CLINICOPATHOLOGICAL CONFERENCE

A 63-year-old man with persistent pyrexia

AR Chang, TWT Leung, J Kew, KF To

Presentation of case

Dr AR Chang*: On 21 February 1994, a 63-year-old man was admitted to the Prince of Wales Hospital with a history of weight loss of 20 pounds, nocturnal fever, and sweating with temperatures up to 37.8°C, and progressive anaemia with increased atypical lymphocytes and monocytes. Investigations by his general practitioner had failed to find a cause for the fever.

On admission, the patient related right upper quadrant abdominal pain of more than one month's duration and a poor appetite. His general practitioner had given him some medication and there was no past medical history of note. There was also no relevant drug or allergy history. He was employed as a workman, lived with his family and was a social drinker and non-smoker.

On physical examination there was no pallor, jaundice, oedema or cyanosis. The lymph nodes were not palpable. His pulse rate was 86 beats per minute and blood pressure was 120/80 mmHg; heart sounds were normal and no murmurs could be heard. The patient's lung fields were clear and there was normal air entry. His abdomen was soft and not tender. All other systems were normal. On the first hospital day, his temperature ranged from 37°C to a high of 38.4°C, which was recorded near midnight.

A number of laboratory investigations were undertaken and yielded the following values: red cell count 3.70 (normal range, 4.3-5.1 x 10^{12}/L), haemoglobin 98 g/L (normal range, 140-180 g/L), haematocrit 0.29 (normal range, 0.39-0.49), mean corpuscular volume 77.8 fL (normal range, 76-100 fL), mean corpuscular haemoglobin concentration 340 g/L (normal range, 330-370 g/L), mean corpuscular haemoglobin 26.5 pg (normal range, 27-33 pg), platelet count 254 (normal range, 150-450 x 10^9/L), white cell count 8.6 (normal range, 3.2-9.8 x 10^9/L). The white blood cell differential revealed the following: neutrophils 54%, lymphocytes 24%, monocytes 21%, and eosinophils 1%. The film showed mild polychromasia, microcytosis, hypochromia, and anisocytosis. The screen for infectious mononucleosis was negative. The Widal agglutination titre for *Salmonella typhi* (O+H) and *Salmonella paratyphi* (A, B, C) was less than 1:50. The test for hepatitis B virus was negative. The patient had no history of Epstein Barr virus infection or tuberculosis. Blood cultures for bacteria were negative. Biochemical investigations revealed the following values: plasma sodium 135 mmol/L (normal range, 135-147 mmol/L), potassium 4.2 mmol/L (normal range, 3.5 to 5.0 mmol/L), urea 3.8 mmol/L (normal range, 3.0-6.5 mmol/L) creatinine 53 μmol/L (normal range, 50-110 μmol/L), glucose 6.7 mmol/L (normal range, 3.9-6.1 mmol/L). The total protein was 73 g/L (normal range, 60-80 g/L), the albumin was 23 g/L (normal range, 40-60 g/L), total bilirubin 11 μmol (normal range, 2-18 μmol/L), alkaline phosphatase 96 U/L (normal range, 30-120 U/L), serum glutamate pyruvate transaminase/alanine transaminase 99 U/L (normal range, 0-35 U/L), calcium 2.29 mmol/L (normal range, 2.20-2.58 mmol/L), phosphate 1.0 mmol/L (normal range, 0.80-1.60 mmol/L), urate 240 μmol/L (normal range, 120-420 μmol/L).

His temperature at midnight on the second hospital day was 39.5°C. By 8 am it was 38.5°C and at noon it was 37.5°C. However, when measured at midnight on the third hospital day, the temperature was 39.5°C. Over the next few hours it was 38°C. Paracetamol 0.5 g, four times daily, was prescribed. On the fifth hospital day, the patient was sent home and instructed to return to hospital on 28 February for an ultrasound examination of his abdomen. The examination revealed bilateral adrenal masses, the right one appeared bilobed, and each was approximately 3 cm in length. On the left side, a mass measuring 9 x 4 x 3 cm could be seen. Small multiloculated cystic lesions were present in the liver, one each in the posterior aspects of the left and right lobes, respectively. The pancreas was not enlarged but was heterogeneous and had a coarse texture, suggesting the possibility of previous pancreatitis.

