tration was 87 g/l, platelet count was $123 \times 10^9/l$ and lactic dehydrogenase was 939 U/l.

Surface membrane markers were identified by indirect immunofluorescence and examined with a FACScan flow cytometer (Becton Dickinson, Mountain View, California, USA). The following antibodies were analysed: T3, T4, T8, J5, B4, B1 (Coulter Clone); LeuM5, Leu15, Leu14, IL-2, Leu17 and Leu8 (Becton Dickinson); anti-LFA 1 and anti- β -LFA 1B (Janssen); Cris 1 (Dr R Vilella, Hospital Clinic Provincial, Barcelona); FMC7 (Sera-Lab); IOB8 (Immunotech); and surface immunoglobulins (Kallestad). Mouse rosettes were also sought. Detailed results are shown in the table.

B cell chronic lymphoid leukaemias comprise a broad spectrum of lymphoid proliferations classified according to the cytological and phenotypic features of the leukaemic cells.³ Our case was a mantle zone lymphoma in leukaemic phase, which is a rare form of B cell chronic lymphoid leukaemia (B-CLL). Cytologically, the leukaemic cells had pronounced heterogeneity of size and a fairly pleomorphic appearance. The surface marker analysis of the leukaemic cells (table) showed a monoclonal B cell proliferation that was not characteristic of classic B-CLL. Surface immunoglobulin was strong, FMC7 was positive, and there was no formation of mouse rosettes. All these features differ from typical B-CLL leukaemia but resemble the surface phenotype of prolymphocytic leukaemia and that of follicular lymphoma in leukaemic phase. Overall, it seems that the characteristic phenotypic profile of mantle zone lymphoma in the leukaemic phase includes strong surface immunoglobulin and positivity for FMC7 and CD5. Reactivity with CD10 and mouse rosette formation is variable. Data on the antibodies Leu8, CD11, CD22, CD23, CD25 and CD38 are scarce. Further studies are needed to clarify precisely the phenotype of this particular lymphoid leukaemia.

J SOLER
F TORTUÑO
E RUBIOL
Servei d'Hematologia
Hospital de la Santa Creu i Sant Pau
Avda S. A. M. Claret 167
08025 Barcelona
Spain
R BORDES
Servei d'Anatomia Patològica
Hospital de la Santa Creu i Sant Pau
Avda S. A. M. Claret 167
08025 Barcelona
Spain

- 1 Jaffe ES, Bookman MA, Longo DL. Lymphocytic lymphoma of intermediate differentiation-Mantle zone lymphoma: A distinct subtype of B-cell lymphoma. *Hum Pathol* 1987;18:877-80.
- 2 Pombo de Oliveira MS, Jaffe ES, Catovsky D. Leukaemic phase of mantle zone (intermediate) lymphoma: its characterisation in 11 cases. *J Clin Pathol* 1989;42:962-72.
- 3 Bennet JM, Catovsky D, Daniel MT, et al. Proposals for the classification of chronic (mature) B and T lymphoid leukaemias. *J Clin Pathol* 1989;42:567-84.

Hypercalcaemia and osteolytic lesions associated with chronic lymphatic leukaemia (CLL)

Case 1

A 72 year old man had cervical and axillary lymphadenopathy and an enlarged spleen

palpable 1 cm below the left costal margin. A blood count showed that his haemoglobin concentration was 11.5 g/dl (normal range: 12.5-16 g/dl), his white cell count was: $114.0 \times 10^9/l$ (normal range $4.0-10.0 \times 10^9/l$), his lymphocytes were $105 \times 10^9/l$ and his platelet count $250 \times 10^9/l$ (normal range: $150-400 \times 10^9/l$). A biochemical screen, including that for serum calcium concentration, was normal. A bone marrow aspirate and trephine biopsy specimen showed diffuse infiltration with small mature lymphocytes, and chronic lymphatic leukaemia (CLL) was diagnosed. The disease was easily controlled by short, intermittent courses of chlorambucil.

