

Case Report

Ectopic immature renal tissue: clues for diagnosis and management

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Abstract: Ectopic immature renal tissue has rarely been reported in literature, associated or not with teratoma. Its finding could be matter of concern, owing to the occasional possibility that Wilms tumor may develop in this setting. We report a 1-year-old male patient who underwent surgery for a sacral subcutaneous small teratoma with a prevalent component of immature renal tissue. The lesion appeared completely excised and, in absence of features of malignancy, only follow-up was suggested. The patient was alive and well 15 months postoperatively. Whenever ectopic immature renal tissue is detected, a proper histological interpretation is mandatory, in order to plan a suitable treatment of the patient. From an extensive analysis of cases reported in literature we draw some practical suggestions for the diagnosis and treatment of this rare condition.

Keywords: Ectopic renal tissue, Wilms tumor, teratoma, metanephric tissue

Introduction

Extra-renal presence of structures consistent with ectopic immature renal tissues (EIRT) has rarely been reported, both in teratomas, or unassociated with a teratoma [1-44]. A broad nomenclature has been used for these unusual findings: ectopic immature renal tissue [10, 30, 32, 33, 35], mesonephric remnant tissue [32], hamartoma with primitive renal tissue [38], extrarenal nephrogenic rests [38, 40], extrarenal nephrogenic blastema [39], heterotopic nephrogenic rests [41], ectopic nephrogenic rests [42, 44], and extrarenal nephroblastomatosis [43].

We analyzed EIRT's cases reported in literature (25 unassociated and 31 associated with teratoma), in order to draw useful informations for diagnosis and therapy. In addition, we describe a small lumbo-sacral lesion, prevalently composed of nests of nephrogenic tissue, in which an accurate search eventually disclosed scarce amounts of nervous and meningeal tissues, and rare glandular epithelial structures, confirming its teratomatous nature.

Case report

A 1-year-old male infant was admitted to our hospital for the removal of a subcutaneous

sacral nodule. The specimen consisted of fat tissue, containing a 1,5 cm central fibrous core histologically characterized by the presence of islets and nests of immature-appearing renal structures, recalling metanephric tissues, composed of stroma, blastemal tissue, and epithelial tubules, with occasional glomeruli containing dystrophic calcifications (**Figure 1A**). Deeper sectioning revealed scarce amounts of nervous and meningeal tissues, embryonal rhabdomyoblastic fibers, a single small focus of cartilage and few mature-appearing acinar and glandular structures. At immunohistochemistry, nervous and meningeal tissue strongly expressed glial fibrillary acidic protein and S-100 protein or epithelial membrane antigen, respectively. A diffuse and strong nuclear immunoreactivity for WT1 (**Figure 1B**) and PAX8 was observed in the blastemal cells, in tubular epithelium and glomerular epithelial cells. Tubular structures showed positivity to cytokeratin 7 (**Figure 1C**) and cytokeratins AE1/AE3. Ki-67/MIB-1 labeling index reached 35% in the blastemal areas (**Figure 1D**), although mitoses were rare and never atypical. The final diagnosis was mature, non-cystic, teratoma with nephroblastomatosis-like component. The lesion appeared completely excised, with adipose tissue at the periphery and, in absence of features of malignancy.

