A Female Van Driver with a Swollen Arm

Charles D Forbes,* William F Jackson,**

A 28-year-old female van driver presented with a 5 day history of a swollen, painful left arm. The swelling had started shortly after she had lifted a heavy box while loading her van. At the time she felt no pain in her arm or shoulder and had noticed no weakness or other symptoms. She had no significant past medical history nor had she received any recent medication. In particular she was not taking the oral contraceptive pill and she was a non-smoker.

Question 1: The patient's left arm was tender. Comment on the clinical appearances shown in Fig. 1.

Answer: The left arm is swollen from the shoulder downwards (and there was a trace of pitting oedema on the dorsum of the hand). The dominant feature was a collateral venous circulation around the shoulder with the direction of the blood flow in this circulation towards the chest. There are also two small bruises on the forearm which, the patient said, were of traumatic origin.

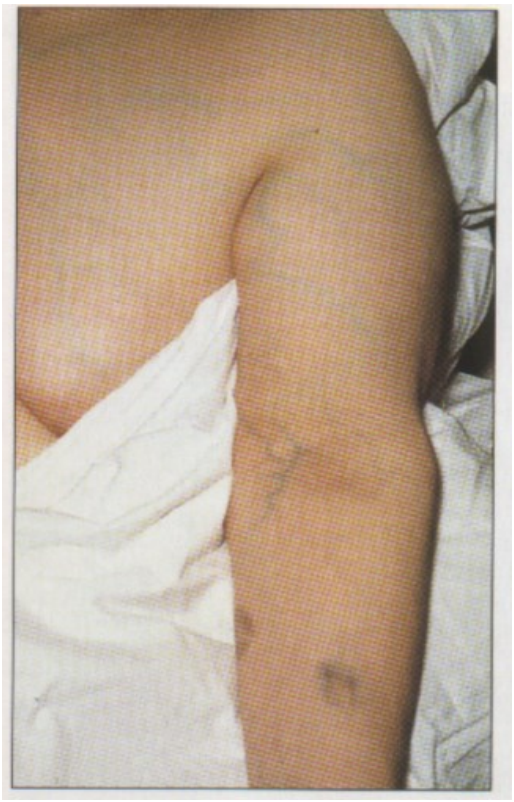

Fig. 1: The patient's left arm on admission.

There was local tenderness on palpation of the arm at the shoulder but movements were normal. The tender cord of the axillary vein was palpable in the axilla. There were no lymph nodes palpable in the axilla or neck. Neurological examination was unremarkable. Chest and abdominal examination were normal.

Question 2: What is the provisional clinical diagnosis?

Answer: The provisional diagnosis is a venous thrombosis in the left axillary vein. There was no evidence to suggest any cause. No cervical rib was palpable.

*) Professor of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland.
**) Formerly Honorary Consultant, Department of Medicine, Guy's Hospital, London.

Question 3: What initial investigations are required?
Answer:

Haematology				
	Haemoglobin	13.9g/dl		
	RBC	$4.82x10^{12}/1$		
	PVC	0.409		
	MCV	84.8 fl		
	MCH	28.8 pg		
	MCHC	33.9g/dl		
	WBC	$13.4x\ 10^{9}/1$		
	Platelets	$285\ x\ 10^{9}/1$		
	MPV	9.6 fl		
	Blood film showed 'marked lymphopenia'			
	ESR	140mm in 1st hour		
Biochemistry				
	Sodium	142mmol/l	Bilirubin	5μmol/l
	Potassium	4.3mmol/l	Alkaline phosphatase	101μ/1
	Bicarbonate	30mmol/l	Albumin	41g/l
	Urea	6.3mmol/l	Protein	80g/l
	Creatinine	80μmol/l	Uric acid	140μmol/l
	Corrected calcium	2.26mmol/l		
	Phosphate	1.28mmol/1		

Radiology
The chest X-ray and a left arm venogram are shown opposite.