Three years from diagnosis and while not receiving treatment, the patient was admitted with a two week history of thirst, malaise, and vomiting. Examination showed that he was dehydrated, had enlarged cervical lymph nodes, an enlarged liver palpable 3 cm below the right costal margin and an enlarged spleen palpable 4 cm below the left costal margin. The haemoglobin concentration was 9.1 g/dl, the white cell count 14.8 (small mature lymphocytes $9.1 \times 10^9/l$, pro-lymphocytes $3.9 \times 10^9/l$), and the platelet count $142 \times 10^9/l$. Serum calcium was 3.66 mmol/l (normal range 2.20-2.65 mmol/l), phosphate 0.9 mmol/l (normal range 0.70-1.30 mmol/l), and alkaline phosphatase activity 101 IU/l (normal range 28-142 IU/l). Serum albumin was 34 g/l (normal range 35-45 g/l). The urea, creatinine, and electrolyte concentrations were normal. The serum parathormone concentration was $<0.1 \mu g/l$ (normal range $<0.5 \mu g/l$) and vitamin D concentration was $10 \mu mol/l$ (normal range 15-100 $\mu mol/l$). A skeletal survey showed generalised osteoporosis and multiple lytic lesions throughout the skull. No serum or urinary paraprotein was detected.

Treatment with chlorambucil 6 mg/day, prednisolone 40 mg/day, frusemide 40 mg/day and intravenous fluids was begun, and after three days the calcium had fallen to 3.0 mmol/l. Intravenous mithramycin (25 $\mu g/kg/day$) for three days was given, after which the calcium concentration was 2.05 mmol/l. Two weeks later a further course of mithramycin was necessary as the calcium concentration had risen to 3.7 mmol/l. A further short-lived response was achieved but three weeks later the patient fell, fractured his femur and pelvis, and died shortly afterwards from bronchopneumonia.

Case 2

A 70 year old woman had Binet stage A CLL. No treatment was needed for four years after which short intermittent courses of chlorambucil controlled a rising lymphocyte count and lymphadenopathy.

About six years after diagnosis she fell and fractured the left humerus. Radiographs showed lytic lesions at the site of fracture and also throughout the skeleton. She had progressed to stage C CLL at this time. There was no evidence of a second primary malignancy. During the next six months further lytic lesions developed in association with severe generalised osteopenia. Crush fractures of several vertebrae occurred. Death from bronchopneumonia ensued 10 months after she fractured her humerus.

Biochemistry screens (including serum calcium, phosphate, and alkaline phosphatase) were normal throughout the last year of life

and no serum or urinary paraprotein was present.

Hypercalcaemia is a rare complication of CLL which occurs most frequently in the setting of advanced disease.¹ Hypercalcaemia, however, has also been reported in patients with early stage disease but in many of these patients coincidental primary hyperparathyroidism has been found.² Where hyperparathyroidism is not detected the cause of the hypercalcaemia has been attributed to increased osteoclastic activity secondary to secretion of osteoclast activating factor by malignant lymphocytes.³

The prognosis for patients with advanced disease and normal or low serum parathyroid hormone activity was generally measured in weeks despite treatment directed at both the CLL and the hypercalcaemia.¹ In contrast, hypercalcaemia complicating early stage disease or secondary to hyperparathyroidism may be associated with survival for several years.^{2,4,5}

Hypercalcaemia and osteolytic bone lesions may complicate CLL. The prognosis is generally poor but primary hyperparathyroidism should be excluded as this group of patients, if correctly treated, fare much better.

TJ LITTLEWOOD
APM LYDON
CJ BARTON
Department of Haematology,
Royal Berkshire Hospital,
Reading

- 1 Norby K, Vikrot O. Hypercalcaemia in chronic lymphatic leukaemia. *Scand J Haematol* 1975;15:132-8.
- 2 Wang JC, Steiner W, Aung MK, Tobin MS. Primary hyperparathyroidism and chronic lymphatic leukaemia. *Cancer* 1978;42:1964-9.
- 3 Mundy GR, Luben RA, Raisz LG, Oppenheim JJ, Buell DN. Bone resorbing activity in supernatants from lymphoid cell lines. *N Engl J Med* 1974;290:867-71.
- 4 Jordan GW. Serum calcium and phosphorus abnormalities in leukaemia. *Am J Med* 1966;41:381-90.
- 5 David NJ, Verner JV, Engel FL. The diagnostic spectrum of hypercalcaemia. *Am J Med* 1962;33:88-110.

