Metanephric Adenoma: A Rare Benign Tumour of the Kidney: Case Report

Metanefrik Adenoma: Böbreğin Nadir Görülen Benign Tümörü

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ÖZET Metanefrik adenoma küçük, üniform, embriyonik görünümlü hücrelerin oluşturduğu, nadir bir epitelyal tümördür. Kadınlarda daha fazla olmak üzere, çocuklarda ve erişkinlerde görülür. Bu tümörlerin yaklaşık %50'si rastlantısal olarak saptanır ve böbreğin benign metanefrik tümörleri olarak sınıflandırılır. 31 yaşındaki kadın hastaya karın ağrısı şikayeti ile ultrasonografik inceleme yapıldı ve sağ böbrekte kitle saptandı. Bilgisayarlı tomografide sağ böbreğin üst pol medial kısmında yerleşmiş, 3.5x3 cm boyutlarında kistik renal kitle görüldü. Laboratuar bulgular normal sınırlarda idi. Renal karsinoma kuşkusu ile hastaya parsiyel nefrektomi uygulandı. Patolojik incelemede, makroskopik olarak, 3.5x3x3 cm boyutlarında merkezi kanamalı kistik yapıda, kesit yüzü gri-kahverengi kitle izlendi. Mikroskopik olarak, sıkıca bir araya gelmiş, üniform, küçük, yuvarlak tubüler ve asiner yapılardan oluşan, kalın bir fibröz kapsül ile çevrelenmiş, oldukça selüler tümör saptandı. Tümör hücrelerinin, küçük üniform ince kromatinli, yuvarlak-oval nükleuslu, belirgin nükleol içermeyen, monoton görünümde olduğu izlendi. Sitoplazmaları soluk ve dardı. Gevşek ödemli ve fokal hiyalinizasyon gösteren bir stroma vardı. Tümör çevresinde, çok sayıda psammom cismi dikkati çekti. Mitotik figür görülmedi. İmmünhistokimyasal olarak, tümör hücreleri WT-1, vimentin ve yüksek moleküler ağırlıklı keratin ile yaygın ve kuvvetli nükleer boyanma gösterdi. Çoğu tümöral hücre sitoplazmasında orta düzeyde CD57 boyanması da saptandı. EMA, CK7 ve düşük moleküler ağırlıklı keratin ile yalnızca fokal pozitif boyanma gözlendi. CD10 ve RCC negatifti. Metanefrik adenoma, karakteristik histopatolojik özellikleri ile nadir görülen, morfolojik olarak ayrı bir tümör tipidir. Boyutuna karşın, bu tümör benigndir ve başlıca, papiller renal hücreli karsinoma, tip 1 ve Wilms' tümöründen ayrılmalıdır. Metanefrik adenomanın kendine özgü bulguları, patolojik ve klinik olarak tanınmalıdır.

Anahtar Kelimeler: Böbrek tümörleri; immünohistokimya

ABSTRACT Metanephric adenoma is a rare epithelial tumour composed of small, uniform, embrionic-appearing cells. It occurs in children and adults with female predominance. Approximately 50% of these tumours are incidental findings and they are categorized as benign metanephric tumours of kidney. A 31-year-old female patient suffering from abdominal pain underwent ultrasonographic examination and a right renal mass was detected. Computerized tomogaphy revealed a cystic renal mass located in the medial portion of upper pole of right kidney, which measured 3.5x3 cm in dimension. The laboratory findings were in normal range. With the presumption of renal carcinoma, she underwent partial nephrectomy. Pathological examination, macroscopically, revealed a centrally cystic mass of 3.5x3x3 cm in dimention, with central haemorrhage and cut surface of grayish-tan in colour. Microscopically, a highly cellular tumour composed of tightly packed small, uniform, round tubular and acinar structures, encapsulated with thick fibrous tissue was seen. The tumoural cells were monotonous, with small uniform round to oval nuclei with delicate chromatin and inconspicious nucleoli. The cytoplasms were pale and scant. There was loose oedematous and focally hyalinized stroma. At the periphery of the tumour, there were many psammoma bodies. No mitotic figures were seen. Immunohistochemically, the tumour cells show diffuse and strong nuclear staining for WT-1, and cytoplasmic staining for vimentin and high molecular weight keratin. Also, moderate CD57 staining was detected in most tumoural cell cytoplasms. EMA, CK7 and low molecular weight keratin showed only focal positive staining. CD10 and RCC were negative. Metanephric adenoma is an uncommon, morphologically distinct tumour type, with characteristic histopathological features. Despite its size, it is benign and should be distinguished particularly from papillary renal cell carcinoma type 1 and Wilms' tumour. These unique features of metanephric adenoma should be pathologically and clinically recognized.

