Case Report

Bilateral Extrarenal Inguinal Nephroblastomatosis - A Rare Event

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Objective: To report an unusual case of extrarenal nephroblastomatosis involving bilateral inguinal regions.

Background: Nephroblastomatosis and nephrogenic rests are usually found in neonatal kidneys sub-clinically or associated with Wilms tumor. Extrarenal occurrence of this immature renal tissue is reported in literature as an incidental finding seen in inguinal canal, retroperitonium, along with a teratoma and sometimes associated with development of Wilms tumor. Involvement of bilateral inguinal regions is quite unusual and is not yet reported. Proper histological diagnosis is mandatory to distinguish them from Wilms tumor. After diagnosis a conservative therapeutic approach and regular follow-up is all that is required in these cases.

Case Presentation: A 5 months old female baby presented with bilateral inguinal swellings since birth. Initially FNAC was performed, a diagnosis of small round blue cell tumor was made and excision was advised. On H&E slides of excised specimen a diagnosis of bilateral extrarenal nephroblastomatosis was made and a close follow-up was advised.

Conclusion: Bilateral extrarenal nephroblastomatosis is a rare event. It has a close association with Wilms tumor. Considering the risk a thorough histological examination with proper diagnosis is required to plan appropriate treatment options for the patient. Regular follow-up for early detection of malignant transformation is also mandatory.

Key Words: Extrarenal nephroblastomatosis, Nephrogenic rests, Wilms tumor, Nephroblastoma

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Introduction

Nephroblastomatosis and nephrogenic rests are considered to be congenital dysembryonic/ dysontogenetic lesions rather than true neoplasms. They have a close histogenic relationship with Wilms tumor (nephrolastoma), which is characterized as a dysontogenetic tumor due to close resemblance to organs or tissue from which it arises[1]. Usually these lesions are found in infantile kidneys sub-clinically or associated with Wilms tumor. Their presence at various extrarenal sites is rare. Total 56 cases have been reported till date, out of these 31 cases were associated with and 25 cases were unassociated with teratoma[2].

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Common sites of occurrence are inguinal canal, retroperitonim, scrotum and sacral region in children associated with spinal dysraphism[2]. Bilateral extra renal presentation is an extremely rare event and this case report might be the first one to report it.

A wide range of nomenclature is used for this condition in the literature for example: ectopic immature renal tissue (EIRT)[2,3,4] hamartoma with primitive renal tissue[2,5] mesonephric remnant tissue[2,4] extrarenal nephrogenic blastema[2,6,] heterotopic nephrogenic rests[2,7] extrarenal nephrogenic rests[2,5,8] and extrarenal nephroblastomatosis[2,9]. These lesions can be single, multifocal, unilateral and bilateral but when microscopic in size they are called nephrogenic rests. When they are diffuse, massive and multifocal they are referred as nephroblastomatosis [1,10,11].

The exact mechanism behind the development and persistence of these extra renal rests is unclear. Purpose of this report is to describe the clinical and morphological features of this entity and to discuss

various differentials especially Wilms tumor (nephrolastoma) that can be a source of confusion.

Case Report

A 5 months old female baby presented with bilateral inguinal swellings since birth. She was otherwise healthy with no congenital syndrome. On physical examination there were diffuse, firm thickening in right and left inguinal regions measuring roughly 3x2 and 2x2 cm respectively. Ultrasonography of inguinal regions revealed oval shaped, multiple, variable sized heterogeneous lesions. Abdominal ultrasound was unremarkable with normal bilateral kidneys. CT scan of abdomen and pelvis revealed two well defined, oval shaped, heterogeneously enhancing soft tissue density lesions in both inguinal regions measuring 15.7x21.4x30.4 mm and 18.7x21.9x31.3 mm in AP x T x CC dimensions. No calcification or internal necrosis seen. (Figure. 1). A provisional diagnosis of conglomerate nodal mass was made and FNAC was advised.