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The rest of the abdominal scan was unremarkable. The overall impression was that the adrenal lesions were metastatic tumours and the patient was advised to have an ultrasound-guided biopsy and a computerised axial tomography examination. Temperature readings during this period in hospital fluctuated between 37°C during the day and 38.5°C in the early hours of the morning. A plasma amylase reading was 57 U/L (normal range, 0-130 U/L) and the faecal occult blood test was negative. His blood clotting profile was normal. The patient was discharged home on 3 March 1994 and given an appointment to return to hospital on 8 March for an ultrasound-guided adrenal biopsy. He was also prescribed paracetamol 0.5 g to be taken as necessary. When he was contacted on 7 March, he refused admission for his biopsy and stated that he was going to return to his general practitioner.

Almost four weeks later on 1 April 1994, the patient was re-admitted to hospital. He was still having night sweats and had experienced further weight loss. He also had peri-orbital oedema which had been present for the past month. In addition, he had a facial rash. On examination, he was pale. There was a left chest scar and this was said to be due to a left empyema which had been drained when he was aged two years. The facial rash which had a "butterfly" distribution and the marked peri-orbital oedema were confirmed. His pulse was 110 beats per minute; temperature was 37.5°C, and blood pressure was 140/70 mmHg. There was no evidence of heart failure. The apex beat was in the fifth intercostal space at the mid-clavicular line. The heart sounds were normal but a systolic ejection murmur 2/4 was heard; all pulses were present. There was marked bilateral ankle oedema. The respiratory system was normal. The abdomen was soft. There was no hepatosplenomegaly and bowel sounds were normal. A non-itchy rash was also present over the neck and back. The urine had 3 plus protein. A blood screen yielded the following values: red cell count 3.23 x 10^{12}/L (normal range, 4.3-5.1 x 10^{12}/L), haemoglobin 81 g/L (normal range, 136-172 g/L), haematocrit 0.250 (normal range, 0.39-0.49), mean corpuscular volume 77.4 fL (normal range, 76-100 fL), mean corpuscular haemoglobin 25.1 pg (normal range 27-33 pg), mean corpuscular haemoglobin concentration 324 g/L (normal range, 330-370 g/L), platelet count 207 (normal range, 150 to 450 x 10^9/L), white cell count 7.4 (normal range, 3.2-9.8 x 10^9/L).

In the time interval between the second and sixth hospital days the patient's condition was described as being stable and his chest was clear. His fluid intake was restricted to one litre daily. Temperature readings during this period ranged from 38°C in the mornings to 39°C recorded in the late afternoon or early evening. He was prescribed paracetamol 0.5 g, four times daily. Biochemistry tests revealed the following: sodium 114 mmol/L (normal range, 135-147 mmol/L), urea 3.2 mmol/L (normal range, 3.0-6.5 mmol/L), potassium 3.6 mmol/L (normal range, 3.5-5.0 mmol/L), creatinine 68 μmol/L (normal range, 50-110 μmol/L), spot urine sodium 24 mmol/L, spot urine potassium 33 mmol/L, spot urine osmolality 604 moSm/kg, plasma osmolality 238 moSm/kg. He developed urinary retention on the seventh day and a Foley catheter was inserted. On the eighth hospital day he was given 250 μgm Synathen intramuscularly. Left lower zone haziness was seen on chest X-ray and crepitations were heard on auscultation. Urine output over the previous 24 hours was described as poor. Several subcutaneous nodules were found in the upper abdominal wall. A skin biopsy was taken from the epigastric region. He commenced intravenous hydrocortisone the same day. The plasma creatine phosphokinase was 1169 U/L (normal range, 42 to 218 U/L), lactate dehydrogenase 2261 U/L (normal range, 87 to 213 U/L); bilirubin was 29 μmol (normal range, 2-18 μmol/L), alkaline phosphatase 178 U/L (normal range, 30-120 U/L), serum glutamate pyruvate transaminase/alanine transaminase 65 U/L (normal range, 0-35 U/L), albumin 13 g/L (normal range, 40-60 g/L). His prothrombin time was 19.5 seconds (normal range, 10-12 seconds), and the activated partial thromboplastin time was 52 seconds (normal range, 27-37 seconds), and calcium 2.03 mmol/L (normal range, 2.20-258 mmol/L), uncorrected. His general condition was poor; he was less alert and he had a rapid pulse (100 beats per minute). There was little improvement over the next 24 hours and in the afternoon of his ninth hospital day the patient collapsed and did not respond to resuscitation.