Key Words: Kidney neoplasms; immunohistochemistry

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Metanephric adenoma (MA) is a rare renal cortical neoplasm which has first described in 1980 as "Le néphrome néphronogène" in the French literature.[1] It has only recently become well characterized with the publication of two large series in 1995.[2,3] Then the immunohistochemical,[3,4] genetic,[3,5,6] and cytologic[5,6] studies were performed. MA is now widely regarded as a distinct clinicopathological entity and it now has a place among renal adenomas/benign tumours of the kidney according to the World Health Organization (WHO) classification of tumours.[7]

CASE REPORT

A 31-year-old female patient suffering from abdominal pain underwent ultrasonographic examination and a right renal mass was detected. Computerized tomography revealed a cystic renal mass located in the medial portion of upper pole of right kidney, which measured 3.5x3 cm in dimension. The laboratory findings, including blood counts and biochemical data, were in normal range. With the presumption of renal carcinoma an operation was planned and she underwent partial nephrectomy. Pathological examination, macroscopically, revealed a centrally cystic mass of 3.5x3x3 cm in dimention, with central haemorrhage and cut surface of grayish-tan in colour. Microscopically, a highly cellular tumour composed of tightly packed small, uniform, round tubular and acinar structures, encapsulated with thick fibrous tissue was seen. The cells were monotonous, with small uniform round to oval nuclei with delicate chromatin and inconspicious nucleoli. The cytoplasms were pale and scant. There was loose oedematous and focally hyalinized stroma. At the periphery of the tumour, there were many psammoma bodies (Figure 1). Approximately 50% of tumours contain papillary structures, usually consisting of tiny cysts into which protrude stubby papillae reminiscent of immature glomeruli (Figure 2). No mitotic figures were seen. Immunohistochemically, the tumour cells show diffuse and strong nuclear staining for WT-1 (Figure 3), and cytoplasmic staining for vimentin and high molecular weight keratin. Also, moderate CD57 staining was detected in most tumoural cell cytoplasms. EMA, CK7 and low molecular weight keratin showed only focal positive staining. CD10 and RCC were negative.

DISCUSSION

Renal MA is a rare renal cortical neoplasm with an incidence of 0.2% in a consecutive series of 405 adult renal epithelial neoplasms.[8] It is a recently described tumour and is now widely regarded as a distinct clinicopathological entity.[7] Most reported cases of MA have occured in adults, and only four

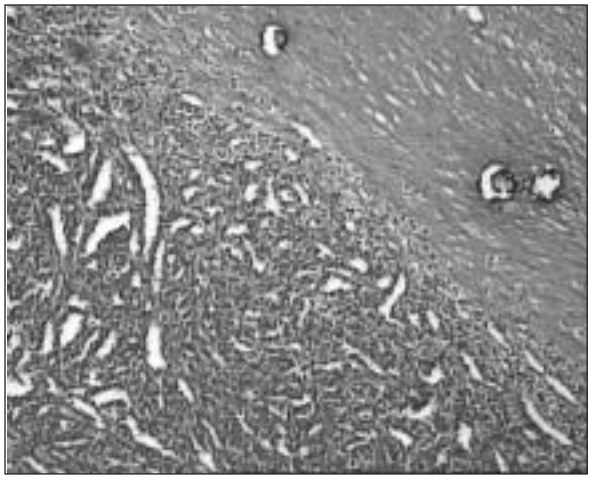

FIGURE 1: Metanephric adenoma. A highly cellular tumour with tightly packed, uniform tubular structures, psammoma bodies, encapsulated with thick fibrous tissue (HEx40)

