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Case Report

Is it a teratoma? is it a nephroblastoma? no, it is a teratoma with nephroblastoma: a rare tumor in pediatric oncology

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ABSTRACT

Mixed extragonadal teratoma with malignant nephroblastoma (TWN) is an exceptionally rare and complex combination of solid tumors which has been referred to as "teratoid Wilms tumor," "teratoid nephroblastoma," or "teratoma with nephroblastoma." Here we report a seven-year-old male who presented with a large retroperitoneal mass outside of the right kidney with lung metastases and diagnosed with a malignant mixed germ cell tumor with mature teratoma and extensive malignant nephroblastoma. Our case report highlights the controversial pathogenesis of this rare tumor and describes the variety of treatment regimens delivered for this type of tumor. In this case report, we described a young child with metastatic TWN who was successfully treated with multimodal approach based on Wilms tumor management including surgery, chemotherapy, and radiation.

Keywords: Wilms tumor, Nephroblastoma, Extragonal teratoma, Teratoma with nephroblastoma, Teratoid Wilms tumor, Teratoid nephroblastoma

INTRODUCTION

Mixed extragonadal teratoma with malignant nephroblastoma is an exceptionally rare and complex combination of solid tumors, posing significant clinical challenges. This rare tumor also known as teratoid Wilms' tumor is a scarce variant of nephroblastoma characterized by an abundance of teratoid elements in the tumor, has only been documented in less than 75 reported cases in the medical literature to date.[1-3] Due to the rare nature of this tumor, management and prognosis have not been well established.

Further research and documentation of such cases are crucial to advancing the understanding and management of this unique clinical entity. The purpose of our report is to present the case of a child with this rare tumor and provide an overview of the clinical presentation, diagnosis, management, and relevant literature.

CASE REPORT

A 7-year-old male presented to the pediatric emergency department with a complaint of fever, acute right lower quadrant abdominal pain, and lethargy. On examination, he was febrile at 38.2, tachycardic, and hypertensive. His abdomen was distended and rigid with guarding. Labs were remarkable for an elevated white blood cell count of 17 K/ul, elevated CRP, and LDH, but complete metabolic panel including renal function was normal. Additional labs including serum alpha fetoprotein and beta hCG were normal, homovanillic acid and vanillylmandelic acid in urine were unremarkable.

Computed tomography scan (CT) of the abdomen and pelvis with contrast revealed a dumbbell or peanut shaped mass in the right retroperitoneum which measured 13.4 cm oblique craniocaudal and 8.1x7.5 cm in short axis. The lesion extended towards the right inguinal canal and

at the superior margin has a dystrophic calcification measuring 7.7 mm (Figure 1). This mass deformed the obstructed kidney and there is loss of intervening fat plane with the kidney, ascending colon, junction of the duodenum, and uncinate process of the pancreas. There is a more solid lenticular component measuring 4.2 cm at the right lateral margin. It was noted that there was also omental/mesenteric involvement with lymphadenopathy, and metastatic deposits in the pelvis. CT of the chest showed multiple solid rounded pulmonary nodules in all lobes of both lungs compatible with pulmonary metastases (Figure 2).

The mass was causing compression of the right kidney and ureter, resulting in hydronephrosis, therefore the patient underwent a total retroperitoneal mass resection. Intraoperatively, the tumor was found to have ruptured into the peritoneum. It was noted that there was an intra-abdominal clot which grossly appeared to be possible tumor which arose from the retroperitoneum.

Pathology showed malignant mixed germ cell tumor with mature teratoma (10%) and extensive malignant nephroblastoma (90%). It was noted that there was in-situ tumor capsule rupture and spillage is noted, with the presence of tumor in the abdominal fluid washings. Sampling of lymph nodes was negative for tumor. Section of the retroperitoneal mass show a mature teratoma arising in the extra-renal, extra-adrenal soft tissues. The teratoma includes somatic tissues comprised of epidermis, adipose, and mesenchymal structures (cartilage and bone). Most of the tumor mass was comprised of malignant component resembling nephroblastoma with typical triphasic morphology with abundant nodules of cellular primitive blastema, interrupted by less cellular spindled mesenchyma and scattered primitive nephrogenic tubules. There was also ischemic-type necrosis associated with hemorrhage. Cytogenetics showed no evidence of loss of heterozygosity (LOH) 1p, gain 1q, LOH of 11p or LOH of 16q.