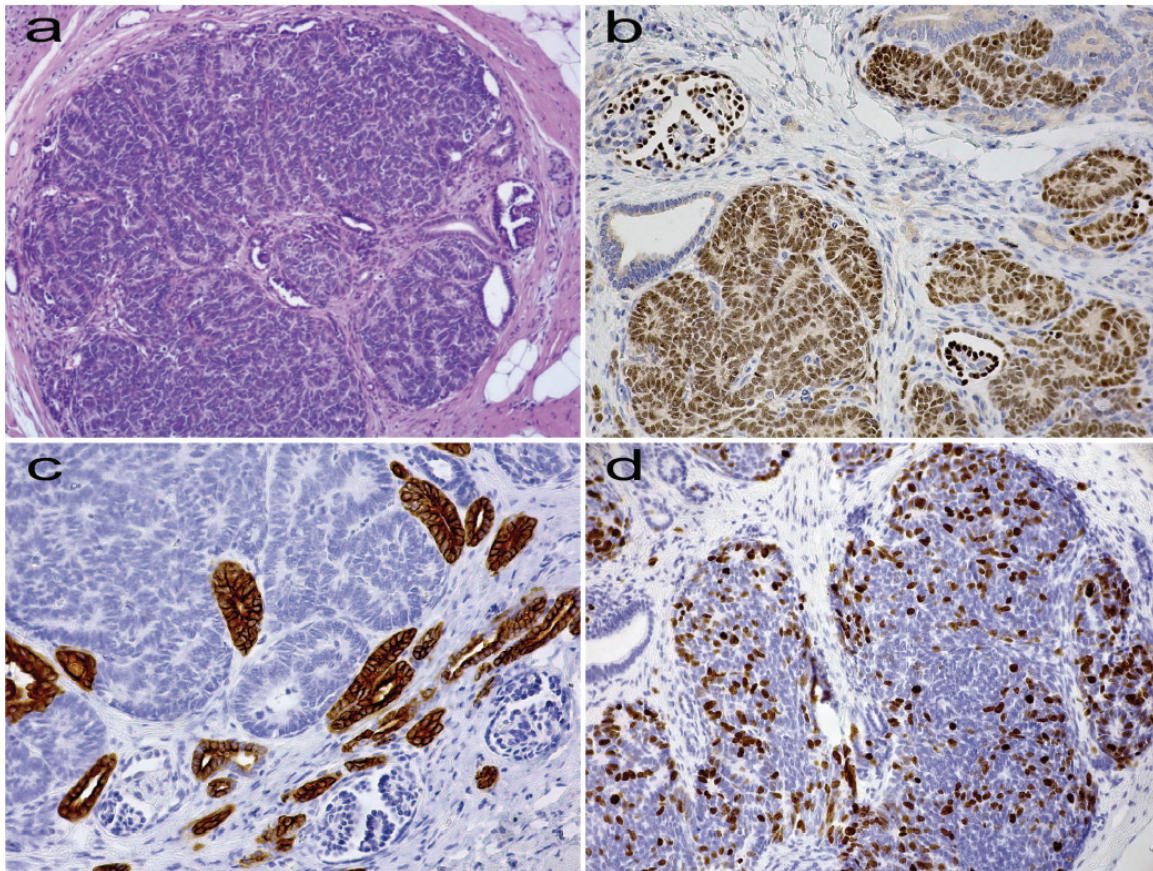


Figure 1. Histological picture of ectopic immature renal tissue in a lumbosacral teratoma. A: Blastemal area characterized by small, closely packed cells, with tubular structures and abortive glomeruli. HE, x 100. B: Primitive, blastemal cells and epithelial glomerular elements show nuclear WT1 expression, whereas differentiated tubules are negative. X 200. C: Immunohistochemistry for cytokeratin 7 shows strong cytoplasmic reactivity in tubular structures. X 200. D: Cell proliferation index after immunohistochemistry for Ki-67/MIB1. x 200.

nancy, only follow-up was suggested. The patient was alive and well 15 months later, without evidence of recurrent or metastatic disease.

Discussion

Extra-renal presence of structures consistent with EIRT has rarely been reported. From a histological standpoint, EIRTs are generally described as aggregates of blastemal tissues, tubules and occasional glomeruli, with a variable amount of admixed fibrous stroma. An extensive review of the literature showed occurrence of EIRT both associated and unassociated with a teratoma, and we found a total of 56 cases. This finding mostly regards children in the first decade of life, with no gender differences [1-44]. **Table 1** shows EIRT's age, gender, site distribution, association with teratoma and follow-up.