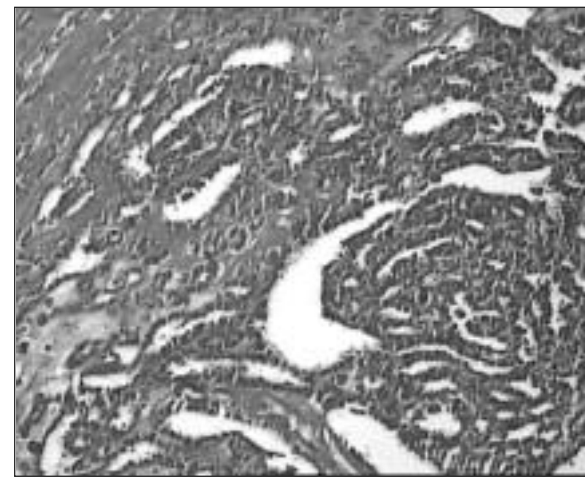

FIGURE 2: Tiny cysts with stubby papillae reminiscent of immature glomeruli (HEx100).

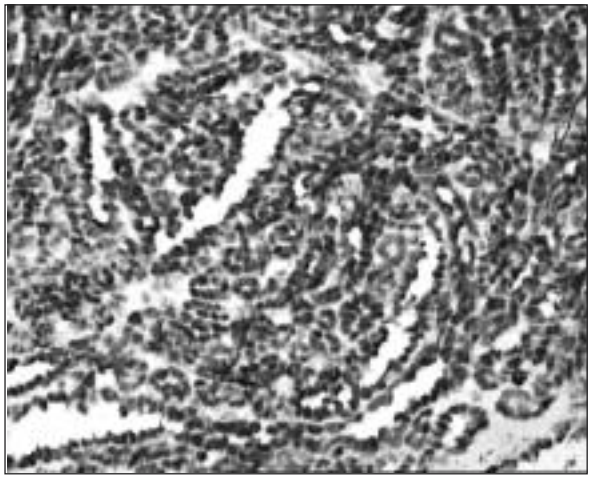

FIGURE 3: Immunohistochemical positivity of the tumour cells for WT-1 (x200).

cases have been reported in children younger than 10 years of age.[2,9] In a study of 50 patients with MA which the mean patient age was 41 (range from 5 to 83 years) with a female predominance (F:M=2.6:1) and with no racial predilection, most of the tumours were detected incidentally by ultrasound or computerized tomography scans, without any clinical findings.[2,9] In symptomatic cases, presenting symptoms included abdominal pain, abdominal mass, hematuria, fever, and/or hypertension. Most MAs reported in the literature have been 30-60 mm in diameter,[2] and the largest tumour reported until today measured 200 mm in diameter.[10] It is used to known that epithelial tumours larger than 30 mm in diameter are generally considered as carcinomas, but metanephric adenoma is an exception with its rather large size and central haemorrhagic necrosis on its cut surface. It has characteristic histopathological features. Typically, MAs are densely cellular neoplasms composed of tightly packed small round acini, long branching, or angulated tubular structures. At low magnification these structures may be mistaken for a solid sheet of cells. The cells of MA are monotonous, with small, uniform hyperchromatic nuclei and inconspicuous nucleoli. The nuclei are only a little larger than those of lymphocytes and are round to oval with delicate chromatin. The cytoplasm is scant and pale or light pink. Mitotic figures are absent or rare. Often, the stroma is inconspicuous, but sometimes it is hyalinised or oedematous. Hyalinized scar and focal osseous metaplasia of the stroma are present in 10-20% of tumours. Approximately 50% of tumours contain papillary structures, usually consisting of tiny cysts into which protrude stubby papillae reminiscent of immature glomeruli. Psammoma bodies are common and sometimes numerous. Although more than 75% of MAs lack pseudocapsules, the junction with the kidney is usually sharp. Radiologically, the imaging characteristics of MA are nonspecific.[11] However, the images often contain foci of calcification which is a feature seen much more frequently in MA than any other renal tumour.[2]