After an extensive literature search and consultation with experts in pediatric renal tumors, the decision was made to treat the patient per Wilms tumor therapy due to the predominance of malignant nephroblastoma in the tumor. Consequently, he was considered stage IV due to the presence of lung metastases and was treated per high-risk favorable histology Wilms children's oncology group (COG) protocol (AREN0533) with vincristine, dactinomycin, and doxorubicin (DD4A). Radiation to the whole lung and abdomen with concurrent chemotherapy was done immediately after tumor resection. Disease evaluation scans 6 weeks after initiating chemotherapy and radiation showed positive response with resolution of the multiple lung nodules and enhancement of the abdominal wall, mesentery, and omentum; therefore, his treatment was not changed to a more intensive regimen. Disease evaluation scans at the end of treatment did not show any evidence of disease.

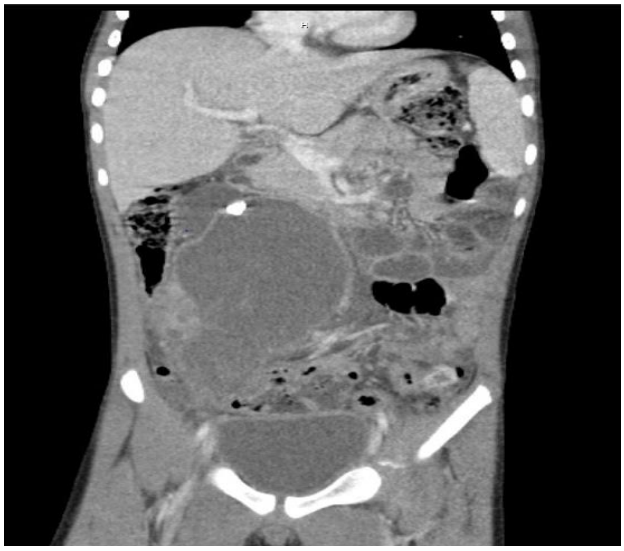

Figure 1: Retroperitoneal dumbbell shaped mass arising from retroperitoneum, measuring 13.4×8.1×7.5 cm.

