CASO CLÍNICO/CASE REPORT

Hemiathetosis-Hemichorea as Initial Manifestation of Brain Metastases from Urothelial Carcinoma

Hemiatetose-Hemicoreia como Manifestação Inicial de Metastização Cerebral de Carcinoma Urotelial

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DOI: https://doi.org/10.46531/sinapse/CC/246/2026

Informações/Informations:
Caso Clínico, publicado em Sinapse, Volume 26, Número 3, julho-setembro 2026. Versão eletrónica em www.sinapse.pt;
Case Report, published in Sinapse, Volume 26, Number 3, July-September 2026. Electronic version in www.sinapse.pt

Keywords:
Brain Neoplasms/secondary;
Carcinoma, Transitional Cell/secondary;
Chorea/etiology;
Movement Disorders/etiology;
Urinary Bladder Neoplasms.

Palavras-chave:
Carcinoma de Células Transitórias/secundário;
Coreia/etiologia;
Neoplasias da Bexiga Urinária;
Neoplasias Encefálicas/secundário;
Perturbações do Movimento/etiologia.

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Recebido / Received: *2026-07-01*
Aceite / Accepted: *2026-08-17*
Ahead of Print: *2026-09-19*

Abstract

Brain metastases rarely present with movement disorders. We report a case of a 77-year-old woman with invasive urothelial carcinoma who developed right hemichorea-hemiathetosis as the initial manifestation of multiple brain metastases. The patient presented to the emergency department with behavioral changes, disorientation, and involuntary movements of the right hemibody lasting five hours. Brain magnetic resonance imaging revealed multiple intra-axial secondary lesions, including a left subthalamic lesion. She was treated with dexamethasone and haloperidol for symptomatic control. The patient died three weeks after admission. This case illustrates a rare presentation of brain metastases and reinforces the importance of considering neoplasia in the differential diagnosis of acute-onset hemichorea-hemiathetosis, particularly in oncological patients.

Resumo

As metástases cerebrais raramente se manifestam com distúrbios do movimento. Apresentamos o caso de uma mulher de 77 anos com carcinoma urotelial invasivo que desenvolveu hemicoreia-hemiatetose direita como manifestação inicial de metastização cerebral múltipla. A doente apresentou-se ao serviço de urgência com alteração comportamental, desorientação e movimentos involuntários do hemicorpo direito com cinco horas de evolução. A ressonância magnética cerebral revelou múltiplas lesões secundárias intra-axiais, incluindo lesão subtalâmica esquerda. Foi medicada com dexametasona e haloperidol para controlo sintomático. A doente faleceu três semanas após o internamento. Este caso ilustra uma apresentação rara de metástases cerebrais e reforça a importância de considerar neoplasia no diagnóstico diferencial de hemicoreia-hemiatetose de início súbito, particularmente em doentes oncológicos.

Introduction

Hemichorea-hemiathetosis (HCA) is a rare hyperkinetic movement disorder characterized by involuntary, abrupt, large-amplitude movements affecting one side of the body.[1,2] Traditionally associated with contralateral subthalamic nucleus lesions, recent studies demonstrate that only a minority of cases present with direct involvement of this structure and may result from lesions in various locations of the basal ganglia, thalamus, or even cerebral cortex.[3,4]

The most frequent etiologies of HCA include cerebrovascular disease (responsible for approximately 50% of non-genetic cases) and non-ketotic hyperglycemia.[1,4] Brain neoplasms, primary or secondary, constitute a rare cause of HCA, being more frequently described in primary central nervous system lymphomas.[1]

Brain metastases represent the most frequent intracranial tumors in adults, affecting 10-20% of oncological patients.[1,2] The most common symptoms include headache, focal neurological deficits, cognitive changes, and epileptic seizures.[1,3,4] Initial manifestation with movement disorders is exceptional, occurring in less than 1% of cases, and is generally associated with lesions involving the basal ganglia or adjacent structures.[1,5,6]

We report a case of HCA as the initial manifestation of multiple brain metastases in a patient with invasive urothelial carcinoma, illustrating an unusual clinical presentation of this pathology.