MAs are distinguished from papillary renal cell carcinoma (RCC) type 1 by their lack of encapsulation, the sharp interface between the tumour and the kidney, the absence of nucleoli, and the relative lack of mitotic activity. Papillary adenoma and papillary RCC do not react with antibody to *WT1.* Additionally, CK7 is largely absent in MA but frequently present in papillary RCC. There is a clear histopathological resemblence between metanephric adenoma and adult nephroblastoma (Wilms' tumour). MA should particularly be distinguished from diffuse nephroblastoma (Wilms' tumour), both blastemal and the differentiated epithelial patterns, as nephroblastoma has a malignant course. Nephroblastoma is the most common neoplasm of the kidney in children, while most MAs occur in adults. The cells of blastemal pattern are small, round to oval, and high nucleocytoplasmic ratio, and are characterised with brisk mitotic activity and nuclear overlapping. MA could be recognised with its bland cytological appearance, absence or paucity of mitotic activitiy, and absence of blastemal component. Immunohistochemically, all nephroblastomas stain for vimentin. Primitive blastemal and epithelial patterns of nephroblastoma are immunreactive for *WT1*, while differentiated epithelial and stromal patterns are not. In the three large series[2,3,9] published in the mid-ninties, authors reviewed the previous cases which were all found to be consistent with MA, but diagnosed mostly as nephroblastoma or RCC. Metanephric adenofibromas (MAF) are distinguished from MAs by the pre-

sence of spindle cell component consisting of fibroblast-like cells with oval to fusiform nuclei. MAF is a composite tumour in which nodules of epithelium identical to MA are embedded in sheets of moderately cellular spindle cells. The border of the tumour with the kidney is typically irregular and the spindle cell component may entrap renal structures as it advances. In MAF, angiodisplasia and glial, cartilaginous, and adipose differentiation occur occasionally.

The literature suggests that MAs do not have a consistent immunoprofile,[3,12] however, with a clear evaluation of the distinct morphologic features of the tumour, both at macroscopic and microscopic level, and by using the immunohistochemical methods the diagnosis of MA could be reached in most cases. As it is shown that MAs have generally carry a normal karyotype,[3,6,12] in problematic cases which raises the suspicion of RCC or adult nephroblastoma, cytogenetic studies may help to reach the exact diagnosis. Recently, a renal MA with previously unreported cytogenetic abnormalities has been reported in a 10-year-old boy.[13]

This rare entity, MA, is not well recognized yet by either clinicians or pathologists. So far, it was thought to be of benign course. However, two well documented cases of typical MA that metastasized to the regional lymph nodes have been reported to date.[14,15] It is desirable to have criteria to diagnose MAs preoperativeley in order to modify the treatment and/or the type of operation, and also avoid overtreatment. Adherence to strict histopathological criteria and awareness of discriminating features should discourage misdiagnosis of malignant renal tumours. There have been several reports in the literature supporting partial nephrectomy for MA.[16,17] However, the exact histopathological diagnosis of the tumour may not be evident during the operation and it may cause problems in differentiating the tumours from papillary RCC in adults, and from Wilms' tumour particularly in children.

It should be always kept in mind that solid papillary (chromophil) RCC, particularly the basophilic variant is suggested to be the most common malignant tumour that is confused with MA. Distinction of MA from solid papillary (chromophil) RCC is important because of the latter to be multifocal, bilateral, and to behave in a low grade malignant fashion.[18]

In conclusion, despite its size, MA is almost always cured by excision and the prognosis for this tumour is excellent. Unfortunately, most of the follow-up has been relatively short and based on patients who have been resected completely. Although MA is widely accepted as a benign tumour of the kidney, follow-up of these rare cases should be reassessed. Both clinicians and pathologists should be aware of a possible metastatic behaviour of this so far considered benign tumour.

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