Thoracic aortitis due to salmonella

Case report

A 62 year old college lecturer was admitted with a six month history of night sweats, arthralgia, and lethargy. Two weeks before admission he developed haemoptysis, hoarseness, and continuous left shoulder pain. There was no history of recent foreign travel, nor diarrhoeal illness in the patient or family, nor a notable medical history. On examination he had fluctuating fever up to 38.5°C. His blood pressure was 110/80 mm Hg in both arms with a systolic murmur at the left sternal edge and a pericardial rub. A chest x ray picture, which had been normal four months earlier, showed a left hilar mass. His white cell count was raised at $18.6 \times 10^9/l$, with an erythrocyte sedimentation rate of 116 mm/hr. C3d was moderately increased at 17 units/ml and an IgG cryoprotein was detected. Six blood cultures and culture of urine were negative. At bronchoscopy the left vocal cord was seen to be paralysed, with extrinsic compression of the trachea and left main bronchus. Culture of bronchial washings was negative. A computed tomogram of the thorax (figure) showed aneurysmal dilatation of the thoracic aorta; this was confirmed at

Computed tomogram of the thorax showing aneurysmal dilatation of the thoracic aorta containing thrombus.

aortography as a false aneurysm of the aortic arch which had originated at the left subclavian artery.

At thoracotomy an apparent hole in the aorta was oversewn with removal of slough from a false aneurysmal cavity adjacent to the upper lobe of the left lung. Cultures from pericardial tissue, the wound drain, and stools grew *Salmonella enteritidis*. He was given intravenous ampicillin 2 g four times a day. While apparently recovering, he suddenly collapsed and died 18 days after surgery from a massive haemoptysis. At necropsy it was impossible to identify the source of blood loss. The left lung contained a ragged cavity partly lined with thrombus in its upper lobe, with no evidence of vascular patency into this area. There was a small true aneurysm between the left carotid and subclavian ostia where a suture line was intact. The aorta showed moderate to severe atherosclerosis.

Although *Salmonella* thoracic aortitis is rare,¹ salmonellas have been incriminated in 18–35% of infected aneurysms.^{2,3} The elderly are particularly liable to the complications of salmonella bacteraemia, with 25% developing an endothelial infection.⁴ Clinical presentation may be with chronic sepsis unresponsive to antibiotics,³ or with features of a primary focus, such as osteomyelitis.

Alternatively, the symptoms may relate to the presence of an aneurysm or its rupture. Frequently there may be no such signs, even after rupture.³ A review of 34 cases of infected aortic aneurysms reported fever in all cases, positive blood cultures in 53%, and preoperative rupture in 79%. In 73% of cases the

patient was over 60 years old.³

The tendency for Gram negative infections to progress rapidly and rupture² makes urgent surgery imperative following diagnosis. If not treated surgically, mycotic aneurysms are invariably fatal.⁵ Successful management requires prompt diagnosis, appropriate antibiotics based on culture sensitivities, and intraoperative Gram stain with culture of the aorta and contents. Wide resection of infected tissue is necessary, with extra-anatomic grafting through clean tissue planes.² Cholecystectomy has been advocated if *Salmonella* is identified preoperatively, as the biliary tree is often a sanctuary for organisms and for continued sepsis.⁵

MJ STEIGER
IDA JOHNSTON
Department of Medicine,
University Hospital,
Queen's Medical Centre
Nottingham NG7 2UH

- 1 Cooper CB, Flinn J. *Salmonella* typhimurium and rupture of the thoracic aorta. *Thorax* 1987;42:391–2.
- 2 Jarrett F, Darling RC, Mundth ED, Austen G. Experience with infected aneurysms of the abdominal aorta. *Archives of Surgery* 1975; 110:1281–6.
- 3 Bennett DE, Cherry JK. Bacterial infection of aortic aneurysms—a clinical pathological study. *Am J Surg* 1967;113:321–6.
- 4 Cohen PS, O'Brien TF, Schoenbaum SC, Medeiros AA. The risk of endothelial infection in adults with salmonella bacteraemia. *Ann Intern Med* 1978;89:931–2.
- 5 Ewart JM, Burke ML, Bunt TJ. Spontaneous abdominal aortic infections. Essentials of diagnosis and management. *Am Surg* 1983; 49:37–50.

