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Feature Articles

An Unusual Case of Haematuria

Jim Cassidy and Stanley B. Kaye

A 40-YEAR-OLD MAN presented with a 3-month history of painless haematuria. He had been tetraplegic from the age of 21 following a road traffic accident, and had a neurogenic bladder with frequent episodes of urinary infection. He was otherwise well with no history of weight loss and no symptoms referable to the respiratory or cardiovascular systems. He was a life-long non-smoker, lived with his wife and an adopted daughter. Despite his disability he was in full-time employment as a bank clerk. He had no prior exposure to chemicals or asbestos, and at presentation was taking only muscle relaxants for lower limb spasms.

Examination on referral revealed that he was tetraplegic in keeping with his history of cervical trauma. He was otherwise well with no evidence of weight loss and no palpable lymphadenopathy. Examination of the chest and abdomen revealed no abnormality. At presentation he had an indwelling urinary catheter.

His full blood count was normal, but routine biochemistry revealed the following abnormalities; sodium 124 mmol/l [normal range (NR) 135–144] chloride 89 mmol/l (NR 97–108), creatinine 59 μmol/l (NR 60–110), calcium 2.19 mmol/l (NR 2.20–2.65) with a normal serum albumin at 37 g/l. Liver transaminases, gamma glutaryltranspeptidase and bilirubin were all within normal limits. Chest X-ray was normal and urinary cytology was uninformative.

An intravenous urogram and cystogram was performed which revealed some clubbing of the renal calyces with loss of cortex but the appearances had not deteriorated in comparison with a prior examination some 5 years ago. The bladder had a typical neurogenic appearance with marked wall thickening but no space-occupying lesion could be demonstrated, even after direct introduction of contrast to the bladder via the urinary catheter.

Correspondence to J. Cassidy.
The authors are at the Department of Medical Oncology, Beatson Oncology Centre, Western Infirmary, Glasgow G11 6NT, U.K.
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He then proceeded to cystoscopy which revealed a white lesion occupying the dome of the bladder. Biopsies were taken which revealed infiltration of the bladder wall and muscle by a undifferentiated small cell carcinoma. Histologically this was indistinguishable from bronchial small cell carcinoma. Staining for gonadotrophins was negative, no other special stains were used. Tumours of this type are rare but can occur as primary bladder carcinoma and carry a poor prognosis [1]. In histological appearances they are indistinguishable from small cell bronchial carcinoma, and tend to behave in a similarly aggressive manner. Ectopic hormone production has been recorded [2, 3]. The pathological diagnosis prompted the performance of an isotope bone scan which was normal, and a computed tomography (CT) scan of abdomen and pelvis. The CT appearances of the lung and mediastinum were normal. The bladder was seen to be contracted with tumour infiltration through the wall; there was evidence of bilateral involvement of the lymphatics of the external and common iliac chains. The appearance of the kidneys was in keeping with chronic pyelonephritis. No other abnormality was seen.

Our current treatment policy in "good prognosis" bronchial small cell carcinoma is intensive combination chemotherapy followed by consolidation radiotherapy to the chest. Therefore, we decided to adopt a similar treatment for this patient. We anticipated that myelosuppression may be very troublesome in view of our experience with this regimen and because of his chronic bladder infections we were concerned that this might further compromise his tolerance of therapy, we therefore chose to use doses around 25% lower than in lung cancer patients. Bone marrow was not performed as this is not currently part of our staging policy for bronchial small cell carcinoma. He was commenced on ICE (ifosfamide 5 g/m^2, mesna 8 g/m^2, carboplatin 300 mg/m^2, etoposide 150 mg days 1 and 2 intravenously and 300 mg orally on day 3, all given in a 4-week cycle), with continuous administration of a co-trimoxosole (two tablets twice daily) as prophylaxis of neutropenic septicaemia. On day 12 he was readmitted with a fever over the preceding 24 h. On

admission he was found to be profoundly neutropenic with a total white cell count of 0.4 and no neutrophils seen on a blood film. He was also thrombocytopaenic with a nadir platelet count of 7×10^9/l. He was treated with intravenous broad spectrum antibiotics and platelet transfusion. Serial blood cultures and urine culture failed to detect a causative organism but his condition improved with recovery of haematological indices by day 17.