Question 4: Comment on the changes in
(a) the X-ray of chest (Fig. 2).
(b) the venogram (Fig. 3).

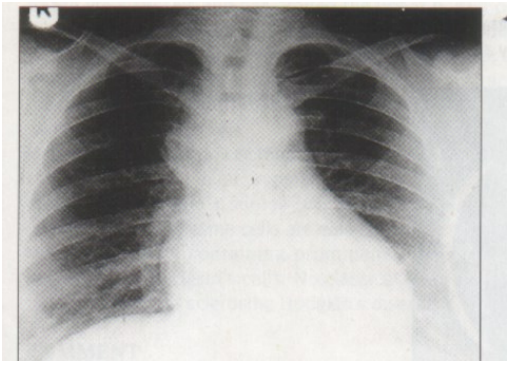

Fig. 2: Chest X-ray on admission.

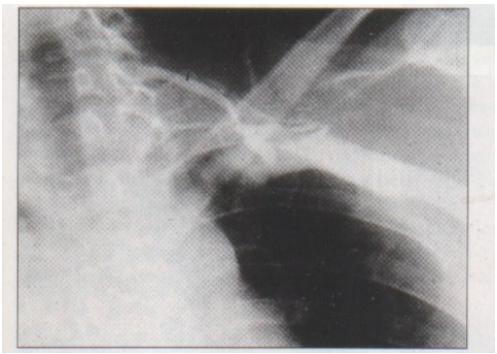

Fig. 3: Left arm venogram, 2 days after admission.

Answer:
(a) There is a large space-occupying lesion in the upper mediastinum, seen on chest X-ray.
(b) This upper limb venogram shows obstruction of contrast in the subclavian vein at the thoracic inlet presumably due to thrombus and there is an extensive collateral circulation. A space-occupying lesion can also be seen in the upper mediastinum.

Question 5: What is the differential diagnosis of this upper mediastinal lesion?
Answer: Thymoma, teratoma, bronchial carcinoma, lymphoma or retrosternal goitre.

Question 6: What further investigations are now required to define this mediastinal mass?

Answer:
(a) Computed tomography of thorax (Fig. 4).
(b) Mediastinoscopy and biopsy (Figs 5 & 6).

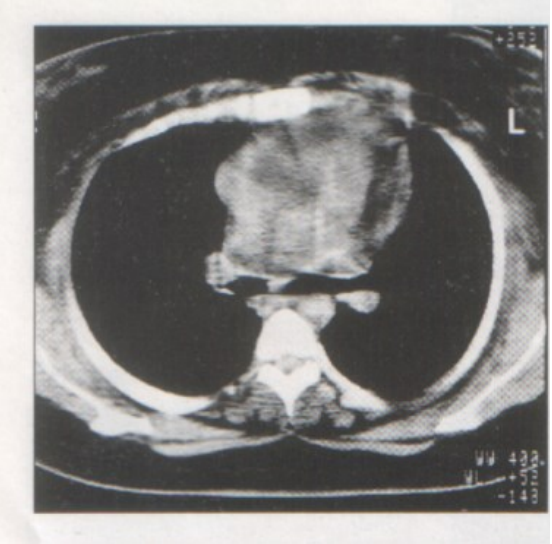

Fig 4: CT scan of thorax on admission.

