

Case Report

Metanephric Stromal Tumor with Unusual Heterologous Adipose Differentiation: A Case Report and Literature Review

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A 10-year-old Thai boy with a metanephric stromal tumor (MST) with unusual adipose differentiation is reported. It has been described that the heterologous tissue element including fat is exceptionally demonstrated in MST cases. Multifocal grossly detected intratumoral adipose tissue as shown in this present case has not been elucidated and illustrated before. The presence of the fatty component may perhaps make it difficult in distinguishing the MST from its differential diagnoses such as Wilms tumor, metanephric adenofibroma, mixed epithelial stromal tumor, and lipomatous renal tumors including angiomyolipoma. The recognition of this rare entity is important and can prevent the patients from complications and unnecessary treatment.

Keywords: Kidney neoplasm, Metanephric, Pediatric

J Med Assoc Thai 2013; 96 (12): 1621-7

Full text. e-Journal: <http://www.jmatonline.com>

Metanephric stromal tumor (MST) is a very rare, benign, pediatric renal neoplasm^(1,2) and currently designated as the stroma-dominant end of the metanephric tumor spectrum which histogenetically arises from the primitive metanephric blastema⁽³⁾. Rare cases are reported in adults⁽⁴⁻⁶⁾. The metanephric tumor continuum ranges from the purely epithelial metanephric adenoma to the intermediate mixed epithelial and stromal metanephric adenofibroma (MAF) to the predominantly stromal MST⁽³⁾. Two of 39 MST cases (5%), 31 cases from the largest series of National Wilms Tumor Study Pathology Center (NWTSPC)⁽¹⁾ and 8 cases from subsequent reports⁽⁴⁻¹⁰⁾, contained focal areas of only glial tissue. There were no other heterologous tissues including adipose tissue reported. However, the unusual adipose differentiation was mentioned but not illustrated in the AFIP textbook⁽⁷⁾.

The aim of this case presentation was to underline the rarity of MST with adipose differentiation possibly making unfamiliarity and difficulty to general

pathologists to give the diagnosis. The first gross and microscopic demonstrations are reported and its differential diagnoses are discussed.

Case Report

A 10-year-old healthy Thai boy presented with epigastric pain for 1 week. On physical examination, the patient was found to have a large abdominal mass located in the left upper quadrant. Neither hypertension nor hematuria was noted. Computerized tomography scan of the whole abdomen demonstrated a 12 cm well-defined heterogeneous mass arising in the left kidney with fatty component (Fig. 1). The right kidney appeared normal. Chest X-ray was not remarkable. The presumptive diagnosis was suspected to be a Wilms tumor of the left kidney.

The patient subsequently underwent exploratory laparotomy with left radical nephrectomy. He had a postoperative course without any complication.

The specimen was carefully examined and disclosed a kidney with attached unremarkable ureter, totally weighing 820 g. The kidney measured 14x12x10 cm. Its capsule was easy to peel off, revealing light brown and smooth cortical surface. Cut surfaces showed a well-circumscribed, rubbery, gray white, fibrous whorl-like mass resembling a uterine leiomyoma measuring 12x11x10 cm. The tumor was

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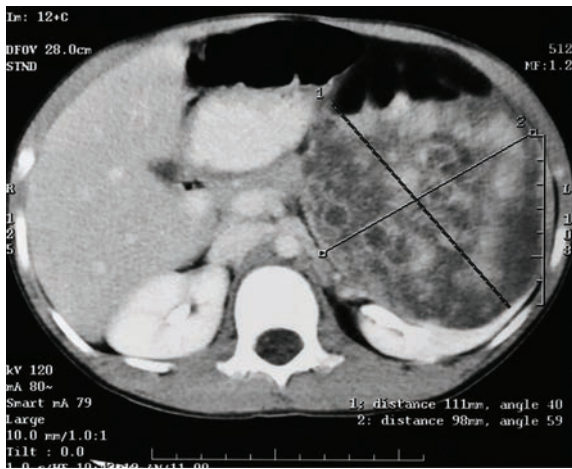


