Brain Metastasis of Wilms Tumor in Adult

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Key words
- Brain metastasis
- Nephroblastoma
- Wilms tumor in adult

Abbreviations and Acronyms
MRI: Magnetic resonance imaging
WT: Wilms tumor

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BACKGROUND: **Wilms tumor is a rare renal tumor in adults. To the best of our knowledge, only a small number of cases of brain metastasis have been reported in the literature. We report the case of a 29-year-old female with headache and dizziness, with a parietal mass and pathologic diagnosis of Wilms tumor metastasis.**

CASE DESCRIPTION: **The patient was admitted with a 3-month history of lumbar pain and 2 months of progressive headache associated with dizziness. Abdomen magnetic resonance imaging showed a renal mass. Post nephrectomy, the neurologic signs worsened and a head magnetic resonance imaging presented in the right parietal lobe, convexity, heterogeneous lesion with little perilesional edema. The patient underwent a complete surgical resection with success. The adjuvant treatment was chemotherapy.**

CONCLUSIONS: **Few cases of brain metastasis of Wilms tumor exist in the literature. Surgical management is considered in cases with intracranial hypertension or focal signs. The adjuvant treatment options are immunotherapy and chemotherapy.**

INTRODUCTION

Nephroblastoma, or Wilms tumor, is a malignant renal neoplasm commonly found in children with a probability of 5%, considering all possible tumors. In adults it is rare, accounting for 0.5% of all renal neoplasms, an incidence of 0.2 cases per million. Only 3% of all nephroblastomas are reported in adults. Brain metastasis is equally rare with a frequency of 1%–2% in children and is unknown in adults due to its rarity.[1,2]

The most common neurologic symptoms are linked to elevated intracranial pressure. Brain magnetic resonance imaging (MRI) is the best imaging examination despite its heterogenic nature and unspecific findings.[3-5]

To the best of our knowledge, there are no official neurologic treatment guidelines available; however, a consensus showing better outcomes in patients undergoing a brain metastasis resection exists.

The aim of this study is to describe a rare case of Wilms tumor with brain metastasis in an adult.

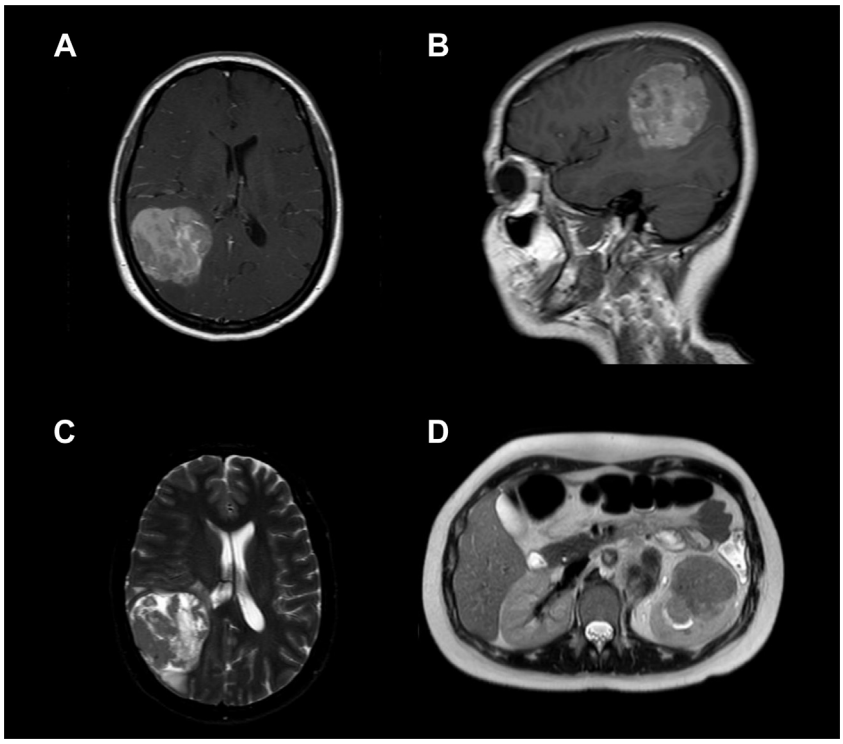

Figure 1. (**A** and **B**) Magnetic resonance imaging (MRI) in axial and sagittal gadolinium showing a solid cystic parietal mass effect lesion with heterogeneous contrast enhancement. (**C**) MRI with axial T2 sequence, which shows posterior parietal area of brain edema. (**D**) Abdomen MRI with left kidney primary lesion.

CASE REPORT

A 29-year-old Caucasian woman had a 3-month history of progressive left lumbar pain without irradiations. Two months later a progressive right temporal headache and dizziness occurred.

