Correspondence

Mature renal teratoma and a synchronous malignant neuroepithelial tumour of the ipsilateral adrenal gland

The main problem associated with renal neoplasms is the potential for metastatic disease. Renal cell carcinoma, angiosarcoma, and nephroblastoma are the most common renal tumours. Other primary renal neoplasms include primitive neuroectodermal tumour (PNET), embryonal tumour of metanephric blastemal derivation, which often contains diverse epithelial and stromal tissues. Diagnostic problems are often encountered when tumours contain a variety of heterologous elements. It is this variant that can be confused with a teratoma. Renal teratomas are rare and most have been dismissed as cases of teratoid nephroblastoma or retroperitoneal teratomas secondarily invading the kidney. The differentiation between these two neoplasms in the kidney is often problematic.

Neurogenic tissues in the kidney can be found in primary tumours or as part of metastatic tumours. The primary tumours are nephroblastoma, which may contain ganglion cells, neuroblast, and neuroglial tissue, and PNET. Adrenal neuroblastomas can directly invade the adjacent kidney. We describe the pathology of a right renal mass in a 3 year old child and discuss the differential diagnosis.

A 3 year old girl presented with abdominal pain and diarrhoea. On examination she was found to have signs of pulmonary tuberculosis and was started on antituberculous treatment. Subsequently, a large, firm, tender, right flank mass clearly separate from the liver was detected and she was referred to the Regional Paediatric Surgical Unit for further investigation and management.

On admission, the child was apyrexic, emaciated, and weighed 13 kg. She had bilateral coarse cracks and a wheeze. The abdomen was distended and a non-tender 3 cm hepatomegaly was palpated. Furthermore, a 10 × 12 cm non-tender, firm, non-pulsatile right flank mass was detected.

Results of routine laboratory tests were as follows: haemoglobin, 90 g/litre (normal, 112–143); white blood cell count, 8.2 × 10⁹/litre (normal, 5.5–15.5); and platelet count, 224 × 10³/μl. Urinary catecholamine values were as follows: normetanephrine, 0.279 μM/mM creatinine (CRT) (normal, 0–0.08); metanephrine, 0.023 μM/mM CRT (normal, 0–0.035); dopamine, 0.67 μM/mM CRT (normal, 0–1.13); vanillylmandelic acid 9 μM/mM CRT (normal, 0–1.5); and homovanillic acid, 11 μM/mM CRT (normal, 0–15). Renal and liver function tests were normal.

Computed tomography (CT) scan of the abdomen revealed a large tumour involving the right side of the abdomen. There were also multiple hepatic lesions consistent with metastases. A fine needle aspiration biopsy of the mass was performed. After a cytological diagnosis of neuroblastoma the child was started on the appropriate chemotherapy protocol consisting of vincristine, actinomycin, cyclophosphamide, and adriamycin. She suffered seizures while on chemotherapy, which was subsequently decreased to 75% dosage. A CT scan of the brain was normal. The child died two weeks after commencement of chemotherapy. A necropsy was performed.

Necropsy revealed an enlarged right kidney measuring 16 × 10 × 8 cm and weighing 1200 g. There was a well demarcated tumour mass in the upper pole of the kidney, which measured 7 × 6.5 × 5 cm (fig 1). The upper pole mass was encapsulated (fig 1; arrows), predominantly firm in consistency, and had yellow and white areas. There was a small area of soft, friable tumour present within the mass, close to the junction of the adjacent kidney. On the capsular surface the upper pole mass was clearly demarcated from the remaining kidney. It was not possible to recognise normal renal tissue because the remaining kidney was diffusely swollen, pale, soft, and contained focal areas of necrosis (fig 1). The right adrenal gland was not identified despite serial sectioning. There was extension of the tumour into the right renal vein and inferior vena cava. Tumour spread into the ureter was also observed. There were multiple greatly enlarged para-aortic lymph nodes containing metastatic tumour. Metastatic tumour deposits were present in the liver, vertebrae, and both lungs. In addition, caseous nodules were identified in the lungs and hilar lymph nodes. The left kidney and adrenal gland were normal. The rest of the postmortem examination was normal.