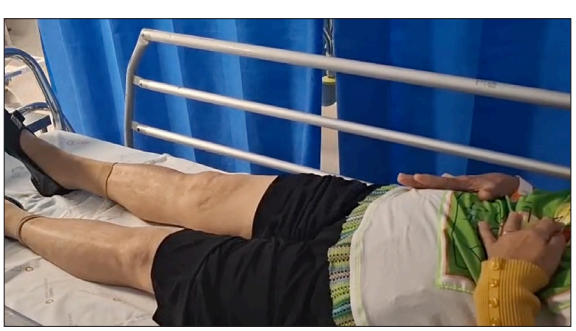
Case Report

A 77-year-old female patient, independent for activities of daily living, living with her husband, presented to the emergency department with behavioral changes, temporal and spatial disorientation, disorganized behavior, and slurred speech with one day of evolution, associated with altered movement of the upper and lower limbs with five hours of evolution.

Relevant personal history included high-grade invasive urothelial carcinoma with extensive invasion of the lamina propria and muscularis propria, without angiolymphatic invasion (pT2), diagnosed two years earlier. She had a history of early recurrence after first transurethral bladder resection, with invasion of the lamina propria but without invasion of the muscularis propria (pT1NxMx). She underwent radical cystectomy with cutaneous ureterostomies seven months before the current admission. Additionally, she had thyroid nodules with hypothyroidism, arterial hypertension, dyslipidemia, and spondylosis with L4-S1 disc degeneration. She had undergone adjuvant chemotherapy with gemcitabine and carboplatin, completing up to the first dose of the sixth cycle, which was discontinued due to hematological toxicity. She was proposed for treatment with pembrolizumab.

Usual medication included lactulose as needed, oral potassium chloride on alternate days, levothyroxine 0.025 mg daily and megestrol 160 mg oral daily. She had no regular use of metoclopramide or other antidopaminergic drugs. She had no known allergies.

On admission to the emergency department, the patient was agitated and restless. Further examination revealed continuous, involuntary, irregular movements of the right lower and upper limbs, that flowed randomly from one body segment to another. The right upper limb demonstrated both distal choreoathetosis with purposeless movements of the hand and fingers, and more proximal movements with flinging motions of the shoulder and arm. The right lower limb showed similar distal choreoathetosis in the foot and toes. These movements were continuous, unpredictable in timing and location, and appeared to worsen with anxiety and attempts at voluntary movement. The patient occasionally attempted to incorporate these involuntary movements into seemingly purposeful gestures (parakinesia). Thus, a clinical diagnosis of hemiathetosis-hemichorea was made (**Video 1**).



Video 1. Right-sided, distal-predominant, involuntary writhing movements (choreoathetosis), most prominent in the hand, but also noticeable in the foot. The proximal shoulder movements were less frequent and not captured in this video. (see the video)

Additional neurological examination showed involvement of the face with irregular grimacing and perioral movements and left kinetic hemiataxia, manifested by dysmetria and intention tremor during finger-to-nose

and heel-to-shin testing. No language deficit was observed. Motor strength could not be reliably assessed in the right limbs due to the continuous involuntary movements, but appeared grossly preserved in the left limbs. Deep tendon reflexes were symmetrical and normoactive. Plantar responses were flexor bilaterally. Sensory examination was unremarkable.

She was hemodynamically stable, afebrile, with capillary blood glucose of 99 mg/dL. Cardiopulmonary auscultation revealed no abnormalities, she had no peripheral edema, and the abdominal physical examination was normal.

Brain computed tomography revealed multiple intra-axial secondary lesions, including a left subthalamic lesion.

Treatment was initiated with a bolus of 10 mg of intravenous dexamethasone followed by a progressive oral taper and, for symptomatic control of hemichorea-hemiathetosis, haloperidol 0.5 mg three times daily. The patient was evaluated by the neurosurgery and urology teams, with no directed surgical measures proposed. She was admitted to the oncology ward for symptom management and palliative care.

Brain magnetic resonance imaging (**Fig. 1**) confirmed multiple secondary intra-axial supra and infratentorial lesions, including both subthalamic nuclei, the right thalamus and the right caudate head. Additional lesions were observed in the right lateral and medial mid-temporal regions, left lateral pons and left posterior cerebellar hemisphere. Interestingly, both the right temporal and left cerebellar hemispheric lesions showed significant surrounding vasogenic edema, with only mild edema around the left subthalamic nucleus lesion.

Despite mild improvement of the extrapyramidal symptoms, the patient's consciousness and overall status continued to decline. She did not start radiation therapy due to the rapid deterioration of her functional status. She eventually became comatose and died 34 days after admission.