Differential diagnosis

Dr TWT Leung†: This patient is a 63-year-old man with fever, which is a common symptom. However, something tells us that he has a severe problem and this is supported by his 20-pound weight loss over a short period of time. For a 63-year-old man this magnitude of weigh loss has nothing to do with his diet and not eating. The second important factor is his temperature. I reviewed his hospital record and noted that before admission, he had had an elevated temperature and a fever for several months. Hence, he had a long-lasting pyrexia, and not just a simple fever. The pa-

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tient's temperature pattern is also interesting—it was higher in the evenings and at night time, and lower in the day time. This pattern is also not very typical of fever due to a viral infection. Therefore, this indicates a serious problem. On his first admission, a few investigations were performed, including liver function tests which revealed that both total protein and albumin levels were low. Although these are very non-specific findings, they do suggest something is suppressing protein synthesis. A low serum albumin level usually suggests a chronic illness and malignancy is one of the possible causes. His peripheral blood profile showed anaemia, with a haemoglobin level of 9.8 g/dL. The peripheral blood film showed mild polychromasia, microcytosis, hypochromasia and anisocytosis. The referring medical practitioner also found increased atypical lymphocytes and monocytes. All these findings, although not diagnostic of a particular blood disorder, make us think there is probably something affecting the blood, and it may be due to irritation of the bone marrow. All these findings indicate a serious illness.

Pyrexia of unknown origin is the presence of a temperature for a few weeks with no obvious causes. The clinician needs to undertake investigations for the following causes: infection, malignancy, or immunological disorder. When considering infections, occult sepsis, tuberculosis and fungal infection ought to be considered. Of course, there are other possibilities. In this case, investigations for typhoid fever, viral infections, and other infections were carried out. However, none of the investigations were positive. Consequently, tests were undertaken to exclude a malignancy, as his pattern of nocturnal fever and night sweating was consistent with malignant fever. Investigations for an immunological disorder, and more specifically an autoimmune disease, were also performed. It is also important to eliminate an infection contracted when travelling overseas and the patient should be carefully questioned. Drugs may also contribute to a fever. However, this patient's history did not support any of these causes. Fever is due to stimulation of the thermal regulating system caused by tissue injury. Thus, fever can be due to immunological defence, autoimmune disease, or malignancy. The immune system actively combats malignancy and produces pyrogens which cause fever. Hence, fever is very common in cancer patients and it usually indicates a rapidly growing, aggressive tumour. Many cancers cause fever, including lymphomas and leukaemia. It is not necessary to have a superimposed infection as some tumours, because of their aggressive nature during their progression and proliferation, produce a lot of pyrogens. Other tumours such as renal cell carcinoma, pancreatic carcinoma, sarcoma, lung cancer, and bowel cancer, are all possible in a 63-year-old man. In order to identify a possible site of origin of the tumour, we need to look for particular symptoms such as haematuria, pain, abnormal lumps and bumps, change of bowel habit, cough or haemoptysis. We also need to carry out a thorough physical examination for any enlarged lymph nodes, enlarged liver or spleen. Furthermore, we need to undertake a peripheral blood examination, to look for immature cells or blast cells that are suggestive of leukaemia, in order to arrive at the correct diagnosis. Up to this point, a malignancy is very high on our differential diagnosis list. However, we still have to establish the site of the primary tumour. Dr Kew will now discuss the radiological findings.