Histological examination of the well demarcated upper pole mass showed a tumour composed of multiple heterologous tissue elements. Tissues derived from all three germ layers—ectoderm, mesoderm, and endoderm—were present. The yellow areas corresponded to mature adipose tissue microscopically. In addition, striated muscle, smooth muscle, and fibrous tissue were present, as were small islands of neuroglial tissue. The epithelial component was variable and consisted of small tubular structures lined by cuboidal epithelial cells with clear cytoplasm. Also present were larger cystic structures lined by respiratory epithelium. Adjacent to these cysts were small closely packed acini composed of mucin containing epithelium. A prominent feature was the presence of several cysts lined by keratinising stratified squamous epithelium with hair follicles and hair shafts (fig 2). Small round tumour cells diffusely infiltrated the remaining kidney. These were arranged predominantly in solid sheets, but focal neuroectodermal canals and rosettes were also identified (fig 3). In addition, there was microscopic evidence of metastases in the lungs, liver, ovaries, and vertebrae. The metastatic tumour in all sites consisted of the primitive small, round cell component. Sections taken from the region of the right adrenal gland showed a diffuse infiltrate of small round blue cells, but no residual adrenal gland tissue was identified. There were no nephrogenic rests in the kidney.

A panel of immunohistochemical stains was performed on the small cell malignant tumour to detect cytokeratins (AE1/AE3, CAM5.2), synaptophysin, neurone specific enolase (NSE), chromogranin, WT1, desmin, muscle specific actin, S100 protein, glial fibrillary acidic protein, O13, leucocyte common antigen, and epithelial membrane antigen. The small round cells showed immunoreactivity for NSE, synaptophysin, and chromogranin. The cells were non-reactive for the remaining markers.

Histology confirmed tuberculosis of the lungs and lymph nodes. Acid fast bacilli were identified. To diagnose a renal teratoma, the primary tumour should be unequivocally of renal origin and the tumour should exhibit unequivocal heterotopic organogenesis clearly recognised as evidence of attempts to form organs other than the kidney. It is the second criterion that often presents a problem. The question is: what constitutes unequivocal organogenesis? The presence of bone, cartilage, muscle, fat, neuroglial tissue, and mature epithelium cannot on their own be regarded as
evidence of organogenesis. Indeed, all of these tissues can be present in both teratomas and teratoid nephroblastomas. In mature teratomas, skin with the dermal appendages, bronchial structures with bronchial glands and cartilage, brain (neuroglial tissue), and teeth are commonly present, and regarded as evidence of organogenesis.

Those nephroblastomas that are characterised by the presence of neuropil and ganglion cells can be readily differentiated from PNET. It is the undifferentiated nephroblastoma, in which neuropil and ganglion cells are sparse or absent, that is sometimes difficult to differentiate from PNET. The immunohistochemical profile and cytogenetic data are helpful in this instance. PNET characteristically demonstrates diffuse membrane positivity with O13 (mic2 gene product) and is also immunoreactive for vimentin, cytokeratin, and NSE.¹ Another highly characteristic feature of PNET/Ewing’s sarcoma is the presence of a specific reciprocal translocation: t(11;22)(q24;q12).²

Our case presents a unique constellation of pathological features, which pose a diagnostic problem. The cell circumscribed and encapsulated upper pole mass could be interpreted either as a renal teratoma or a teratoid nephroblastoma. After much deliberation and consultation, we prefer the diagnosis of a primary intrarenal teratoma. Most of the heterogeneous elements can as, alluded to earlier, occur in a nephroblastoma. The presence of hair shafts is evidence of terminal differentiation, which is seen in teratomas. Although structures resembling hair follicles have been described in nephroblastoma, to the best of our knowledge, hair shafts have not been described in nephroblastoma.

The small round cell tumour presents a more difficult problem. We have documented neural differentiation in these cells with immunoreactivity to NSE, synaptophysin, and chromogranin. It is also quite clear on morphology and immunohistochemistry that this component represents a malignant neuroepithelial tumour. The latter is probably an undifferentiated nephroblastoma arising in the adrenal gland and invading the kidney, mainly along the hilum.

Our case posed a problem often faced by pathologists who regularly examine renal tumours in children. Furthermore, it highlights the need for a refinement of the diagnostic criteria for renal teratoma. We believe that the differentiation between these two neoplasms must lie in their respective genetics. For example, deletion of the short arm of chromosome 11 should favour a nephroblastoma; whereas a renal teratoma would be detected by the presence of nephrogenic rests.

We thank Professor LP Dehner, St Louis, USA for reviewing the histology.

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the cost effectiveness of a practice for which there are no current grade A recommenda-

tions.