On admission the patient presented with a Giordano sign at the left lumbar region, without pupillary changes or focal signs. The urology team conducted MRI of the abdomen, which showed a left renal lesion with mass effect, hypointense in T1 and hyperintense in T2 presenting heterogeneous contrast enhancement. A total nephrectomy with regional lymphadenectomy was performed. Postoperatively, the patient's right temporal headache and dizziness got worse and MRI of the head was performed for investigation. It showed a mass evolving in the right parietal, temporal, and occipital lobes, with a diameter of 6 cm. It presented with a heterogenic pattern in contrast sequence, hyperintense in T2 and hypointense in T1. A complete resection of the cranial mass was performed, and the patient evolved without deficits. On supplementary investigation small lesions were found in the lungs and liver (Figures 1 and 2).

The pathologic study showed focal WT1 expression to the renal lesion and a diffuse WT1 and PAX 8 positivity in the encephalic lesion. No *BRAF* mutations were identified (Figure 3).

The patient was classified by Tumor, Node, Metastasis staging with T3 No M1. The adjuvant treatment was performed with radiotherapy, and chemotherapy with savolitinib was initialized following the SAVOIR clinical trial in Phase III study protocol.

DISCUSSION

Also called nephroblastoma, Wilms tumor (WT) is a rare renal tumor that originates from the totipotent cells of the metanephrogenic blastemal remnants. Histologically it is characterized by 3 possible cell patterns: stromal, epithelial, and blastemal cells. In adults it is uncommon for the 3 patterns to be present in the same case, presenting blastemal predominance, which is possibly the most malignant component.[6-8]

The immunohistochemical study shows positivity to WT-1, one of the first genetic alterations that is associated with 11p13 deletion. Other possible mutations are loss of heterozygosity of 1p and 16q, WT-2 expression due to the *11p15* gene, and abnormalities in chromosomes 7p, 17p, and 19q. Pax-8 and Pax-2 antibody expression is sensitive for epithelial and blastemal components.

In our patient the epithelial pattern was prevalent with immunohistochemical positivity for WT−1 diffusely, Pax-8, and vimentin.[7,9-11]

The main Wilms tumor classification was proposed by the National Wilms Tumor Study Group being divided in 5 stages: I—tumor limited to kidney and completely excised; II—tumor extended beyond kidney, the excision is complete; III—residual tumor limited to abdomen; IV—hematogenous metastases; V—bilateral renal involvement at diagnosis.[12]

Metastasis rates are superior in adults, accounting for 29% compared with 10% in children. It is most common in the lungs, followed by liver, bone, lymph nodes, skin, orbit, and the contralateral kidney. Brain metastases occur in 1%−2% of children and are uncertain in adults due to pathology rarity.[2,13]

The most common neurologic symptoms are the elevation of intracranial pressure, focal signs like headache, dizziness, vomiting, visual alterations, paresis, paresthesia, seizure, and mental confusion.[2,4,13]

Neuroimage examination with MRI is the best image method to detect the WT brain metastasis; however, it shows unspecific findings like heterogenic signal in T1 and T2 sequences, with homogenic enhancing post gadolinium administration in small lesions and heterogenic enhancement for larger tumors. The surrounding edema can be extensive, presenting a bright signal in T2 and flair sequences.[3,4]

The main differential diagnoses of brain metastasis of WT are glioblastoma, brain