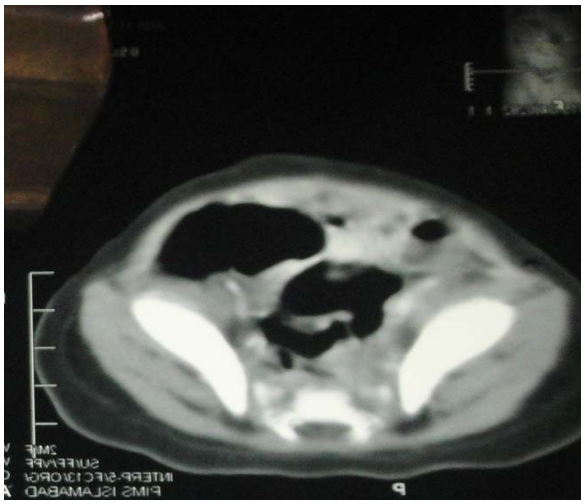


Figure. 1- CT scan showing soft tissue densities in inguinal regions bilaterally

On FNAC a diagnosis of small round blue cell tumor was made and excision was suggested. Excision specimens consisted of two soft tissue pieces from right and left inguinal region measuring 2x1.5 and 2x1.8 cm respectively. Microscopic examination of paraffin embedded sections revealed a nodular lesion with multiple nodules of blastemal tissue admixed with variable sized tubules along with immature glomeruloid structures (Figure. 2). The blastemal component was in the form of round to oval cells, hyperchromatic nuclei and scant cytoplasm. Scattered mitotic figures were seen with a mitotic count of 4-6/10 HPF. No atypical mitosis, necrosis and definitive invasive component was seen.

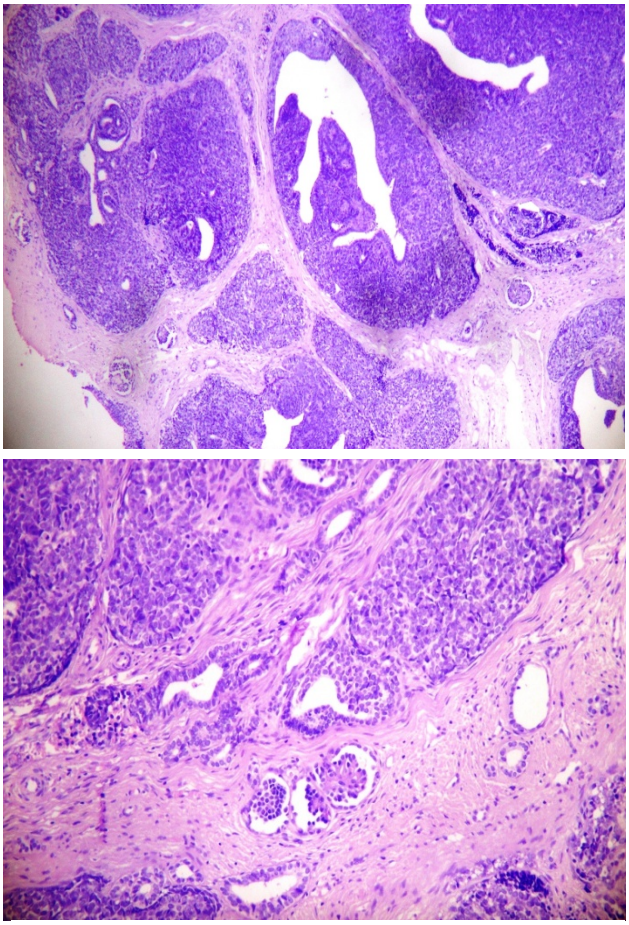


Figure. 2- Histological picture of the case showing blastemal component in the form of small round closely packed cells with tubules and abortive glomeruli. (H&E X 40 and H&E X 100).