The important issue that Dr Murphy raises relates to why thrombophilia tests are per-
formed; are they to explain why an individual develops thrombosis or when the discriminating approach suggested by the 1990 guidelines quoted by Dr Murphy will increase the proportion of tested patients who are found to have a laboratory abnormality. However, testing is performed to optimise clinical decisions when there is no rational basis for such a recommendation given the data that are currently available. There is no evidence that the predictive value of thrombophilia testing is in any way superior to that in the categories of patients outlined above to that in other patients with venous thromboembolism. For example, a patient with a first event after the age of 45 years in the absence of a family history might still be at risk of recurrence in the future. Therefore, the issue is whether testing patients with venous thromboembolism for laboratory evidence of thrombophilia has predictive value. The presence of a raised titre of anticardiolipin antibodies indicates a higher risk of early recurrence and therefore might be considered an indication for continued anticoagulation (grade B). Because the lupus anticoagulant activity is also indicative of antiphospholipid activity it might also be considered an indication for continued anticoagulation. The predictive value of testing for heritable thrombophilia is becoming clearer as I indicated in my leader. There is no evidence to support a higher intensity or extended duration of anticoagulation in most patients with laboratory evidence of heritable thrombophilia; those patients might be patients with the homozygous or combined heterozygous defects (grade B). In my own practice I find testing valuable for assessing risk in family members, particularly female patients who are considering pregnancy or oestrogen/progestagen contraceptive pill use. If a thrombophilic defect has been detected in the symptomatic index family member then that specific defect may be looked for in the relatives who are requesting counselling. This obviates the need for an expensive comprehensive screen in all of the family members and avoids confusion as to whether an abnormal result is relevant or not.

Like all clinicians responsible for the judicious use of scarce health care resources Dr Murphy has to decide whether thrombophilia test results influence his clinical practice. If they do not then there is no necessity to do them.

BAGLIN

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Illustrated Pathology of the Spleen by Bridget Wilkins and Dennis Wright is a beautiful book. It is a pleasure to hold it and browse through it because of its size, layout, and the quality of the print and figures. But that is only the exterior. At least equally important is the contents. These match the style.

The authors aim with this book to demystify the spleen, putting forward a systematic, analytical approach to the interpretation of splenic pathology. The authors succeed by using numerous illustrations and the book is indeed a combination of an atlas and a textbook.

The book is well written and very readable. Most textbooks are reference works where one can look up a specific problem. This book is also a guide. The problem with splenic pathology is where to start and what to look for. The first two chapters ("Introduction" and "Normal structure, development and functions of the spleen") serve as a firm basis on which the approach to the pathology of splenectomy specimens is built. The last chapter ("Summary: some key points in splenic differential diagnosis") provides an easy approach for some common situations. These three chapters include about 50 pages of text and illustrations and the evening it will cost studying them is a worthwhile investment. The other chapters deal with the disorders expected in the spleen, such as haematopoietic and infectious diseases, but there is also a chapter on post-traumatic and incidentally removed spleens, illustrating the practical approach of the authors.

Are there no complaints? Of course there are a few points that can be made. Not all of the illustrations are perfect; for instance, splenic marginal zone lymphoma, a difficult to recognise lymphoma is not very well illustrated, especially the low power figure, which is not very informative. The references are well chosen, run into 1998, but the number is rather low. The importance of plasmacytosis ("splenitis") is not described. Nevertheless, the value of the book clearly outweighs these remarks and the book is recommended for each practising pathologist who occasionally is confronted with splenic pathology and feels uncomfortable when there is histology that does not look familiar.

AVARGAS


This book is introduced as being "suitable for cytogenetic technologists and clinicians alike", and at first glance, appears to provide a comprehensive overview of all aspects of clinical cytogenetics. However, on closer examination, the book is a rather curious mixture of information. The introductory chapters are perhaps the most confusing. The overview of the biochemistry of genetics is brief, to the point that oftentimes a reader is left without a full understanding of the processes of replication, transcription, and translation to understand the chapter, thereby rendering it largely surplus to requirements. The chapter on chromosome nomenclature and the current nomenclature of chromosome 21 truncation of the Paris ISCN and because the authors are only too happy to refer the reader to suitable manuals for laboratory methodology, it would seem appropriate to do so for this topic also. There is a general lack of cohesion about the book, almost as though none of the chapters had any knowledge of the contents of the other chapters. That said, several of the chapters on clinical cytogenetics provided very useful discussions and several included comprehensive tables of data pooled from various sources to give an easily manageable reference for aetiology of several classes of chromosome disorder. The chapters on cancer genetics, although in its presentation of tumour specific breakpoints, fails to expand on the specific biochemical and genetic results of the rearrangements specified. I felt that this was particularly remiss in the present climate of molecular genetic discovery, because only a few well selected and well described examples would be necessary to whet the reader’s appetite for further discovery. The reader should also be aware that the book is marred by shoddy proofreading. Diagrams are

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mislabelled, and typographical errors are frequent and often misleading—in the chapter on chromosome nomenclature several examples are given using a chromosome band that does not exist. Overall, I found the book to be a useful aide memoire for several topics, and although perhaps an expensive luxury for the individual, I would recommend the book as an addition to any laboratory or hospital library.