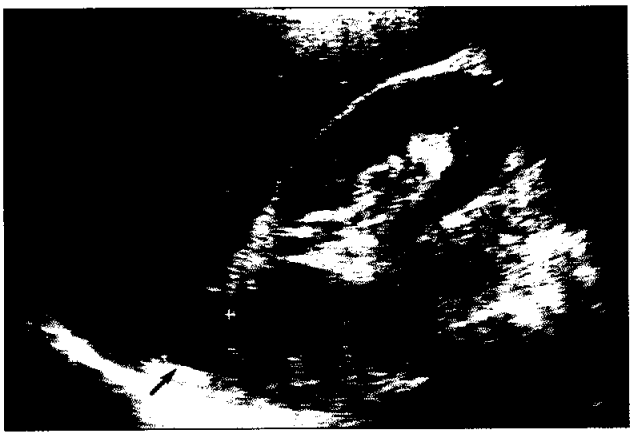

Fig 1. Ultrasound (longitudinal section) showing the right lobular solid adrenal mass (arrows) cephalad to the kidney (arrowhead)

Dr J Kew‡: Bilateral solid lobular adrenal masses could be seen on ultrasound, the right being bilobed and measuring approximately 3 x 2 cm (Fig 1). The left adrenal mass was 9.5 x 4 cm (Fig 2). No calcification or necrosis can be seen. The spleen is homogeneous and measures 10 cm in maximum length. Small cystic areas can be seen in the caudal aspect of the right lobe of the liver adjacent to the inferior vena cava. The pancreas is within normal limits and no mass is evident. No overt para-aortic lymphadenopathy is seen. The differential diagnoses for bilateral adrenal masses include hyperplasia, inflammation, haemorrhage and metastases. Primary adrenal tumours are usually unilateral. The cystic liver lesions could represent cysts, cystic metastases, infection, or lymphoma. A chest X-ray performed on initial admission shows irregularity of the left 10th rib and is in keeping with

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a previous thoracotomy. No active pulmonary tuberculosis or mass lesion is seen.

Dr Leung: I am afraid at this stage it was apparent that the patient had enlarging tumours in both adrenal glands, and other areas were relatively clear. Hence, it was important to get a histological diagnosis and an ultrasound-guided biopsy of this tumour was arranged. Unfortunately, the patient did not keep the appointment. Four weeks later, the patient's condition had deteriorated. When the patient was admitted for the second time, his anaemia was more severe. He had protein in his urine, a rash on his face and still the same undulating temperature. The patient deteriorated further and subsequent investigations revealed an elevated creatine phosphokinase and also lactate dehydrogenase (LDH). These enzymes are very non-specific, but they were elevated and this suggested tissue injury. An increased LDH level can indicate the presence of an aggressive non-Hodgkin's lymphoma or Hodgkin's lymphoma. Consequently, malignancy—possibly lymphoma—was still a valid diagnosis. To complete the story, I have prepared a slide to assist with a discussion of adrenal masses (Table).