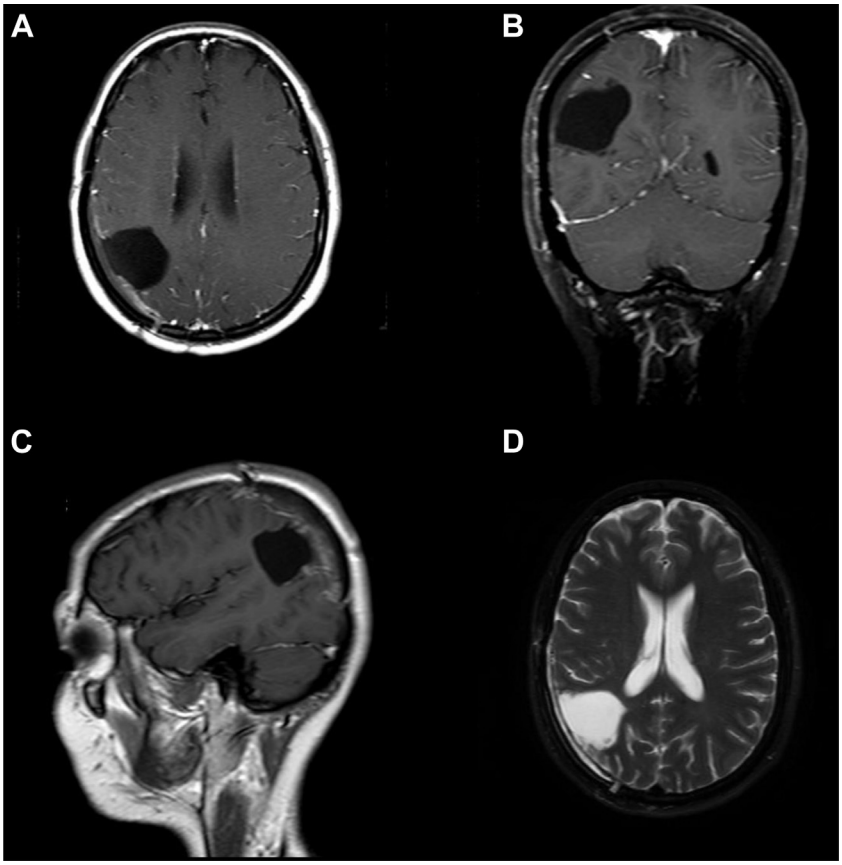

Figure 2. (**A**−**C**) Postoperative magnetic resonance imaging (MRI) in axial, coronal, and sagittal gadolinium showing complete tumor resection. (**D**) MRI with axial T2 sequence, showing edema resolution post tumor resection.

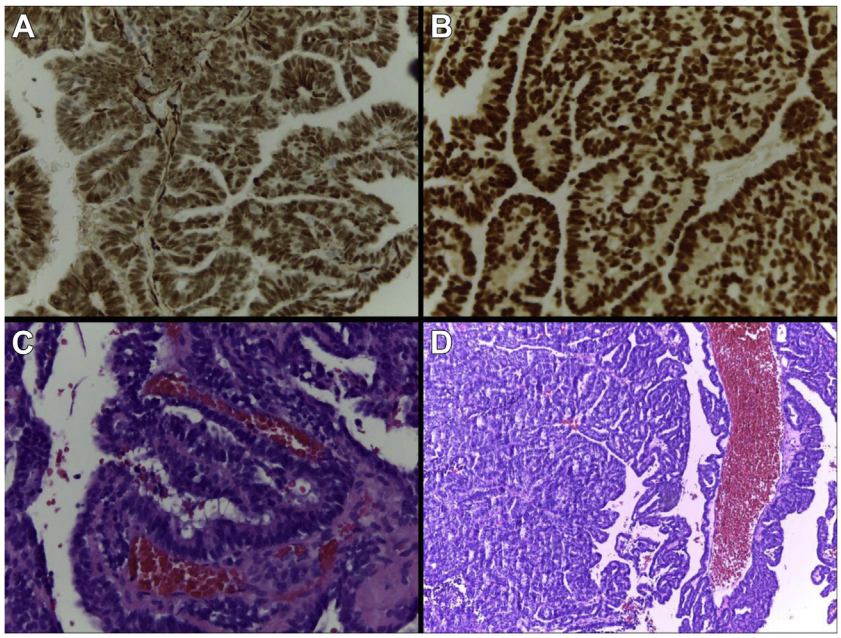

Figure 3. Biopsy images. (**A**) WT-1 expression positive. (**B**) PAX-8 expression positive. (**C** and **D**) Eosin-hematoxylin stain showing epithelial pattern.

abscess and other metastatic tumors. In these cases, the clinical history, surgical findings and a simple histological analysis can differentiate it. In some cases of metastasis the immunohistochemical confirmation tests confirm diagnosis.[2-4,13]

There is no official guideline for Wilms tumor brain metastasis treatment, but an association by surgery, radiotherapy, and chemotherapy are actually the treatment of choice. Surgical resection is important, bringing benefits like improvement of focal signs caused by mass effect and control of intracranial hypertension. Vincristine, actinomycin D, doxorubicin, and cyclophosphamide are the most commonly used chemotherapy drugs, despite ifosfamide and etoposide recently showing superior results. Other adjuvant treatment option is immunotherapy, with drugs like sunitinib and savolitinib, which are inhibitors of c-MET receptor tyrosine kinase.[14-17]

CONCLUSION

Brain metastasis of Wilms tumor shows unspecific clinical and radiologic findings. It needs to be suspected if the patient with history of Wilms tumor has neurologic signs like headache or neurologic deficits. The diagnosis is confirmed by immunohistochemical positivity to WT-1.

The gross total resection seems to provide a survival benefit and should be attempted always, if possible (i.e., if the patient's clinical condition permits).

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