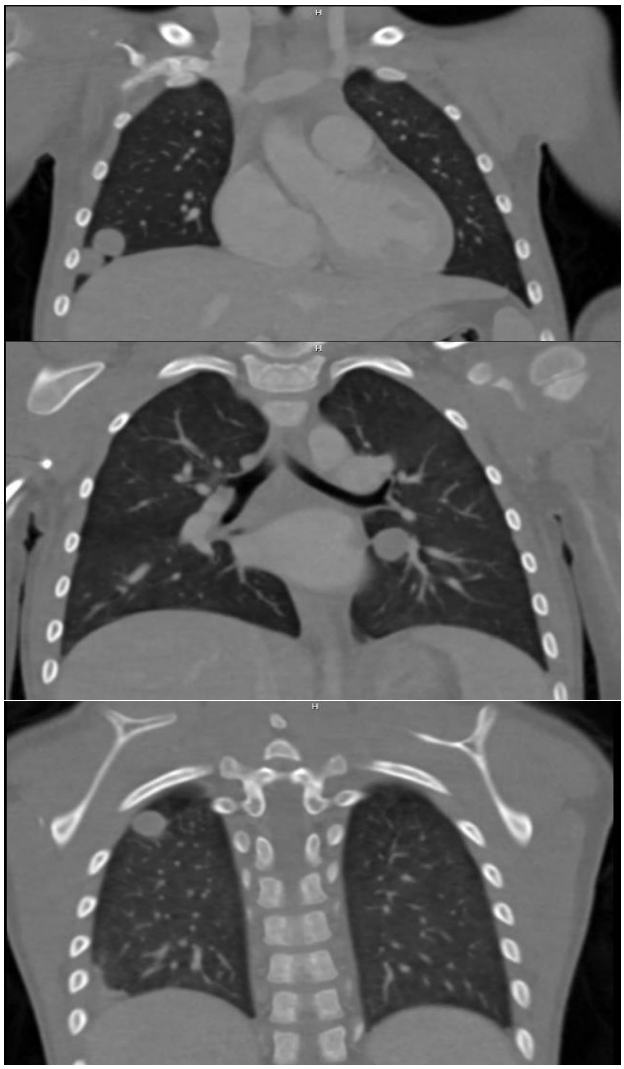

Figure 2: CT of chest showing multiple large lung nodules.

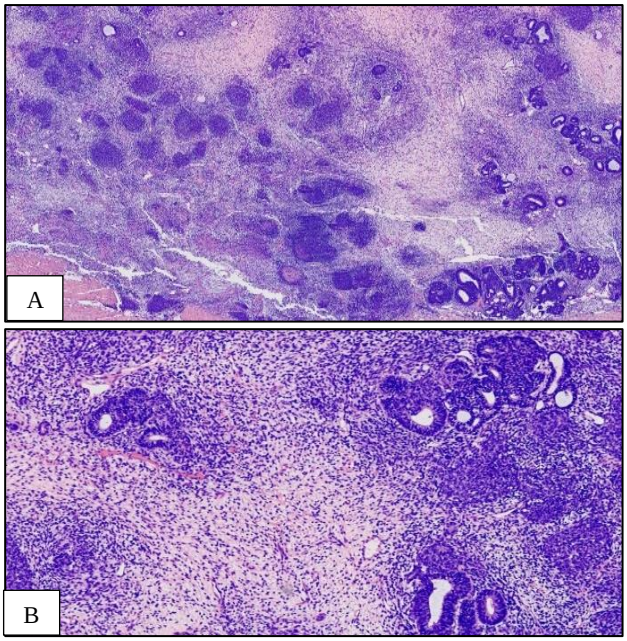

Figure 3 (A and B): 50x_H and E: Low power image of the dominant nephroblastoma component. 200x_H and E: High power of the nephroblastomatous component showing typical triphasic nephroblastoma harboring epithelial tubules, primitive mesenchyme and spindled stroma.

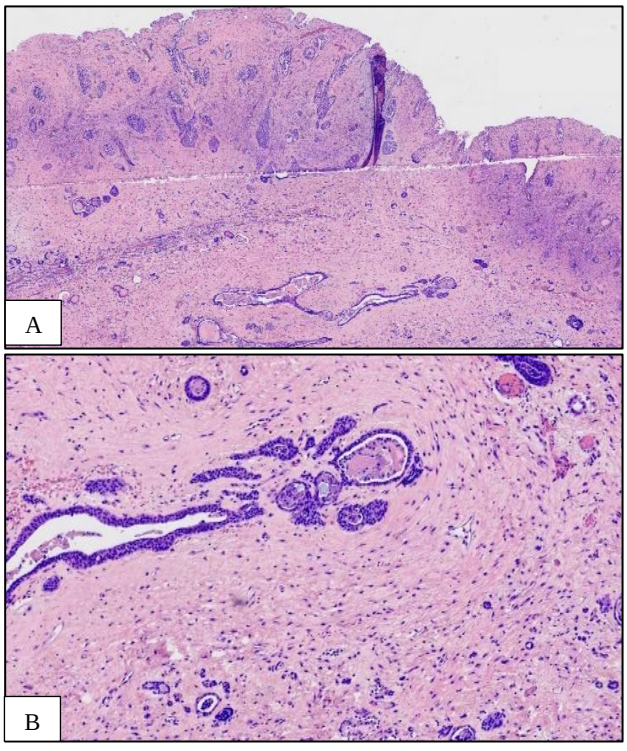

Figure 4 (A and B): 40x_H and E: Teratomatous component characterized by epidermal lining (top) and underlying epithelial cysts with occasional seromucinous glands (bottom). 200x_H and E: Higher power of the teratomatous epithelial cysts corresponding to somatic tissues within the mass.