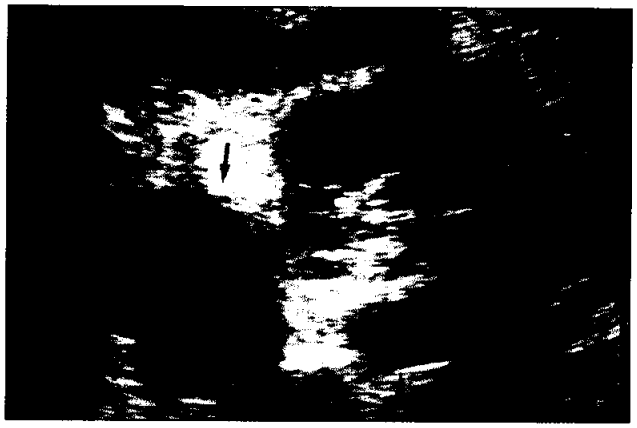

Fig 2. Ultrasound (longitudinal section) showing the left adrenal mass (arrows), measuring 9.5 x 4 cm (arrowhead = kidney)

Table. Common primary tumour sites linked to adrenal metastasis

- Renal cell carcinoma
- Carcinoma of the lung
- Carcinoma of the breast
- Lymphoma

mine whether it is a benign or malignant tumour. If it is a malignant tumour, we have to establish whether it is a primary or secondary tumour. Dr Kew mentioned that this is a bilateral condition. Hence, a primary adrenal tumour is unlikely, but secondary malignant tumours are more likely, in this circumstance. Primary adrenal cortical neoplasms, which are relatively common, usually occur in one of the adrenals. Weight loss may be present. However, in this patient there was no feminisation or virilisation, and there was no Cushing's syndrome because these tumours commonly produce hormones. In addition, there were no nodal or distant metastases. We also need to consider other common primary tumours if it is an adrenal metastasis, such as kidney, lung, breast, and lymphoid system. Of course, the patient is a male, so the breast is a very unlikely primary tumour site. The patient had a clear chest X-ray, but we cannot exclude a very small occult lung primary carcinoma. The kidneys also appeared to be clear, but again an occult renal primary may be possible. Lymphoma is another possibility, but this patient did not have enlarged peripheral lymph nodes. The liver and spleen did not appear to be involved. So at this stage, if it had been possible to obtain a histological diagnosis, treatment was still possible especially if he had a treatable condition, such as lymphoma or even small cell lung cancer. With the use of chemotherapy it is still possible to achieve a remission.

Clinical diagnosis:
Bilateral adrenal metastatic tumours—primary site unknown

Dr Leung's diagnosis :
Bilateral adrenal metastatic tumours—primary site unknown

Pathological discussion

Dr KF To[§]: The subject was a middle-aged man of normal body build with a striking skin rash over the malar, forehead, peri-orbital, and peri-oral regions. There was a small left chest wall scar related to a previous old chest drain site and also a recent abdominal skin biopsy scar. Multiple small abdominal subcutaneous nodules were lipomas. Internal examination confirmed bilateral enlargement of the adrenal glands. The left adrenal gland measured 10 cm in its maximum dimension and weighed 87 grams (Fig 3). The right adrenal gland measured 6 cm in its maximum dimension and weighed 27 grams. Both adrenal glands were diffusely replaced by grey tumour tissue with a fish-flesh appearance and there were areas of haemorrhage. It was difficult to identify any normal residual

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Fig 3. Left adrenal gland showing diffuse enlargement

adrenal gland in the gross specimen. The liver and spleen were enlarged. The liver weighed 2149 grams. The cut surface of the liver had a mottled appearance, and a simple cyst was present. The spleen weighed 294 grams and no obvious tumour was evident. The para-aortic lymph nodes were slightly enlarged. The left lower lobe was consolidated and there was bilateral pulmonary congestion and oedema. All the other organs were grossly unremarkable.