B HOLLAND


In the UK between January 1989 and December 1999 there were 164 279 reports to the Communicable Disease Surveillance Centre of cases of gastroenteritis caused by rotaviruses—an average of 14 934 each year. Rotaviruses were discovered in animals in the early 1960s and in humans in the early 1970s. For several years, electron microscopy was the only widely available method used for diagnosing infection. Since the early 1980s, molecular, serological, and cell culture methods have come into use and fruitful research on these important pathogens has resulted. This excellent new book provides detailed protocols for these methods.

The central chapters begin with an up-to-date review of the relevant field, all of which are clearly written, informative, and excellently referenced. The editors have provided a short, but introductory chapter aptly titled “Basic facts”. In a chapter contributed by BV Venkataram Prasad and Mary Estes, on electron cryomicroscopy and computer image processing techniques, the structure–function studies of rotaviruses are beautifully illustrated with computer-generated three dimensional reconstructions of rotavirus particles. A chapter by Mary Ramsay and David Brown describes the epidemiology of rotavirus infections and concentrations on surveillance and the, surprisingly high, disease burden caused by rotaviruses. The other chapters, all of which are of the same high standard, include rotavirus replication, cell entry, genetics, immunology, animal models, serotyping, and genotyping.

G BEARDS

CD-ROM review


This CD ROM of stomatology-ENT is a reference image database of the field of ENT. It is in English and in French. It contains macroscopic and histopathological pictures of the main lesions in the field of oral pathology and ear, nose, and throat pathology. Clinical, radiological, cytological, immunohistochemical, or ultrastructural pictures of some of these lesions are present. Indeed, this CD ROM contains a large number of pictures of most lesions in this area. The images of interest are very easy to find using a list or keyword driven search. The quality of the photographs is variable; most of them are sharp, but others are not always focused or are very dark. The data sheet contains all relevant information about the picture but this information is often scanty. However, additional information about different lesions is supplied by separate text slides. There are three fields containing a selection, image, and database window. It is a nuisance that the database window stays on the screen when another program (such as Word or PowerPoint) is used. The program is easy to use and it is very easy to copy the pictures to PowerPoint slides for use in presentations. In addition, they can be copied to a photo editor (such as Photoshop) so that the pictures can be edited.

In conclusion, this CD ROM contains a wealth of photographic material, which can be used for diagnostic or educational purposes. The layout, however, could be improved.

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Haematological Morphology and Leukaemia Classification for Cytogeneticists

29 March 2001, St Mary’s Hospital, London, UK

Further details: The Academic Secretary, Department of Haematology, St Mary’s Hospital Campus of ICSM, Norfolk Place, London W2 1PG, UK. (Fax +44 020 7262 5418)

6th European Forum on Quality Improvement in Health Care

29–31 March 2001, Bologna, Italy

Further details: BMA/BMJ Conference Unit, BMA House, Tavistock Square, London WC1H 9JR, UK. (Tel +44 020 7383 6409; fax +44 020 7383 6869; email Quality@bma.org.uk; website www.quality-bmj.com)

Diagnostic Histopathology of Breast Disease

23–27 April 2001, Hammersmith Hospital (Imperial School of Medicine), London, UK

Further details: Wollstone Conference Centre, Hammersmith Hospital, Du Cane Road, London W12 ONN, UK. (Tel +44 020 8383 3117/3227/3245; fax +44 020 8383 2428; email wcc@ic.ac.uk)

Gynecologic and Obstetric Pathology

26–29 April 2001, Fairmont Copley Plaza, Boston, Massachusetts, USA

Further details: Department of Continuing Education, Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA. (Tel +1 617 432 1525; fax +1 617 432 1562; email hms-cme@hms.harvard.edu)

BSCC Northern Spring Tutorial: Gynaecological Cytology

8 March 2001, Manchester, UK

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Urological Surgical Pathology for the Practising Pathologist

24–26 March 2001, Sanibel Harbour Resort and Spa, Fort Myers, Florida, USA

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Diagnostic Consultation on the Diagnosis of Noninvasive Urothelial Neoplasms

11–12 May 2001, University of Ancona School of Medicine, Torrette, Ancona, Italy

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BSCC Annual Scientific Meeting

9–11 September 2001, Majestic Hotel, Harrogate, UK

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Calendar of events

Full details of events to be included should be sent to Maggie Butler, Technical Editor JCP, The Cedars, 36 Queen Street, Castle Hedingham, Essex CO9 3HA, UK; email: maggiebutler@pilotree.prestel.co.uk

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Haematology Morphology

26–27 March 2001, St Mary’s Hospital, London, UK

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Histopathology of the Bone Marrow

28 March 2001, St Mary’s Hospital, London, UK

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