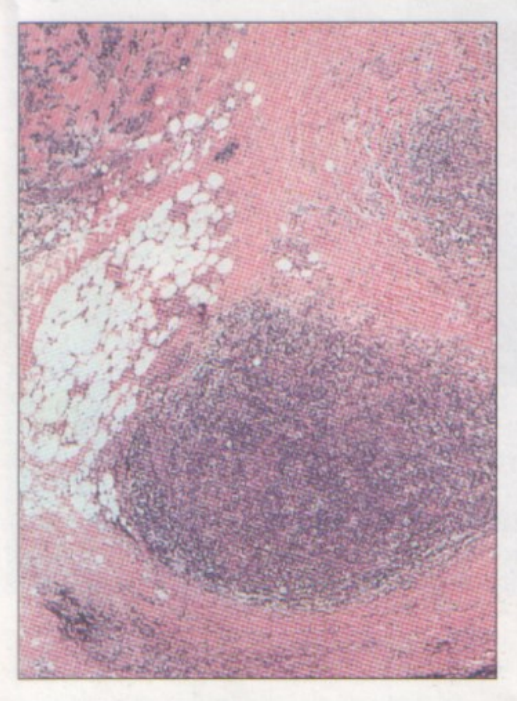

Fig. 5: Histology of paraffin section of mediastinal mass.

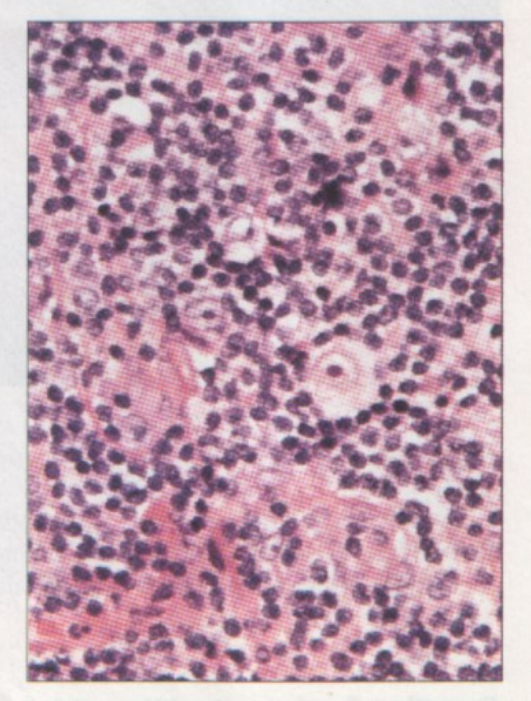

Fig. 6: Close-up histology of mediastinal mass.

Question 7: Comment on these investigations.

Answer: The CT scan (Fig. 4) shows a large anterior mediastinal mass which is attached to the great vessels and has eroded the upper border of the manubrium sterni. There is thickening of the pericardium on the left side and this may represent tumour spread.

The possibilities are thymic tumour, lymphoma or teratoma. Mediastinoscopy confirmed the presence of a large tumour which was attached to the left lung and pericardium and had eroded the posterior surface of the manubrium. Multiple biopsies were taken.

Histology. The low power (Fig. 5) view of this paraffin section shows separate nodules of lymphoid tissue in fat, in areas delineated by broad bands of fibrous tissue. On high power (Fig. 6) the nodules are composed largely of lymphocytes but scattered eosinophils and plasma cells are also seen. As can be seen there are several large cells with clear nuclei containing prominent eosinophnic nucleoli. These are typical of mononuclear Hodgkin's cells. No classical Reed-Sternberg cells were seen. This is the picture of nodular sclerosing Hodgkin's disease.

Comment:

The presenting feature in this lady was axillary vein thrombosis. The commonest cause of this is venous compression, usually by a cervical rib, but occasionally by the first rib, the anterior scalene or pectoralis minor muscles, or a fracture of the clavicle. Rarely, there is a congenital web in the vein. In this patient no apparent cause could be palpated. Venography showed the presence of venous thrombosis at the thoracic inlet in relationship to a large mass in the upper mediastinum. A decision was made to anticoagulate the patient with intravenous heparin while the central mass was investigated, to prevent propagation of the thrombus. Heparin is a short acting anticoagulant and can be stopped at short notice to allow mediastinoscopy and biopsies to be carried out.

Staging of Hodgkin's lymphoma traditionally follows the Ann Arbor classification (Table 1). Pathological stage is further determined by histological examination of biopsied tissues. A recommended staging procedure is shown in Table 2.