Microscopic examination of the skin biopsy specimen showed epidermal atrophy, sparse superficial perivascular chronic inflammatory infiltrate and pigmentary incontinence. The histological features were those of Poikiloderma which is not a specific histological entity, but is an association with dermatomyositis. Some muscle blocks showed inflammatory myopathic changes. The patient had features of dermatomyositis, which is a cutaneous manifestation associated with underlying malignancy. The adrenal glands were diffusely infiltrated by malignant tumour. High-power microscopy revealed medium- to large-sized atypical lymphoid cells with hyperchromatic, multilobed or clefted nuclei and a scanty to moderate amount of amphophilic cytoplasm. The morphological features were those of non-Hodgkin's malignant lymphoma. However, a striking feature was that these malignant lymphoid cells were confined within the lumina of blood vessels (Fig 4). The lymphoma cells were plugging medium-sized vessels as well as capillaries (Fig 5). In some vessels, the tumour cells had adhered to fibrin and platelets. Only a minority of the lymphoma cells had escaped from vascular lumina and were in the peri-vascular interstitium. The tumour cells were positive for leucocyte common antigen and also positive for B cell markers (L26, 4KB5), and negative for T cell markers (MT1, UCHL1). This indicated a B-cell linkage. The liver, spleen, lymph nodes, and bone marrow were also infiltrated by the lymphoma cells. In the liver, a distinct sinusoidal infiltrate was evident. The splenic red pulp, bone marrow, and lymph nodes were diffusely replaced by the lymphoma cells. In the lungs, there were bronchopneumonic changes in the left lower lobe, and lymphoma cells plugged the septal capillaries (Fig 6). Intravascular involvement by the lymphoma cells was also noted in the heart, pancreas, kidneys, brain, subcutaneous tissue, and skeletal muscle. In the kidney, distinct glomerular capillary involvement was evident.

The overall picture at autopsy confirmed the diagnosis of intravascular lymphomatosis. This is an uncommon non-Hodgkin's lymphoma and most cases, including this case, are of B-cell linkage. It is uncertain why the lymphoma cells are confined to the vascular lumen. One explanation offered is that it may be a homing mecha-

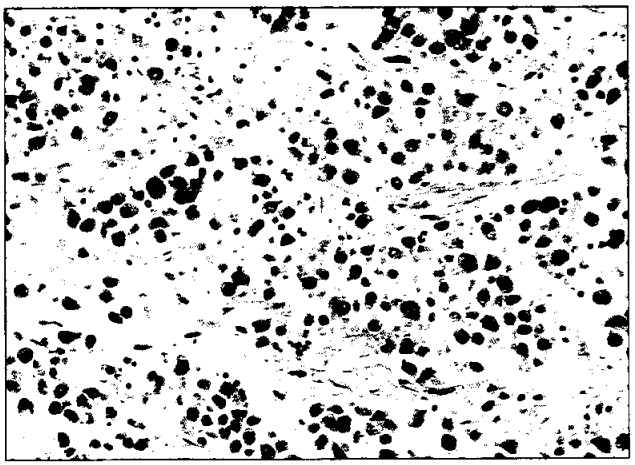

Fig 4. Section of adrenal gland showing lymphoma cells within the lumina of blood vessels (x 100)

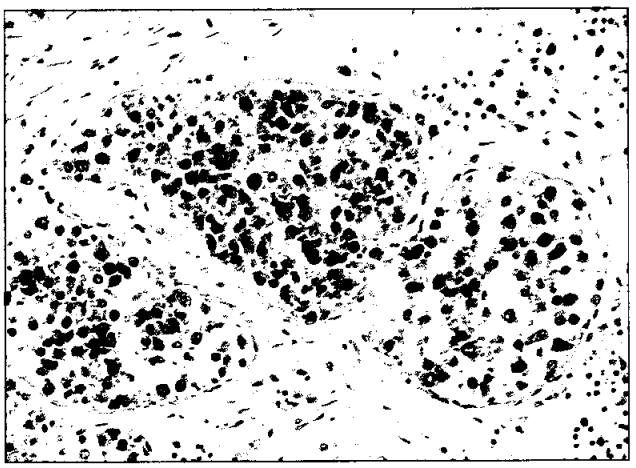

Fig 5. A section showing medium-sized vessels in the adrenal capsule plugged with lymphoma cells (x 400)

