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Tuberous Sclerosis Associated with Biphasic Adult Wilms' Tumor: A Case Report and Review of Literature

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Abstract

Tuberous sclerosis is an autosomal dominant genetic disorder characterized by lesions in the skin and benign tumors in various organs—retina, lungs, heart, brain, skin, and kidneys. Wilms' tumor is rare in adults. We present a unique case of Wilms' tumor in an adult with tuberous sclerosis. A 17-year-old girl presented with chief complaints of a large abdominal lump in the left loin region, associated with multiple acne-like dark skin patches all over the body (suggesting tuberous sclerosis), of 2 months' duration. Contrast-enhanced computed tomography suggested a large left renal tumor along with multiple variably sized, heterogeneously enhancing lymph nodes at preaortic, left para-aortic, left hilar, and mesenteric regions. She underwent laparoscopic radical nephrectomy and regional lymphadenectomy. Histopathology suggested a biphasic Stage 1 Wilms' tumor and was started on 16-week chemotherapy regimen of vincristine and dactinomycin. A patient with tuberous sclerosis complex presented with an abdominal mass and was diagnosed with biphasic Wilms' tumor as per the histopathology report. This presentation is unique and needs management accordingly.

Keywords
- tuberous sclerosis
- Wilms' tumor
- adult
- urology
- medical oncology

Introduction

We present a case of biphasic adult Wilms' tumor in a girl with tuberous sclerosis complex (TSC). TSC is an uncommon autosomal dominant neurocutaneous genetic disorder caused by mutations in the *TSC1* (chromosome 9q) or *TSC2* (chromosome 16p) gene, which encode tumor suppressor proteins—hamartin and tuberin, respectively.[1,2] Most of these mutations are sporadic.[3] Its incidence is 1 in 10,000 and is characterized by lesions in the skin and benign tumors in various organs—retina, lungs, heart, brain, skin, and kidneys.[1] Angiomyolipomas, unilateral or bilateral, are the most frequent manifestations of renal lesions seen in most of the patients.[1] Wilms' tumor is uncommon in adults, more so in a patient with tuberous sclerosis.

Case Summary

A 17-year-old girl who presented in the outdoor clinic with chief complaints of an abdominal lump in the left loin region associated with intermittent pain of 1 month duration. There was a history of multiple acne-like dark skin patches all over the body since the past 2 months (►**Fig. 1A, B**). There was no history of similar illness in the family.

At examination, there was a palpable nontender lump of 15×10 cm in the left hypochondrium and lumbar region, suggesting a left renal mass. Contrast-enhanced computed tomography suggested a large 20×12 cm well-defined heterogeneously enhancing soft tissue density lesion in the left kidney, indicating a complex, solid mass characteristic of malignancy such as renal cell carcinoma (►**Fig. 2**). There

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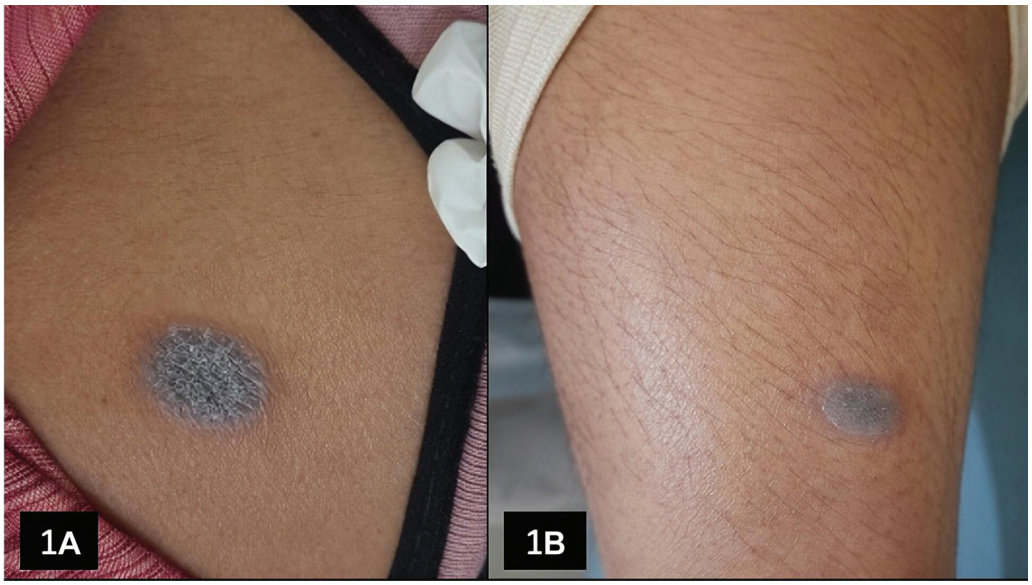