Fig. 1 Computerized tomography of abdomen with intravenous contrast material reveals a 12.0x11.1x9.8 cm, well-defined, heterogeneous, enhancing mass with central low density portion of left kidney. There is fat component noted at the anterior part of the mass. Calcifications are not detected.

located at the renal medulla and confined to the kidney. Few occasional smooth walled microcysts and cysts were also present intratumorally varying from 0.1 to 1 cm in maximal diameter. Scattered foci of fatty tissue were obviously noted, 6 cm in maximal dimension, and mostly located at periphery of the mass. Areas of necrosis and hemorrhage were not present. The renal pelvis was compressed by the tumor and appeared slit-like space. Non-neoplastic kidney was light brown, ranging from 0.8 to 1.5 cm thick and revealed a well-defined cortico-medullary junction (Fig. 2A).

Microscopically, the renal mass without a capsule showed a scalloped and delicately infiltrative border with surrounding kidney (Fig. 2B). The tumor was predominantly composed of a proliferation of bland spindled cells with abundant fibrocollagenous stroma with focal sclerotic area. There was no stromal hypercellular area. Onion-skin, hypodense, collarette formations by the tumor cells around the entrapped tubules were noted (Fig. 2C). Mitotic figure was not

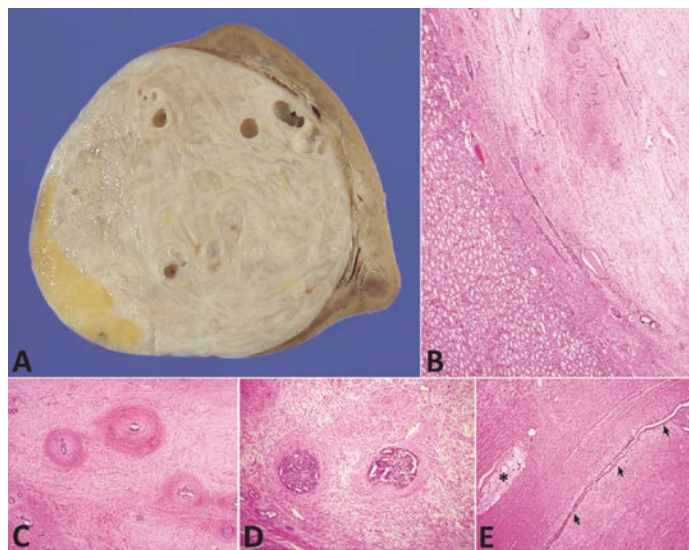


Fig. 2 Metanephric stromal tumor (MST) with heterologous adipose tissue. A) Gross photograph of formalin fixed MST cut section reveals a circumscribed renal mass (12 cm) with fibrous, whorled appearance. Few small smooth-walled cysts are also exhibited within the mass. There is no area of hemorrhage/necrosis. Note scattered foci of adipose tissue with the largest one present at left lower rim of the tumor. B) The interface of MST with nonneoplastic kidney shows scalloped and superficially infiltrative border with unencapsulation; the entrapped native structure containing inspissated Tamm-Horsfall protein is concentrated at the perimeter of the tumor (H&E stained, original magnification x20). C) Characteristic concentric collarette (onionskin ring) formation of hypocellular spindle cells present around the entrapped tubules in fibrocollagenous background, yielding nodular variation in cellularity (H&E stained, original magnification x40). D) Few entrapped native renal epithelial structures showing hyperplastic change are observed near the border of the tumor (H&E stained, original magnification x100). E) Intracanalicular growth pattern is produced by tumor indenting entrapped renal tubule (arrows). A small aggregate of adipose tissue is also present (asterisk) (H&E stained, original magnification x40).