DISCUSSION

Teratomas and nephroblastomas are both well-recognized solid tumors typically encountered in childhood. Teratomas are commonly found in the gonads and along the median line of the body, such as in the sacrococcygeal region, mediastinum, and retroperitoneum, exhibiting a diverse array of elements such as muscle, bone, and cartilage.[2,4,5] Conversely, nephroblastoma predominantly affects young children aged 1 to 4 years, originating as an abdominal mass within the kidney. This embryonic neoplasm arises from the metanephric blastema and is characterized by a classical triphasic histological pattern consisting of blastemal, stromal, and epithelial components.[3-4] Teratoid Wilms tumor also known as TWN is an extremely rare tumor with fewer than 75 cases documented. The true incidence and prognosis are difficult to determine since there are no standardized definitions of these tumors and treatment are not well documented. Although this tumor has been named as “teratoid Wilms tumor,” “teratoid nephroblastoma,” or “teratoma with nephroblastoma,” all masses were composed of heterogeneous tissues including adipose tissue, skeletal and smooth muscles, fibrovascular septa, cartilage, immature glomeruloid elements, and tubular structures; therefore, these masses are likely different manifestations of the same disease.[4]

The pathogenesis of TWN is currently unknown, and the origin is still controversial. Tumors in which there is no evidence of a teratomatous component are considered to arise within embryogenic nests of renal tissue. In contrast, Wilms tumors containing teratomatous components are thought to originate from teratoma. This type of lesion could represent a teratoma with a predominance of nephroblastic elements much like our patient case.[2,4,6] Further studies are needed to evaluate these mechanisms to gain a better understanding of the pathogenesis and development of TWN. This greater understanding may lead to the standardization of treatment for TWNs.

The most common site of TWN is the kidney (57.4%). Atypical locations include the retroperitoneum (13%), testis (5.6%), mediastinum (3.7%), abdomen (3.7%), thoracic cavity (1.9%), stomach (1.9%), neck (1.9%), vagina (1.9%), and uterus (1.9%). In the retroperitoneum, the most common symptom is the presence of an abdominal mass, which occasionally presents with abdominal distension and/or abdominal pain, like our patient.[4]

The literature review reports that patients diagnosed with teratoid nephroblastoma displayed clinical features and ages comparable to classical Wilms tumor cases. The cases predominantly consisted of young children, with an average age of 3.1 years at the time of diagnosis and a male-to-female ratio of 1.35. Common initial presenting symptoms included abdominal pain and the presence of an abdominal mass. Staging at diagnosis varied, and

some cases presented with metastases, primarily in the lungs and lymph nodes. Additionally, some patients exhibited hypertension and congenital abnormalities, such as horseshoe kidneys, inguinal hernias, clubbed feet, Beckwith-Wiedemann syndrome, bilateral cryptorchidism, and an ectopic ureteropelvic system.[3,4,7]

Both ultrasonography and computed tomography may be useful in the diagnosis of this disease, but only a tissue biopsy can establish a definitive diagnosis of TWN by identifying the heterogeneous tissues which makes up this tumor.

Microscopic examination of teratoid Wilms tumor masses is described as a diverse composition, encompassing adipose tissue, skeletal and smooth muscles, fibrovascular septa, cartilage, immature glomeruloid elements, and tubular structures, with the majority of tumors exhibiting favorable histological findings.[6,8] It is important to identify teratomatous elements in order to differentiate TWN from an extrarenal Wilms tumor. Secondly, it is important to determine if the teratoma components are mature since this may dictate the appropriate chemotherapy regimen for the patient.[6] Similarly, as our present case, if the tumor is made up of a mature teratoma with nephroblastoma, it may be more appropriate to treat based on a Wilms tumor regimen. Conversely, if the tumor is made up of an immature teratoma with nephroblastoma, it may be more appropriate to treat based on a combination of a Wilms tumor and germ cell tumor regimen.