Fig. 1 (A, B) Clinical image of acne-like skin lesions.

were multiple variably sized, heterogeneously enhancing lymph nodes, the largest measuring 11 mm in short axis, located in the preaortic, left para-aortic, left hilar, and mesenteric regions. Multiple cortical cysts could be appreciated in the upper and lower poles of the left kidney. In view of the skin lesions, TSC was suspected, and cardiology, ophthalmology, neurosurgery, and dermatology opinions were taken.

The patient underwent laparoscopic radical nephrectomy and regional lymphadenectomy. Intraoperatively, there was a large left renal mass almost replacing the whole kidney, extending from the lower surface of the spleen to the level

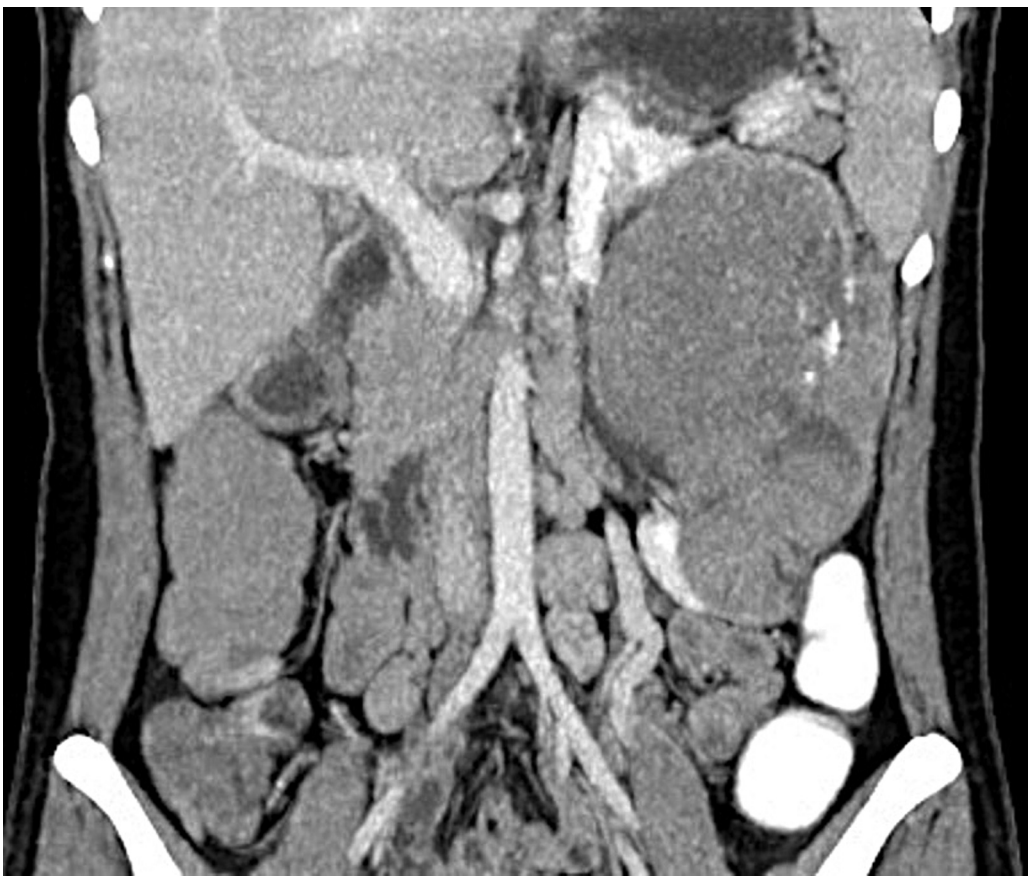

Fig. 2 Computed tomography of the abdomen and pelvis of the patient showing a large 20 × 12 cm well-defined heterogeneously enhancing soft tissue density lesion of the left kidney.

Fig. 3 Image of the excised specimen.

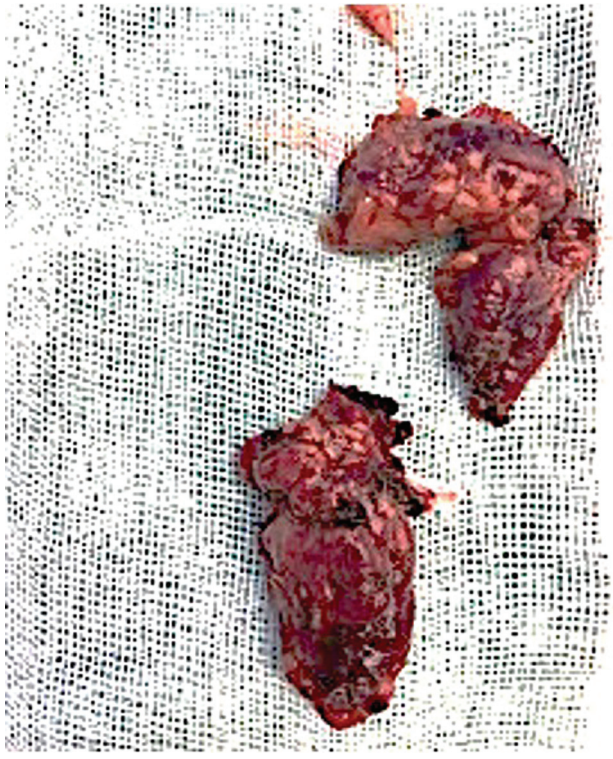

Fig. 4 Image of the excised lymph nodes.

of the iliac vessels. Two renal arteries and one renal vein were identified, and multiple large lymph nodes were noted in the para-aortic and interaortocaval region. Regional lymphadenectomy was done, and a separate specimen was kept in a lap bag and retrieved. ►**Fig. 3** depicts the retrieved specimen, and ►**Fig. 4** depicts the excised lymph nodes.