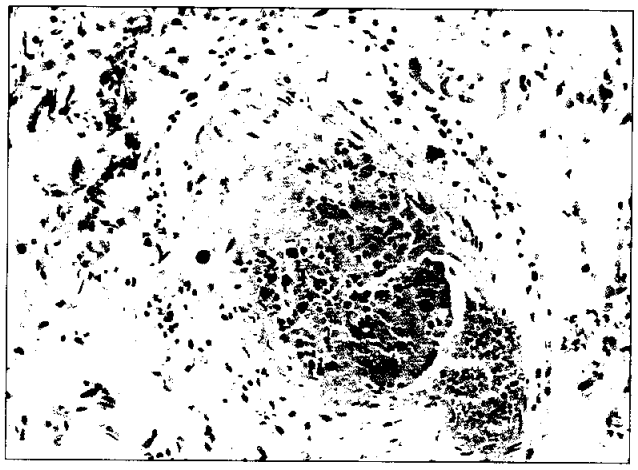

Fig 6. A section of lung showing lymphoma cells associated with thrombi formation (x 400)

nism or that cells are trapped by thrombi.[1]

This lesion was first described by Pfleger and Tappeiner in 1959. At that time, the cellular lineage was uncertain and the condition was designated "angioendotheliomatosis proliferans systemisata". During the following 30 years, the lymphoid nature of the lesion became clear and the term "intravascular lymphomatosis" was recommended.[2-4]

Most patients do have central nervous system and cutaneous involvement and present with neurological or cutaneous symptoms. In this patient, almost all the organs examined revealed lymphoma involvement. However, the skin was not involved and the cerebral involvement was minimal. Also, liver, spleen, lymph node, and bone marrow involvement are unusual, but can be present in the terminal stages.

Prof JCK Lee[‖]: A very interesting story. This is a very uncommon tumour, so do not go away and make such a diagnosis on every patient you see with a fever. However, what is important in this case, is the clinical presentation and how Dr Leung analysed the case. You should learn how to make a differential diagnosis of fever of unknown origin and the various cancers which may cause fever. Any comment from Dr Leung?

Dr Leung: So we have the answer now. I would like to emphasise one thing, this patient had a serious illness and due to a delay in diagnosis he did not receive treatment. He died two months later. Therefore, when you suspect this disease, with all the hallmarks of an aggressive illness, it is important to act quickly, arrive at a diagnosis, and provide treatment.

I just want to briefly talk about the treatment of a non-Hodgkin's lymphoma. Chemotherapy is the main form of treatment. Primary treatment depends on the histological type found, since there is a range of disease, from indolent non-Hodgkin's lymphoma to very aggressive non-Hodgkin's lymphoma, which warrants a different treatment regimen. In the case under discussion, as the patient had a high-grade lymphoma he would probably receive aggressive systemic chemotherapy.[5] The standard chemotherapy regime for non-Hodgkin's lymphoma in this instance is a combination of cyclophosphamide, doxyrubacin, vincristine, and prednisone. The overall prognosis for aggressive lymphoma is an approximately 60% cure rate with combination chemotherapy. Given that the patient had the worst type of non-Hodgkin's lymphoma, combined with his age and also his late stage of presentation, his chance of remission was less.

Prof Lee: I want to raise the question of the clinical diagnosis in this case. I know there was no tissue diagnosis but there must have been a clinical diagnosis.

Dr Chang: When the patient died, the clinical diagnosis was bilateral adrenal metastatic tumours. Lymphoma was a possibility in the background but it was not at that stage confirmed. I think they were uncertain as to the precise nature of the malignancy. As Dr To mentioned, the main problem in this case was the lack of neurological manifestation because in this condition most patients tend to have some neurological symptoms. Also the skin manifestations were not quite typical because one way of obtaining a diagnosis is to take a skin biopsy and to find the tumour cells in the vascular spaces in the dermis. So, this case was a little unusual in that there was an absence of neurological symptoms and skin changes.

