CASE REPORT

METANEPHRIC ADENOMA: CASE REPORT AND REVIEW OF LITERATURE

SHAHIDA NIAZI, MADIHA ARSHAD, NASIR KARIM AND M. H. BUKHARI
Department of Pathology, King Edward Medical University, Lahore – Pakistan

ABSTRACT
Metanephric Adenoma (MA) is a histologically and clinically unique and rare benign renal epithelial tumour. Only a few reports are found in literature regarding this novel tumour entity. We report this neoplasm in a 40 – year old male who presented with flank pain and microscopic haematuria. USG and operative findings were suggestive of Renal Cell Carcinoma. Microscopic examination showed a tumour composed of small bland cells forming small tubular structures in an acellular stroma. Occasional papillary formations were also seen but no blastema was identified. The case was finally diagnosed as Metanephric Adenoma. It has a histological similarity to developing metanephric tubular epithelium and is considered to represent the benign counterpart of Wilms' Tumour. The unique pathological features of Metanephric Adenoma should be recognised because of its invariable indolent clinicobiological behaviour.

INTRODUCTION
Metanephric Adenoma (MA) also designated “Nephrogenic adenoma” or “Embryonal adenoma” is a rare benign renal tumour which is histologically, immunohistochemically and clinically unique, with an indolent clinicobiological behaviour.\(^1,2\) It accounts for only about 0.2% of adult renal epithelial neoplasms with only 130 well documented cases reported in world literature.\(^3\) Origin of this renal mass from persistent primitive metanephric epithelium of the proximal nephron is postulated and partly substantiated.\(^1,2\) Histologically this tumour seems to be related to epithelial Wilms’ Tumour and Nephrogenic Rests and in fact these lesions may coexist.\(^4,5\)

MA occurs predominantly in middle aged females but well documented cases have been reported in children.\(^5,9\) Usually these tumours are asymptomatic and discovered incidentally on investigation for other problems.\(^5,6,9-11\) Symptoms when present include an abdominal mass, flank pain, microscopic haematuria, hypertension and fever.\(^5,12\) About 12% cases of MA are responsible for producing the paraneoplastic syndromes like polycythaemia and hypercalcaemia.\(^5,7\) Radiologically and morphologically these tumours are frequently solid, well circumscribed, calcified and hypovascular.\(^3,12\) From the clinical and diagnostic viewpoint the importance of this tumour depends on differentiating it from nephrogenic rests (nodular renal blastema), epithelial Wilms' tumour, solid papillary renal cell carcinoma and metastatic cancers.\(^5,7,13\) Recognition of this tumour as benign is of utmost importance as conservative tumour resection with organ sparing surgery is sufficient in almost all cases.\(^5,12\)

CASE REPORT
A left nephrectomy specimen of a 40 year old male was referred from the Urology Ward of Mayo Hospital, Lahore to the Department of Pathology, King Edward Medical University, Lahore. The patient had a history of pain left lumbar region and microscopic haematuria for the last 6 months. Abdominal USG findings reported a solid, well circumscribed renal tumour occupying the mid region of the left kidney measuring 5 x 4 x 4.5 cm with the provisional diagnosis of renal cell carcinoma. The right kidney was completely normal. A left radical nephrectomy with removal of the perinephric fat was performed.

Gross examination and sectioning of the renal specimen revealed a well circumscribed white, solid, encapsulated tumour measuring 4 x 4 x 3 cm occupying the central portion of the left kidney. There was no extension of the tumour into the renal vein, Gerota’s fascia or surrounding renal parenchyma. On histological examination post-graduate residents diagnosed the tumour as a round blue cell tumour consistent with the diagnosis of Wilms’ Tumour. The tumour comprised of small, round, uniform dark staining cells forming small acinar and tubular structures with focal areas showing papillary formations. Individual tumour cells had no pleomorphism and no mitosis. Blastema component was not seen. Tumour was surrounded by a distinct well defined fibrous capsule. The case was diagnosed and confirmed as metanephric adenoma.
METANEPHRIC ADENOMA: CASE REPORT AND REVIEW OF LITERATURE

Fig. 1: Low power microscopic image showing the sharp demarcation of the tumour from the surrounding renal parenchyma. The tumour cells are small, hyperchromatic forming small acinar / tubular structures.

Fig. 2: Higher magnification showing the tumour composed of small, round to oval acinar structures separated by scant stroma. Individual tumour cells are bland with hyperchromatic nuclei and scant cytoplasm.

DISCUSSION

In embryonic life the kidney develops from the metanephric blastema. If remnants of this tissue remain within the renal parenchyma in post natal life, they often develop into Wilms’ tumour or rarely into metanephric adenoma.6 Thus Wilms’ tumour and metanephric adenoma are histogenetically related and MA is considered to be the benign counterpart of Wilms’ tumour in adults.4,6,14 Since they arise from the same precursor tissue, metanephric adenoma and Wilms’ tumour may sometimes co-exist and adequate histological sampling is essential to differentiate between the two tumours.4,6 Histologically metanephric adenoma is also very similar to the metanephric hamartomatous element of nephroblastomatosis.5