Postoperative period was uneventful. Per urethral catheter was removed on the first postoperative day, and orals were allowed the same day. The patient was discharged on the third postoperative day. Histopathology suggested a biphasic Wilms' tumor with involvement of the tumor in the pelvicalyceal system but no perineural and perivascular invasion. The renal capsule and hilar sinus were free from tumor, and all margins were free. The 5 hilar and 20 retroperitoneal lymph nodes sent for histopathology were negative for tumor cells. The patient thus had Stage 1 Wilms' tumor and received 16-week chemotherapy regimen of vincristine and dactinomycin. She is presently on follow-up and has no complaints. She has no recurrence at 1-year postchemotherapy.

Discussion

TSC is an autosomal dominant genetic disease characterized by benign tumors in various organs.[1] The most frequent renal tumors in a patient with tuberous sclerosis are angiomyolipomas seen in ~34 to 80% of patients.[1] These usually appear later in life and can present with fatal bleeding (if size is more than 4 cm) and consequently hypovolemic shock.[1] Other renal tumors reported to be associated with TSC are renal cell carcinomas, Wilms' tumor, leiomyosarcoma, liposarcoma, oncocytoma, and leiomyoma.[4] Diagnosis is made usually by dermatological examination and radiological imaging. Renal angiomyolipomas of size more than 4 cm have high risk of hemorrhage and should be embolized under radiology guidance as early as possible.[1]