Immunohistochemical examination revealed strong and diffuse expression of WT1 in the blastemal component. Tubules were positive for cytokeratins AE1/AE3. Ki-67 labeling index was 20-25% in blastemal component (Figure. 3). Based on absence of marked pleomorphism, atypical mitosis and moderately high Ki-67 index diagnosis of extrarenal nephroblastomatosis was favored over extrarenal nephroblastoma and close follow-up was suggested for any recurrence and early detection of malignancy. Currently the baby is healthy and no recurrence is noted after 3 months of surgery.

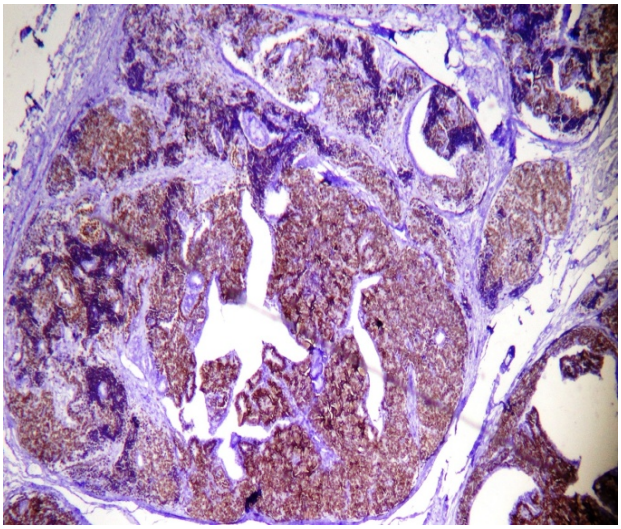
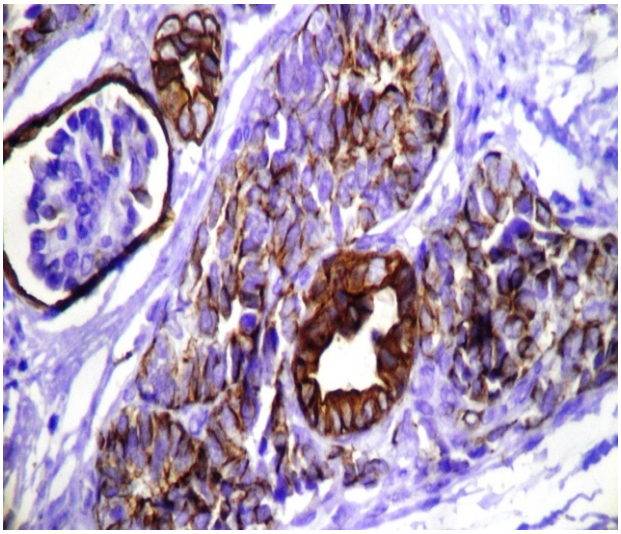
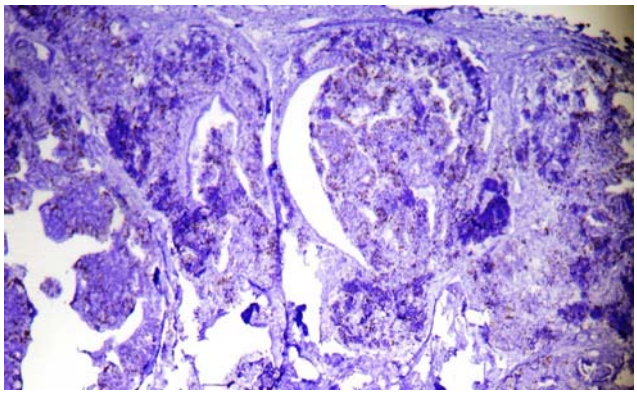


Figure. 3(A)- Immunohistochemistry: WT1 showing diffuse, strong nuclear expression in blastemal component.(H&Ex40)



B- CK-AE1/AE3 showing positivity in tubular structures while negative in blastema (H&Ex100)



C- Ki-67 labeling index reached up to 20-25% (H&Ex40).