identified. The entrapped tubules focally displayed cystic dilatation, micro- and macrocyst formations, and infrequent hyperplastic change of the epithelium (Fig. 2D). Areas of intracanalicular growth pattern of the stroma were occasionally noted (Fig. 2E). Scattered small and large foci of mature adipose tissue were also demonstrated in the stroma (Fig. 2E). A relatively sharp interface between adipose tissue component and neighboring fibrous stromal tissue was noted (Fig. 3). Other heterologous elements, e.g., glial tissue, cartilage, were not detected. By immunostaining, the neoplastic stromal cells were vimentin and CD34 positive in diffuse and patchy fashions, respectively but they did not stain with S100 protein and smooth muscle actin. Stains for pancytokeratin AE1/AE3 highlighted entrapped native tubular epithelia at the perimeter of the tumor.

Discussion

Metanephric stromal tumor (MST) was first described by J. Bruce Beckwith in abstract form in 1998⁽⁸⁾. MST is a rare stromal renal neoplasm composed entirely of stromal element identical to the stroma of metanephric adenofibroma (MAF; previously termed nephrogenic adenofibroma)^(1,2) and classified as a separate unique tumor in the spectrum of metanephric tumor^(1,3,4,9).

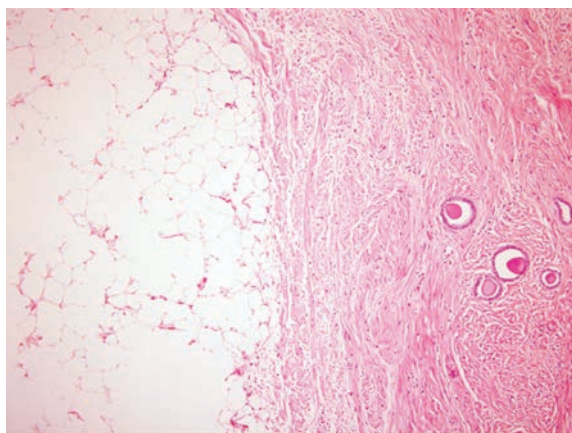


Fig. 3 The interface of adipose tissue and fibrous stroma in mesonephric stromal tumor (MST) is relatively sharp. Adipocytes show slight variation in size and shape. Nuclei are fairly uniform. Few entrapped tubules lined by bland-looking cuboidal epithelial cells with dense intraluminal eosinophilic secretions are also noted in fibrous stromal component of the MST (H&E stained, original magnification x100).

The presence of heterologous differentiation in MST supports a relationship with Wilms tumor (WT) or intralobar nephrogenic rest, since heterologous differentiation is a hallmark of WT and associated lesions.

MST is most commonly presented in childhood with median and mean age at diagnosis being 17.5 and 30 months, respectively^(1,10-13). However, the minority of MST cases (4 in 40 reported cases, 10%) is present in adulthood (53, 55, 72, and 77 years old)⁽⁴⁻⁶⁾. No gender predilection is noted (male:female = 1.1:1.0)^(1,4-6,10-13). When compared to the other renal stromal neoplasms, MST is approximately 10% as common as congenital mesoblastic nephroma (CMN)^(1,9). To the author's knowledge, no more than 8 reports of MST cases have been published in English and Spanish (Table 1). Additionally, 3 MST cases were issued in Chinese^(14,15).

Typical presentation of MST is an abdominal mass, which is localized to the kidney. No bilateral tumors have been reported⁽¹⁾. An outnumbered group of the patients may manifest symptoms/signs of extrarenal angiodysplasia, e.g., hypertension or hemorrhage^(2,3).

Most patients have been successfully treated with simple nephrectomy without additional treatment⁽⁶⁾. Although previously described MSTs have had a benign course with no reports of metastases or even local recurrence⁽¹⁻³⁾ recently, De Pasquale MD et al⁽¹³⁾ proposed a 9-month-old boy of MST who had an initial diagnosis of CMN of the kidney, recurring as a gonadal mass six months after nephrectomy and adjuvant chemotherapy. However, the patient had no evidence of the disease, 31 months after the orchidectomy.