Wilms' tumor or nephroblastoma is the most common pediatric renal malignancy and is derived from primitive metanephric blastema.[5,6] Wilms' tumor is not common in adults and represents less than 1% of all diagnosed renal tumors.[7] The incidence of Wilms' tumor as per Western literature is estimated to be 0.2 per million per year.[8] Adult Wilms' tumor clinically presents with abdominal pain and hematuria.[8] Presentation with distant metastases is also not uncommon.[5]

Preoperative diagnosis is difficult because of the low index of suspicion of Wilms' tumor in adults. The staging criteria and management of adult Wilms' tumor are the same as those for pediatric Wilms' tumor. Histopathologically, adult Wilms' tumor has similar classical triphasic histopathological features of pediatric Wilms' tumor—blastemal, epithelial, and stromal elements.[5] Marked structural diversity has been reported, and the presence of all three elements in the same case is uncommon.[6]

The available literature on TSC-associated Wilms' tumor dates back to 1987, when Grether et al[9] published the association first; however, the abstract is not available in PubMed. In 1991, Occhionorelli et al[10] reported about the abdominal aortic aneurysm in a young female who was a known case of TSC and had undergone nephrectomy for

Table 1 Table comparing the reported cases in the literature with the index case

S/N	Name of the author	Year of publication	Age/sex	Clinical presentation	Management	Molecular diagnosis
1	Occhionorelli et al[10]	1991	Young female	A known case of TSC presented with aortic aneurysm and stenosis with a history of right nephrectomy (mesoblastic nephroma)	Management was surgical	
2	Spreafico et al[11]	2011	Young female	Abdominal pain and distention in a known case of TSC	Nephrectomy for renal tumor—confirmed on HPR as Wilms' tumor (anaplastic)	De novo TSC2 mutation, c.4934–4935delTT, leading to a p. F1645CfsX7 Loss of the constitutional wild-type TSC2 allele, and loss of heterozygosity of the *WT1* gene. Deletion of the *WTX* gene was also present, but it involved the functionally inactive X chromosome
3	Wang et al[12]	2022	One patient	One patient of 93 total studied patients with TSC and renal tumors had a Wilms' tumor	Not mentioned	*TSC1* gene
4	The present case		17 y/female	Abdominal lump with skin lesions	Nephrectomy (histopathology suggesting Wilms' tumor) followed by chemotherapy	Not done

Abbreviation: TSC, tuberous sclerosis complex; HPR, histopathology report.

mesoblastic nephroma. In 2011, TSC-associated Wilms' tumor was reported in a young female by Spreafico et al.[11] In 2022, Wang et al[12] reported one case of Wilms' tumor among 93 patients with renal tumors associated with TSC. The details are tabulated in ►**Table 1**.

Diagnosis is based on well-known criteria described by Kilton et al in 1980[13]—(1) the tumor under consideration should be a primary renal neoplasm; (2) presence of primitive blastemal spindle or round cell component; (3) formation of abortive or embryonal tubules or glomerular structures; (4) no area of tumor diagnostic of renal cell carcinoma; (5) pictorial confirmation of histology; and (6) patient's age should be $>$ 15 years.[8]

Prognosis is poor compared with childhood Wilms' tumor in view of the advanced stage at diagnosis and no definitive protocols for management of adult Wilms' tumor, although multimodality therapy with chemotherapy and radiotherapy is recommended.[14] Long-term follow-up is advised. Genetic testing and counseling can aid in determining the type of TSC and may also allow for gene therapy if possible.

Conclusion

This case is unique as a patient with TSC presented with an abdominal mass and was diagnosed with a biphasic Wilms' tumor as per the histopathology report.

Authors' Contributions

This manuscript has been read and approved by all the authors, the requirements for authorship have been met, and each author believes that the manuscript represents honest work.

Ethical Approval

Waived as it is a retrospective case report.

Patient's Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images; anonymity was maintained.

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None.

Conflict of Interest
None declared.

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