Prof Lee: In fact without a tissue diagnosis, it was impossible to give any definitive treatment. The next question I have is for Dr Kew. In terms of trying to arrive at a diagnosis without a tissue biopsy, if, for example, the liver, the adrenals, and possibly the lymph nodes and spleen are involved by lymphoma, are there any radiological studies that would help us to make a diagnosis of lymphoma?

Dr Kew: No lymphadenopathy was identified on

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the single ultrasound examination performed on the patient's first admission. The most common causes of enlarged bilateral adrenal glands are hyperplasia and secondary tumours (which would include lymphoma). The differential diagnosis for bilateral adrenal masses and lymphadenopathy would include secondaries and lymphoma. Tissue biopsy would still be needed as the ultrasound examination is not specific for either disease. If hepatosplenomegaly was also initially seen, lymphoma would be first on the differential diagnosis list.

Prof Lee: So in fact the ultrasound was performed prior to the patient having tumour in the lymph nodes and other organs. I have a question for Dr To. Is this type of lymphoma, which presents first in the adrenal glands, in the vessels and other sites, common?

Dr To: Approximately half of the reported cases do present with various neurological symptoms and approximately one-third present with skin involvement. In contrast to nodal lymphoma, lymph node involvement is usually not prominent. Although bilateral adrenal gland involvement is not the most common presentation, it is not unusual. For instance, in three of fifteen cases reported by Wick, there was gross adrenal gland involvement.[3] Finally, this patient presented with fever of unknown origin and bilateral adrenal masses and this illustrates the wide clinical spectrum of this unusual lymphoma.

Anatomical diagnosis:
Intravascular lymphomatosis with multi-organ involvement; bronchopnemonia; dermatomyositis

Acknowledgement

We would like to thank Mrs MKH Yau for her meticulous secretarial assistance.

References

1. Jalkanen S, Aho R, Kallajoki M, et al. Lymphocyte homing receptors and adhesion molecules in intravascular malignant lymphomatosis. Int J Cancer 1989;44:777-82.
2. Wick MR, Mills SE. Intravascular lymphomatosis: clinicopathologic features and differential diagnosis. Semin Diagn Pathol 1991;8:91-101.
3. Wick MR, Mills SE, Scheithauer BW, Cooper PH, Davitz MA, Parkinson K. Reassessment of malignant "angioendotheliomatosis": evidence in favour of its reclassification as "intra vascular lymphomatosis". Am J Surg Pathol 1986;10:112-23.
4. Demirer T, Dail DH, Aboulafia DM. Four varied cases of intravascular lymphomatosis and a literature review. Cancer 1994;73:1738-45.
5. Di Giuseppe JA, Nelson WG, Seifter EJ, Boitnott JK, Mann RB. Intravascular lymphomatosis: a clinicopathologic study of 10 cases and assessment of response to chemotherapy. J Clin Oncol 1994;12:2573-79.

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HKMJ — Statistics for the first year

The *Hong Kong Medical Journal* is now one year old. Information about the manuscript review process, which may be of interest to past and future authors, is now available for the first year.

a) From 1 November 1994 to 30 October 1995, 86 manuscripts were received by the editorial office. One CPC and one editorial appeared per issue.
b) In total, 24 papers were rejected, which gave a rejection rate of approx 28%.
c) On average, the time taken to acknowledge receipt of a paper was 4 working days.
d) Two papers were rejected outright, which meant that 98% of submitted papers were sent for peer review.
e) In 1995, 60.5% of the papers received were published.
f) Time to final decision being relayed to authors: for those not peer reviewed and not accepted = 6 weeks; for those that were peer reviewed = 12.5 weeks.
g) The number of reviewers currently being used = 73.
h) At the end of September 1995 there were 5129 listed readers of the journal.
i) Time taken to forward reviewer's comments to authors = 7 weeks.

The editors of the *Hong Kong Medical Journal* thank you for your support during the past year and look forward to your continued interest in the Journal throughout the coming year.