Table 1: Ann Arbor staging in Hodgkin's disease.

Stage I:	Involvement of lymph nodes in a single region (I) or infiltration of a single extralymphatic site (IE)
Stage II:	Involvement of lymph nodes in two distinct regions on the same side of the diaphragm (II) which may also include spleen (Us), localized extralymphatic involvement (IIE) or both (llsE)
Stage III:	Involvement of lymph node on both sides of the diaphragm (IIE), which may include the spleen (IIIs), localized extralymphatic involvement (IIIE) or both (IIIsE)
Stage IV:	Diffuse or disseminated involvement of extralymphatic sites (e.g. bone marrow, liver and lung)
	In addition, the suffix letters A and B are used to denote the absence (A) or presence (B) of any of the additional systemic features of fever, night sweats and loss of 10% of body weight in the previous 6 months.

Table 2: Recommended staging procedures in Hodgkin's disease.

1. Required evaluation procedures

- A Adequate surgical biopsy
- B Detailed history with emphasis on the presence or absence of B symptoms
- C Complete physical examination with special attention directed to the evaluation of lymphadenopathy, liver and spleen size, and the detection of bony tenderness
- D Laboratory studies: FBC and platelet count, liver and kidney function, serum alkaline phosphatase
- E Chest X-ray PA and lateral
- F Bilateral lower extremity lymphangiogram
- G Abdominal CT scan
- H Bone marrow aspirate and biopsy

2. Required evaluation procedures under certain conditions

- A Chest tomography of chest CT scan
- B Bone scan
- C Staging laparotomy including splenectomy

3. Useful ancillary procedures

- A Skeletal radiographs
- B Gallium scan

Difficulties arise, however, when staging patients with so called 'bulky mediastinal Hodgkin's' (defined as the maximum mediastinal mass width divided by the maximum intrathoracic diameter, with a ratio of greater than one-third). Patients such as this do not fit neatly into the Ann Arbor classification, which does not take into account tumour bulk, but tumour bulk is known to be of prognostic significance. Also the criteria for extralymphatic extension (E) are poorly defined in the Ann Arbor classification; thus localized spread in the thorax, in this case involving lung, pericardium and mediastinum may be attributed to Stage IIE or IV (staging procedures showed no spread outside the thorax). The consensus at present is to allocate such patients to Stage IIE.

Stage IIE disease in conjunction with lack of constitutional symptoms suggests a good prognosis. However, anaemia, an elevated ESR, lymphopenia and relative lymphocyte depletion in the tumour mass suggests a more guarded prognosis, as in this patient. Table 3 lists the important prognostic factors in Stage I and II disease.

Treatment in this patient consisted of a combination of radiotherapy and a variant of the 'MOPP' chemotherapy regime (Table 4).

Table 3: Prognostic factors - Hodgkin's disease Stages I and II.

	Favourable	Unfavourable
Age	<40 years	>40 years
Histology	LP and NS	MC and LD
Erythrocyte sedimentation rate (ESR)	'A' and ESR <50	'A' and ESR ≥50
+ systemic symptoms	'B' and ESR <30	'B' and ESR ≥30
Clinical stage	I or II (mediastinal)	II (non-mediastinal)
Laparotomy*	Spleen negative	Spleen positive

*Prognostic significance defined by laparotomy and spenectomy.

Table 4: Principles of 'MOPP' chemotherapy.

1.	Indicated for Stages III and IV and patients with localized disease with poor prognostic features
2.	Should be given in full dose and as intensively as possible. It consists of MUSTINE, VINCRISTINE, PROCARBAZINE and PREDNISOLONE
3.	Treatment should be continued until complete clinical resolution and then for two further courses only. There is no role for maintenance chemotherapy
4.	Careful restaging is required at the end of treatment

References:

- Forbes C.D. and Jackson W.F. Illustrated Case Histories: Clinical Medicine. Mosby-Wolfe, London, 1995.