Discussion

In contrast to development of other epithelial organs that somewhat follow a simple scheme of differentiation i.e to be derived from single primordia and undergoes sequential branching pattern, nephrogenesis has a different story. Nephron the functional unit of kidney is derived from primitive mesenchymal blastemal tissue which undergoes mesenchyme-to-epithelium transition (MET) and leads to the formation of earliest epithelium derived from mesenchyme. The collecting system is ureter derived which undergoes further branching in the course of development. So the whole process of nephrogenesis is based on two pathways; the nephrogenic (mesenchymal) and the ductogenic (ureteric) and interaction between these two is vital in renal development [12].

Nephrogenic (mesenchymal) pathway can be divided in to three successive phases including, the formation of pronephros, mesonephros and metanephros. Development of metanephric or permanent kidney starts at 4-5th weeks and it should complete at around 36th week of gestation. At this time blastemal component should disappear from developing kidney. Failure of its maturation results in persistence of immature blastemal component in the kidney in the form of nephrogenic rests (when microscopic) or nephroblastomatosis (when diffuse and multifocal). According to their location in kidney they are divided in to perilobar and the intralobar types[13].

Extrarenal presence of this immature renal tissue is a rare event. Various ectopic sites have been reported in the literature and most common of them is inguinal canal[6,8] lumbosacral region[5,14] and associated with teratomas[2]. Rarely they can also be seen in thorax, heart, colon, adrenal glands and testis[4,15]. The mechanism behind their origin and persistence is still unclear. According to various theories, they have originated either from mesonephros or metanephros. The cases associated with gonads are thought to arise from mesonephros due to its association with developing gonads[4]. Cases from lumbosacral area associated with spinal dysraphism, thought to arise from metanephros because in lumbosacral region it comes closest to the spinal cord [5, 15]. Like perilobar and intralobar nephrogenic rests which can be source of Wilm's tumor in the kidney (having an association of around 40%) extrarenal rests can also act as a precursor lesions for Wilms tumor[13].

Whenever an immature renal tissue is identified at an ectopic site, it is compulsory to differentiate between extrarenal nephroblastomatosis and extrarenal Wilms tumor (nephroblastoma). At times this distinction can be quite challenging because it is difficult to distinguish a proliferative nephrogenic rest from small Wilms tumor. On histological grounds both entities are composed of blastemal component, epithelial tubules along with immature glomeruloid structures admixed in variable amount of stroma[2].

The distinguishing characteristic of Wilms tumor is marked pleomorphism, atypical mitosis and sometimes presence of disordered structures. Tumor necrosis and presence of anaplastic cells (associated with 5% of Wilms) can also be helpful. In contrast nephroblastomatosis is usually composed of multiple islets and nests of immature renal tissue. Mitotic count is usually scanty. Sometimes proliferative nephrogenic rests exibit high mitotic rates and moderate pleomorphism but they lack atypical mitosis, necrosis and peritumoral capsule associated with Wilms due to its rapid growth[15].

Other possible differentials include teratoma and any metastatic tumor with unknown primary including germ cell tumor. Teratoma was excluded due to absence of other non- nephrogenic component and germ cell tumors were out due to positivity of WT1 and negativity of germ cell immunohistochemical markers.

A conservative therapeutic approach is indicated for these lesions. If they are present sub-clinically and found incidentally during ultrasonography for any reason a "wait and see" policy is favoured[16].For those causing a mass lesion, complete excision of the lesion is advised.

Conclusion

Documented literature regarding this subject is very limited. From this sparse knowledge it can be concluded that though nephroblastomatosis/ nephrogenic rests are considered to be a benign lesion, they have a close association with Wilms tumor and act as precursor lesion for them (up to 40% association). It is mandatory to differentiate them from Wilms tumor (nephrolastoma) because a conservative approach is all what is required in the case of nephroblastomatosis/neprogenic rests and Wilms tumor require chemotherapy alone or with radiotherapy for higher stages. A close follow-up is required to detect any recurrences and to look for malignancy at an early stage

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