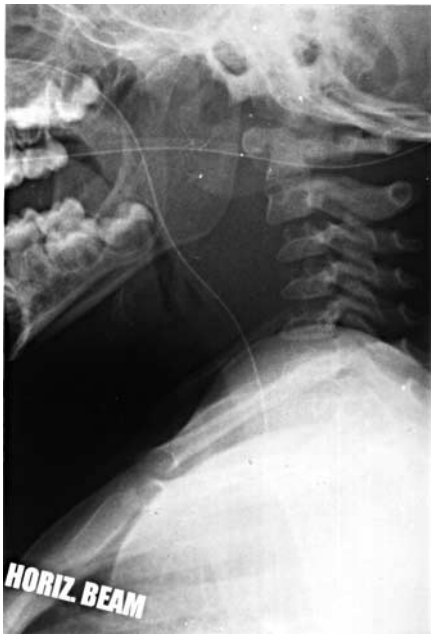

Figure 1 **Plain lateral soft tissue radiograph showing widened prevertebral space**

florid rather than insidious as here. Causes in children include upper respiratory tract infections, foreign bodies, trauma, cystic malformations and tuberculosis[1]. We have found no previous reports of diagnosis as a result of perioperative airway compromise. In this case we presume that the retropharyngeal abscess was secondary to recurrent tonsillitis and caused increasing snoring and stertor by anterior displacement of the adenoidal bed. The anterior bulging might have been spotted at operation but for the bilateral distribution and remarkable symmetry of the abscess.

CT scanning is more sensitive but less specific than lateral neck radiography in the detection of retropharyngeal abscesses. Its accuracy in differentiating abscess from

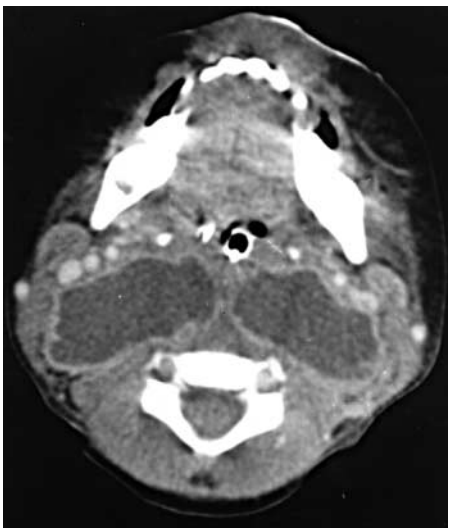

Figure 2 **Axial computed tomographic scan of neck showing a massive symmetrical retropharyngeal abscess**

cellulitis remain in doubt[2,3]. CT scanning is also of use in the identification of an underlying cause[4]. This case highlights an unusual and potentially dangerous presentation and underlines the importance of early radiological investigation.

REFERENCES

1 Hibbert J. Tonsils and adenoids. In: Evans JNG, ed. *Scott-Brown's Otolaryngology*, 5th edn. London: Butterworths, 1987:368–71

2 Boucher C, Dorion D, Fisch C. Retropharyngeal abscesses: a clinical and radiologic correlation. *J Otolaryngol* 1999;**28**:134–7

3 Stone ME, Walner DL, Koch BL, Egelhoff JC, Myer CM. Correlation between computed tomography and surgical findings in retropharyngeal inflammatory processes in children. *Int J Paediatr Otorhinolaryngol* 1999; **49**:121–5

4 Boyer JC, Helenon O, Coste A, *et al.* Contribution of x-ray computed tomography in the diagnosis of cervical suppuration. *Ann Otol Chir Cervicofac* 1994;**111**:59–68