Since its first description by Gruenwald, in a 20-mm human embryo with myeloschisis, we found only 25 cases of EIRT unassociated with teratoma, mainly located in the sacral region, frequently in children with spinal dysraphism [26-44]. In such cases, it is possible that EIRT represents metanephric remnants displaced during embryonic development. Its peculiar presence in the lumbosacral region, in cases of spinal dysraphism, supports the hypothesis that neural tube abnormalities may interfere with migration and morphogenesis of bystander renal tissue [38]. On the other hand, from a cumulative analysis of large series and single case reports of teratomas, we found association with EIRT in thirty-one cases [1-25]. Its actual prevalence in this condition appears to be low (about 1 percent) although difficult to determine with accuracy and probably underestimated.

Ectopic immature renal tissue

Table 1. Cases of ectopic immature renal tissue reported in the literature

	Total (n=56)	Associated with teratoma (n=31)	Unassociated with teratoma (n=25)
Age			
Newborn-10 yrs	43	21	22
≥11 yrs	10	8	2
Unknown	3	2	1
Gender			
Male	24	11	13
Female	28	17	11
Unknown	4	3	1
Site			
Lumbar/sacral	28	16	12
Inguinal canal	8	-	8
Retroperitoneal	6	6	-
Testicular	4	4	-
Ovarian	2	2	-
Other sites	8	3	5
Diagnosis of Wilms tumor	18	14	4 [†]
Follow-up			
Recurrence	3	2	1
Metastases	6	6	-
Dead with malignancy	2	2	-

[†]only suspected in 3 cases.

The strict similarity of ectopic immature renal structures to the foci of perilobar and intralobar nephrogenic rests/nephroblastomatosis occasionally found in neonatal kidneys and recognized potential source of nephroblastoma, could be matter of concern and diagnostic uncertainty [45-48]. Suspicious or obvious features of EIRT malignancy have in fact been reported mainly within teratomas, and treated with additional surgery and chemotherapy: eight (5 children / 3 adults) out of 31 patients showed local recurrence or metastatic disease, with two adult patients dead of disease [3, 6, 7, 12, 14, 18, 23, 24]. On the contrary, only one out of 25 patients (23 children / 2 adults) presenting EIRT unassociated with teratoma had recurrence, lacking features of malignancy, and he (a 22-month-old child) was still alive and free of disease three years later, without adjuvant chemotherapy [44].

Whenever EIRT is found, a differential diagnosis between benign ectopic immature renal tissue and a true Wilms tumor (WT) is mandatory, albeit sometimes it may pose serious difficulties. Typically, nephroblastoma tends to form expanding, spherical nodules, surrounded by a fibrous pseudocapsule, while EIRT usually consists of small multiple microscopic nests and islets. From a cytological point of view, only frank atypias, atypical mitoses and marked pleomorphism are reliable characteristics of WT, high mitotic rates and moderate pleomorphism being found also in EIRT [45]. Therefore, if the immature renal tissue in a teratoma lacks

obvious features of malignancy it should be considered as an “immature component”, in analogy with the more common primitive neuroectodermal component of immature teratomas [49]. In fact, it has been also proposed that areas reminiscent of WT present in teratomas should be reported as nephroblastoma-like when extending for half to a whole microscopic field seen with a 4x objective, and as an immature component when smaller [50].

The conclusion from the scarce literature on this subject is that EIRT generally does not behave in an ominous manner, in particular in childhood and unassociated with teratoma, in which cases a “wait and see” policy with follow-up seems adequate. On the other hand, immature renal tissue within a teratoma (an accurate search for teratoma components is necessary) impose a closer attention: in absence of atypia, it might be considered likewise other immature embryonal-type components, whereas obvious atypias and features of malignancy prompt a diagnosis of nephroblastoma and the patients should receive appropriate treatment.

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