The diagnosis of MSTs can be essentially made based on gross finding and histologic criteria. Grossly, MSTs are characteristically tan, lobulated, fibrous, cystic or solid, mass ranging from 1.6 to 21 cm in maximum diameter (median, 5 cm; mean, 6 cm)^(1,4-6,10-13) centered in the renal medulla. Of interest, the patients with large tumor size (>10 cm) tends to be older than the patients in common age group of presentation. Approximately one-sixth of cases were multifocal⁽¹⁾. Commonly, MSTs have an unencapsulated but subtly infiltrative, scalloped border. The tumor can extend from the intrarenal location to nearby structures. Argani and Beckwith⁽¹⁾ proposed two of 31 cases (6.5%) had polypoid botryoid extension into the renal pelvis. MST case with continuous extension through the bladder to the

Table 1. Metanephric stromal tumor (MST) cases reported in English and Spanish literatures. MST has been commonly encountered in childhood exceptionally diagnosed in adult. The patient age ranges from 2 days to 77 years old. There is no gender predilection. Size of the tumors can vary from 1.6 to 21.0 cm

Authors	No. of case(s)	M/F	Patient age	Tumor size (cm)
Argani P, Beckwith JB 2000 ⁽¹⁾	31	15/16	2 days-11 years	1.6-10.0
Palese MA, et al. 2001 ⁽¹⁰⁾	1	1/0	15 years	4.6
Bluebond-Langner R, et al. 2002 ⁽⁵⁾	1	0/1	53 years	5.5
Lorenzo AJ, et al. 2003 ⁽¹¹⁾	1	1/0	2 years	-
Amat Villegas I, et al. 2006 ⁽⁶⁾	2	2/0	72, 77 years	18.0, 21.0
Rajalakshmi V, et al. 2009 ⁽¹²⁾	1	0/1	1 month	3.0
McDonald OG, et al. 2009 ⁽⁴⁾	1	0/1	55 years	2.5
De Pasquale MD, et al. 2011 ⁽¹³⁾	1	1/0	9 months	10.0
Present case	1	1/0	10 years	12.0
Total summary	40	21/19	2 days-77 years	1.6-21.0

M/F = male/female

prostatic urethra was also reported⁽¹¹⁾. A case of MST with prominent renovascular angiodysplasia and juxtaglomerular cell hyperplasia arising in a patient with neurofibromatosis-1 (NF-1; von Recklinghausen) was stated. This suggests that MST may be an NF-1 associated lesion⁽⁴⁾.

By microscopic examination, MSTs are composed of bland spindle to stellate cells with indistinct cytoplasmic processes. Epithelioid stromal cells are common. The degree of stromal cellularity can range from profoundly hypocellular to extremely hypercellular. Four following distinctive characteristics of MST have been previously described^(1-3,7): 1) Formation of eccentric collarettes (onionskin rings) of stromal cells around renal tubules or blood vessels, the most common feature of consideration of MST. 2) Vascular changes include angiodysplasia of intratumoral arterioles with expansion and disorganization of vascular medial smooth muscle cells due to epithelioid transformation and myxoid degeneration; and juxtaglomerular cell hyperplasia of entrapped glomeruli, results in nodules of polygonal cells with minimal clear cytoplasm at the vascular pole. 3) Nodules of heterologous tissue are noted in 20% of MSTs, such as glia⁽¹⁾, cartilage⁽¹⁾, fat⁽⁷⁾ with glial elements being the most common. The adipose tissue seems to be the rarest heterologous constituent present in the MST. 4) Normal renal elements may be entrapped by the tumor, mainly causing dilatation and cyst formation. Indentation of tubules by the spindle cell component sometimes produces an intracanalicular growth pattern

reminiscent of mammary fibroadenomas/phyllodes tumors.