Teratoid Wilms tumor is widely characterized as a non-aggressive and non-metastatic tumor, displaying a favorable prognosis, though metastatic cases have been reported, including our case.[9] Inoue et al summarizes 16 cases of teratoid Wilms tumor in the literature all arising from the kidneys with 10 unilateral and 6 bilateral. Although 9 cases received preoperative chemotherapy for the treatment of Wilms tumor, all except 1 case was resistant to the therapy. This resistance may be because of the mature, differentiated, heterologous elements that make up a large part of the tumor. The prognosis was excellent for patients who had complete tumor resection. Surgery remains the best treatment if the diagnosis is made preoperatively and the tumor is resectable. In this case series, most patients received postoperative chemotherapy and 6 patients received radiation therapy in addition to chemotherapy. Survival rate was 76% in this case series.[1] Details of the chemotherapy regimen was not described in this case series.

Li et al identified 53 previously reported cases in the literature with almost all being young children except for 6 adult men and 1 woman. A majority of the tumors arose from the kidney (31) and secondly from the retroperitoneum (7). Chemotherapy was administered in 38 patients and chemotherapy protocols that were utilized were not uniform and not described in detail, 19 received preoperative chemotherapy, 11 received both pre and postoperative chemotherapy and 30 only received postoperative chemotherapy, 6 received preoperative radiotherapy and 12 were administered postoperative radiotherapy, 49 of the 54 cases (90.7%) were alive and healthy at last follow up time point.[4]

Chemotherapy regimens for the treatment of TWN have included vincristine and actinomycin-D or vincristine, cyclophosphamide, and actinomycin-D.[2,7] An adult patient with ovarian teratoma with nephroblastoma was treated with 3 cycles of bleomycin, etoposide, and cisplatin followed by 3 cycles of vincristine and actinomycin-D10. Lastly, an adult with extrarenal Wilms tumor of the uterus with teratoid features was treated with 4 cycles of cisplatin and ifosfamide.[10]

The present case was treated based on high-risk favorable histology Wilms tumor regimen since the predominant histology was malignant nephroblastoma. He had a complete surgical resection upfront and postoperative chemotherapy. Due to the tumor rupture and spill into the peritoneum, he received whole abdomen radiation in addition to whole lung radiation for his metastatic disease. He had an excellent response with multimodal therapy which can be partly due to the predominant histology being malignant nephroblastoma which is well-known to be chemo-sensitive with an excellent prognosis. Although the pulmonary nodules were not biopsied at the time of diagnosis, they had a positive response to chemotherapy and radiation; therefore, we can presume that these nodules were chemo-sensitive and are likely to be nephroblastoma histologically. Similarly, Nakabayashi described a 33-year-old woman with metastatic ovarian teratoma with nephroblastoma. Histologic studies of the metastatic lesions in the omentum and spleen confirmed only the presence of only nephroblastoma without any teratoid component.[11] It is highly likely that metastatic cells behave more like classic nephroblastoma and are sensitive to cytotoxic chemotherapy.

CONCLUSION

TWN is a rare tumor that occurs in childhood and the clinical presentation and primary location can be variable. However, a definitive diagnosis can be made based on biopsy with tumors composed of heterogeneous tissues including adipose tissue, skeletal and smooth muscles, fibrovascular septa, cartilage, immature glomeruloid elements, and tubular structures. Despite the classic appearance of these tumors histologically, the pathogenesis remains controversial. Due to the rare nature of this tumor, management and prognosis have not been well established. In this case report, we described a young child with metastatic TWN who was successfully treated with multimodal approach based on Wilms tumor management including surgery, chemotherapy, and radiation. Further research including a tumor registry are needed to study this rare tumor and its biology in order to establish a standard treatment regimen.

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