At cycle 2 the total dose of all agents was reduced by 10% and severe neutropenia was avoided. A repeat CT scan of abdomen and pelvis on the day prior to the planned start of cycle 3 showed complete resolution of the pelvic lymphadenopathy and therefore it was decided to give another two cycles of ICE. Cycle 3 was again complicated by an episode of neutropenic septicaemia, and thrombocytopaenia requiring admission and administration of intravenous antibiotics and platelets. As before, no organism was identified on bacteriological investigation. Accordingly, for the fourth and final cycle of chemotherapy the total doses of drugs were reduced by a further 10%.

A CT scan 1 month after completion of chemotherapy revealed no abnormality in the pelvis and confirmed resolution of the previously noted lymphadenopathy. A repeat cystoscopy was performed and showed no evidence of residual tumour within the bladder. Bimanual examination was also normal.

In view of this encouraging response to chemotherapy he went on to receive consolidation radiotherapy at a dose of 4500 cGy in 20 fractions as a four field technique to the bladder itself. It was felt that treatment of the whole pelvis (that is the potential lymph node bearing area) was not feasible in view of the need to minimise radiation reaction of the bowel and skin. He did develop some diarrhoea but this settled on codeine phosphate.

He completed therapy 2 months ago and is currently well at home and has returned to full-time occupation.

DISCUSSION

Tumours with the histological appearance of carcinoma of the bronchus can arise in other organs. In this patient it seems unlikely in view of the non-smoking history and normal chest X-ray and CT that the bladder tumour was a metastatic manifestation of a bronchial tumour. It is of some interest that he initially had biochemical disturbances in keeping with inappropriate antidiuretic hormone production. Although we chose not to investigate this further it did resolve with effective antitumour therapy which is strong circumstantial evidence that the tumour was producing ectopic antidiuretic hormone. The prevalence of ectopic hormone production in this tumour and in small cell carcinoma of the prostate [4] suggests that these tumours derive from neuroendocrine or amine precursor uptake and decarboxylation (APUD) cells, but as in small cell lung cancer, the precise cellular derivation is uncertain.

Our ICE protocol for small cell lung cancer is known to be effective in inducing remissions in a high percentage of patients with that disease, but is also associated with profound myelosuppression. As expected we did encounter some problems in this respect with this patient, which proved to compromise the dose intensity of chemotherapy that we could actually deliver. One could argue that haematological support using granulocyte colony stimulating factor (CSF) or granulocyte/macrophage CSF may have been appropriate. Despite this reduction in planned chemotherapy dose he did achieve a complete response as judged by CT imaging and cytoscopy with examination under anaesthetic. His tetraplegic state also compromised the ideal treatment volume for consolidation radiotherapy. The (scarce) literature on small cell bladder carcinoma suggests that this is an aggressive tumour not unlike small cell lung cancer in biological behaviour. We could find only one other report of combined radiotherapy and chemotherapy in this disease. In this report patients receiving the combined approach survived longer than those not treated in this manner (78% died at mean follow-up time of 9.4 months). It, therefore, appears that combination chemotherapy may be of benefit in this rare tumour type [5].

Small cell carcinoma of the prostate is a more common entity with similar biology which responds to multi-agent chemotherapy but because of generally late and abnormal presentation carries a very poor prognosis [6].

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Towards an International Register of Cancer Trials: The UKCCCR Register of U.K. Trials

INTRODUCTION

THE UNITED KINGDOM Coordinating Committee on Cancer Research (UKCCCR) is currently developing the UKCCCR Register of U.K. Cancer Trials, covering all phase II and phase III randomised trials. The register is stored as a computer data base that will be made available to clinicians for interactive access [1]. Other European countries are planning to develop similar registers, and the UKCCCR register is expected to become an integral part of the European register of cancer trials that has been proposed under the auspices of the