In addition, the spindle cell stroma may have several architectural growth patterns, including a palisading pattern simulating the Verocay bodies of a schwannoma, a storiform pattern, and a hemangiopericytomatous pattern⁽¹⁾.

MSTs are typically immunoreactive for CD34, but labeling may be patchy as in the present case. Desmin, cytokeratins, and S100 protein are negative, though heterologous glial areas label for glial fibrillary acidic protein (GFAP) and S100 protein⁽¹⁻³⁾.

Based on the pathologic findings, this case was typically consistent with MST. These findings included involvement of renal pelvis, formation of eccentric collarettes of stromal cells around renal tubules and immunoreactivity for CD34.

Cytogenetic alteration of MST has not been precisely conclusive. Recent findings revealed a complex homogeneous gain between bands 17q22 and 17q25.3 described in a 3-year-old boy patient⁽¹⁶⁾. In contrast, a prior cytogenetic testing result of the tumor performed in an adult patient demonstrated normal karyotype⁽⁵⁾.

When the following features of fibrous stroma of MST, such as intratumoral angiodysplasia, onion-skinning, concentric peritubular growth pattern and heterologous differentiation⁽²⁾ are present, we can distinguish MST from its malignant mimickers e.g., CMN, clear cell sarcoma of the kidney (CCSK), monophasic spindle cell synovial sarcoma.

This distinction is important because the patients can be saved from the toxic effects of aggressive chemotherapy/radiation therapy that may be administered if the tumor is misdiagnosed as one of its malignant differentials.

In addition, the entities to be differentiated from MST with adipose differentiation comprise WT, MAF, mixed epithelial stromal tumor (MEST), lipomatous renal tumors including angiomyolipoma (AML), renal teratoma and other rare fat-containing renal tumors.

Stromal predominant WT with varying amount of fat may enter in the differential diagnosis. WT is a malignant embryonal neoplasm of the kidney with potentially differentiating toward epithelial, blastemal, and stromal elements in variable proportions. WT can be excluded by the presence of neoplastic epithelial and/or blastemal structures.

MST and MAF are members of the same morphologically continuous spectrum. Both also share qualitatively identical stroma with rare heterologous element including particularly adipose tissue⁽⁹⁾. Consequently, the distinction between MST and MAF is not always straightforward. When considering the presence of intratumoral epithelial proliferation, type of epithelium and location of the epithelial proliferation are important. Basically, MST can manifest infrequently hyperplastic change of scattered entrapped glomeruli/tubules that are usually concentrated at the perimeter of the tumor as the present case and, in some cases, deeply situated within the tumor. This may be puzzling when discriminating between MST and MAF. Recently, the tumor is classified as biphasic MAF when it contains at least focally a proliferation of embryonal epithelium forming discrete, round, unencapsulated nodule(s), particularly deep-seated and unassociated with native kidney, identical morphologically to pure epithelial metanephric adenoma^(1,9).

Another biphasic renal tumor in the differentials is MEST. Minor component of fat can be found in the stroma of MEST. Unlike MST, typically, MEST afflicts the renal pelvis of perimenopausal women and microscopically, the stroma lacks characteristic concentric onion-skin cuffing. MEST with extensive fatty differentiation which is grossly thought to be an angiomyolipoma (AML) has been reported⁽¹⁷⁾.

The presence of fat in a renal mass is virtually pathognomonic of AML. AML, a rare benign mesenchymal tumor histogenetically arising from

perivascular epithelioid cells, may be found in children and commonly develop in association with tuberous sclerosis complex (TSC). AMLs in TSC are frequently multicentric, bilateral, and fat-poor lesions consisting of predominantly spindle cells, epithelioid cells or vascular elements. Grossly, AMLs are not encapsulated and may be locally infiltrative. Histologically, AMLs have no typical MST's stroma. The neoplastic cells exhibit immunoreactivity for melanocytic markers e.g., human melanoma black-45 (HMB-45), melanin-A⁽¹⁸⁾ but they are negative for CD34.