MA was first described in 1979 by Bove et al.2 in a 7 -year old boy and he proposed an origin of this tumour from the persistent primitive epithelium of the proximal tubule of the nephron which had failed to mature adequately. Pages and Granier6 proposed the name “Nephronogenic nephroma” for this tumour in 1980. Since that time about 130 cases have been reported in world literature.3 The largest series of this rare tumour was published by Davis and colleagues5 in 1995 who reported on 50 Metanephric Adenomas during a 22 – year period from the retrieved files of the Armed Forces Institute of Pathology, Washington DC. This study included 36 females and 14 males (F:M ratio = 2.6:1) with the histological diagnosis of MA. Patients ranged in age from 5 to 83 years. MA was detected incidentally in 20 patients (40%) and 6 patients (12%) had polycythaemia. Presenting complaints included abdominal / flank pain in 11 patients (22%), haematuria in 5 patients (10%) and a palpable mass in 5 patients (10%). Preoperative radiological examination of these tumours demonstrated calcifications of 44% cases.

Regarding age and sex distribution, metanephric adenomas occur mostly in young and middle aged females but cases have also been reported in children and adolescents.8,9,14 Liniger16 reported this tumour in a 15-month old boy, the youngest patient yet to be reported with MA. Loeser and friends8 reported MA in the left kidney of a 2 – year old girl. In both cases, successful tumour resection with nephron sparing surgery was performed. A close association between polycythaemia and hypercalcaemia has been reported in adults and children with MA.5,7,17 A recent cell culture study by Yoshioka and co-workers18 in Japan proved that MA cells produce erythropoietin and other cytokines which may be responsible for the high incidence of erythrocytosis in these patients.

Most imaging studies describe MA as a solid, well circumscribed, hypovascular tumour with frequent calcifications as a rather characteristic diagnostic feature.3,12,19 A study by Bastide and coworkers3 analysed and reviewed the clinical and radiological features of 9 patients with MA. Six patients were discovered incidentally, 2 had microscopic haematuria and 1 had polycythaemia. Preoperative imaging showed all MA’s to be well circumscribed, solid with no vascular flow within the tumours on colour Doppler USG, and frequent calcifications were seen in 6 tumours. However, Patankar20 reported a cystic MA measuring 12 × 5 cm surrounded by a fibrous cyst wall.

Morphologically MA is a solid, well circumscribed, tan pink to gray cortical tumour surrounded by
a fibrous capsule with no extrarenal extension.\(^1,3,6,7\)
Unlike renal papillary adenomas which are by definition less than 5 mm in diameter MA can grow to a large size.\(^12\) Bouzourene \(et \ al^1\) reported the largest MA measuring 20 × 19 × 15 cm. Other studies report variable size dimensions of this tumour. In the largest study on 50 MA's reported by Davis\(^{13}\) the tumours measured from 0.3 cm to 15 cm (mean 5.5 cm) in size. In Jones \(et \ al^6\) on 7 patients, size of MA's ranged from 0.6 to 8 cm and in a case report by Yaqoob\(^19\) at Aga Khan University, Karachi the tumour measured 10 × 8 cm and was largely haemorrhagic and necrotic. Many MA's are mistakenly diagnosed as renal cell carcinoma on gross morphology and imaging studies and total nephrectomies are performed.\(^5,10,11\) Histopathological examination of MA, often prompts an initial diagnosis of Wilms' tumour (as was experienced in our case as well) as both lesions show cellular areas composed of small uniform, round blue epithelial cells forming small acinar and tubular formations in an acellular stroma.\(^37\) Glomeruloid bodies composed of lobulated papillary projections are seen focally and blastema is consistently absent in MA.\(^5,13,14\) Individual tumour cells are bland, with rounded to ovoid nuclei having delicate chromatin, absolutely no pleomorphism or mitosis and scanty cytoplasm.\(^6,11\) Frequent calcifications in the form of psammoma bodies or dystrophic calcification may be present.\(^5,13,19\) Distinction from epithelial Wilms' tumour, nephrogenic rests, the solid variant of papillary renal cell carcinoma and metastatic thyroid carcinoma can be difficult.\(^3,4,7,9,10,13\) Both nephrogenic rests and Wilms' tumour on microscopy contain a blastema component whereas MA has no primitive blastema.\(^5,4,14\) On immunohistochemistry (IHC), MA's are focally positive for CK- and strongly and diffusely positive with antibodies to WT, and CD\(_7\), as are maturing Wilms tumours and nephrogenic rests.\(^1,4\) Papillary renal cell carcinoma has fibrovascular cores containing foamy macrophages and lined by larger cells with pleomorphic nuclei, whereas MA lacks true fibrovascular cores and has bland uniform cells.\(^13\) In the distinction from metastatic thyroid cancer clinical information and immunohistochemical study of TTF-1 may provide assistance.\(^13\)

Almost all MA's follow a favourable, benign clinical course with no metastasis and recurrences.\(^1,5,6\) However Renshaw\(^22\) presented the only reported case of metastatic MA to the regional lymph nodes in a 7 – year old child but no deaths related to the tumour have been reported so far. The unique features of metanephric adenoma should be clinically and pathologically recognised because of its invariably benign course and treatment with conservative local resection.

ACKNOWLEDGEMENTS
The authors acknowledge the V.C of KEMU for providing the facilities to do this work and the Professor of Pathology for encouraging us.

REFERENCES