is indeed worthy of discussion.² The true incidence of these accidents, however, is and probably always will be impossible to assess. Not all cases are diagnosed, nor are they reported: it seems remarkable that not one case of peritoneal metastasis after needle biopsy has even been reported. The variability of survival is also of great importance: 20% of the reported subcutaneous metastases are detected after four years or more.²

Good indications of the true incidence were given by Smith,³ who showed that the actual risks of metastasis after needling were very low (of the order of 0.5/10 000). Bleeding and sepsis after needle biopsy are at least 10 times more common than metastasis.

Puzzled by the question of the number of metastases and being unable to obtain a satisfactory scientific answer, we thought it more relevant to examine the circumstances in which they occurred and found that the occurrence of metastasis seemed to be associated with large needles, core biopsy devices, high numbers of passes, and absence of normal parenchyma covering the tumour.²

Accordingly, we evolved a golden rule for needle biopsy: one pass with a fine needle (22 gauge or larger) through normal parenchyma.² This seems to be well advised because we were unable to find any report of metastasis in such circumstances.

When it can be calculated, the risk of metastasis seems to grow exponentially—for instance, increasing the needle diameter by a factor of two increased the seeding by a factor of 60² (without improving diagnostic efficiency).^{4–6}

In our opinion *good practice* is that needle biopsies of solid masses should be performed by (i) trained teams, (ii) only when taking decisions about the patient's management, (iii) through normal parenchyma, whenever possible, respecting anatomical boundaries, (iv) always with a fine non-cutting needle, (v) the sampling has to be done under suction, which must be maintained when withdrawing the needle, (vi) the sample quality has to be checked later to keep the number of passes to the very minimum.

In our opinion the case² referred to accumulated risk factors, and should, in no way, be used to affirm that the rate of metastasis after needle biopsy, and especially fine needle aspiration, is higher than is usually thought. It could serve, instead, to emphasise the risk factors and how they can be avoided. Large cutting needles, in particular, should not be used when cancer is suspected.

F ROUSSEL
Laboratoire d'Histologie Cytologique — C.H.U.,
Hôpital Charles Nicolle, F
76031 Rouen,
Cédex France

- 1 Denton KJ, Cotton DWK, Nakielnny RA, Goepel JR. Secondary tumour deposits in needle biopsy tracks: an underestimated risk? *J Clin Pathol* 1990;43:83.
- 2 Roussel F, Dalion J, Benozio M. The risk of tumoral seeding in needle biopsies. *Acta Cytol* 1989;6:936–9.
- 3 Smith EH. The hazards of fine needle aspiration biopsy. *Ultrasound Med Biol* 1984;10:629–34.
- 4 Bedenne L, Mottot C, Courtois B, et al. L'aiguille Tru-Cut est-elle plus efficace que l'aiguille fine dans le diagnostic des lésions hépatiques? Etude comparative de 45 ponctions guidées par l'échographie. *Gastroenterol Clin Biol* 1990;14:62–6.
- 5 Roussel F, Genevois A, Lestrat JP, Benozio M. Ultrasound guided FNAC in pancreatic masses: interest of co-performing by radiologist and cytopathologist. *Acta Cytol* (in press).
- 6 Cochand Priollet B, Chagnon S, Ferrand J, Blery M, Hoang C, Galian A. Comparison of cytologic examination of smears and histologic examination of tissue cores obtained by fine needle aspiration biopsy of the liver. *Acta Cytol* 1987;31:476–80.

Drs Denton and Cotton comment:

We are grateful to Dr Roussel for his comments, and we agree with several points, including his assessment of risk factors.

While it is true that most of the measures given should reduce the risk of needle track metastasis, we would dispute his suggestion of maintaining suction while withdrawing the

MATTERS ARISING

Risk of metastasis during fine needle aspiration

Denton *et al* expressed the opinion that there is a systematic underestimation of the risk of metastasis during needle biopsy.¹ This topic