Lipomatous tumors, lipoma and liposarcoma, are easily distinguished from the MST. The former is entirely composed of benign/malignant adipocytes without stroma of fibrocollagenous tissue while the fat composition in the latter is usually a small portion within the mass. Renal lipomas are quite infrequent in children⁽¹⁹⁾. Intrarenal lipomas must be distinguished from AMLs. Generous sectioning is necessary to find smooth muscle and vascular element that help to differentiate the lipoma from lipomatous AML. Melanoma markers on multiple levels are sometimes needed. Renal liposarcomas typically occur in the retroperitoneum and rarely presenting an isolated intrarenal lesion. Many of those are associated with TSC and probably correspond to AMLs⁽²⁰⁾. These cancers do not differ histologically from similar tumors at other sites.

Renal teratoma, which may contain the adipose tissue component, is infrequent and rarely occurs as primary renal tumor. Most cases have been described as either retroperitoneal teratomas with renal extension or Wilms tumors with teratoid features⁽²¹⁾.

Other rare fat-containing renal tumors, e.g., renal oncocytoma and renal cell carcinoma, occur rarely in children and adolescents^(22,23). In case of fat, not true tumoral component, present in such both tumors, the tumors usually invade and/or envelop surrounding perirenal/sinus fat^(22,24).

In conclusion, MSTs are benign pediatric renal tumors exceptionally diagnosed in adults. The most essential characteristics for diagnosis of MST are the eccentric collarettes of stromal cells around renal tubules/blood vessels in concert with the evidence of the tumor cells labeled with anti-CD34. Complete excision is the treatment of choice and the prognosis is excellent. When adipose tissue component incorporated in the MST, it has to be differentiated from the other adipose tissue containing renal tumors such as Wilms tumor, metanephric adenofibroma, mixed epithelial stromal tumor, angiomyolipoma.

Acknowledgement

The author wishes to thank Dr. Anchalee Kruatrachue from the Department of Radiology, Queen Sirikit National Institute of Child Health, Bangkok, Thailand for her assistance in reviewing and providing the CT imaging picture.

Potential conflicts of interest

None.

What is already known on this topic?

It is well established that metanephric stromal tumor is a very rare renal neoplasm and commonly present in children but also its heterologous differentiation is present in an outnumbered group of cases.

What this study add?

This report first demonstrates the adipose differentiation that can be grossly seen in scattered foci of metanephric stromal tumor. The case with this unusual fatty differentiation is described and discussed about its differential diagnoses.

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เนื้องอกเมตาเนฟริกสะโตรมอลของไตที่มีเนื้อเยื่อไขมันร่วมด้วย: รายงานผู้ป่วยและบททวนวรรณกรรม

นรเศรษฐ์ สมานไทย, ทรงคุณ วิญญูวรรณ

รายงานเนื้องอกของไตชนิดเมตาเนฟริกสะโตรมอลในผู้ป่วยเด็กชายไทยอายุ 10 ปี ที่มีเนื้อเยื่อไขมันร่วมด้วย โดยพบเนื้อเยื่อไขมันหลายหย่อมอยู่ภายในก้อนเนื้องอก ซึ่งยังไม่เคยมีการรายงานและแสดงภาพประกอบมาก่อน การได้รู้จักเนื้องอกไตชนิดนี้มีความสำคัญโดยเฉพาะในการวินิจฉัยแยกโรคกับเนื้องอกของไตชนิดอื่น ๆ ที่มีเนื้อเยื่อไขมันเป็นส่วนประกอบ การให้วินิจฉัยโรคที่ถูกต้องนั้นสามารถป้องกันผู้ป่วยจากภาวะแทรกซ้อน และการรักษาที่ไม่จำเป็น