Discussion

This case illustrates a rare presentation of brain metastases manifesting primarily as hemichorea-hemiathetosis. HCA as the initial manifestation of brain neoplasia is exceptional, having been described mainly in cases of primary central nervous system lymphoma and, more rarely, in metastases from breast, lung, and gallbladder carcinomas.[1,5,6]

The pathophysiology of HCA relates to dysfunction of basal ganglia circuits. Classically, this disorder was attributed to contralateral subthalamic nucleus lesions.[4] However, recent reviews demonstrate that the subthalamic nucleus is directly involved in only 27% of cases, and HCA may result from lesions in multiple locations, including putamen, caudate, globus pallidus, thalamus, and even cerebral cortex.[3] In the present case, brain MRI identified a left subthalamic lesion, compatible with the clinical presentation of right hemichorea, although the presence of multiple lesions in the basal ganglia bilat-

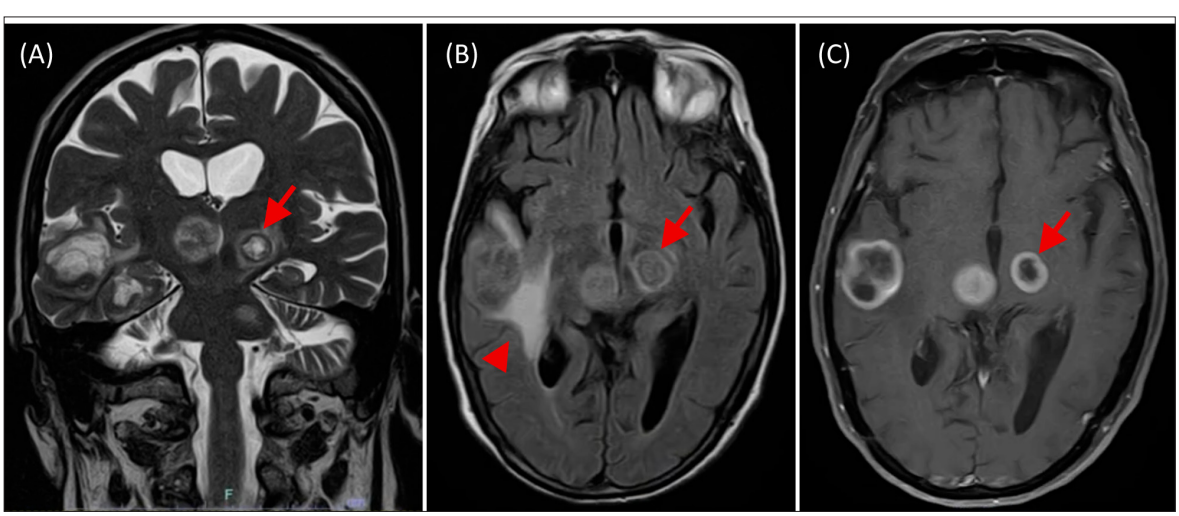


Figure 1. Brain MRI. (A) Coronal T2-weighted image, (B) axial FLAIR image, (C) Axial post-contrast T1-weighted image, showing multiple supra- and infratentorial secondary lesions, including the left subthalamic nucleus (arrows). This lesion caused right-sided hemichorea-hemiathetosis, which led the patient to the emergency department. Additional lesions can be seen in the right subthalamic nucleus, right thalamus, right lateral and medial temporal lobe and left lateral pons. The right temporal lesion is surrounded by significant vasogenic edema (arrowhead).

erally may have contributed to the clinical picture.

Recent studies using functional network mapping have demonstrated that anatomically heterogeneous lesions causing HCA are located in regions functionally connected to the posterolateral putamen, suggesting that HCA results from dysfunction of a specific neuronal network and not just from injury to an isolated structure.[5] This network perspective helps explain the diversity of lesional locations associated with this movement disorder.

The proposed mechanism involves thalamocortical disinhibition secondary to loss of inhibitory control of the internal globus pallidus over the thalamus, resulting from dysfunction of the subthalamic nucleus or other basal ganglia structures.[6,7] SPECT studies have demonstrated decreased cerebral blood flow in the basal ganglia contralateral to the chorea and increased flow in the thalamus, corroborating this pathophysiological hypothesis.[6]

Brain metastases most frequently present with headache (30%-53%), focal motor deficits (20%-35%), cognitive changes (36%), and epileptic seizures (22%-35%).[1,3,8] Manifestation with movement disorders is extremely rare. In a series of 857 patients with breast cancer referred for neuro-oncological evaluation, the most frequent symptoms were headache, focal motor deficit, and sensory complaints, with no mention of movement disorders.[8] Similarly, in a cohort of 254 patients with brain metastases as the initial manifestation of systemic neoplasia, the most common symptoms were headache and motor deficit, without reference to chorea or ballismus.[2]

The rarity of presentation with HCA may relate to the need for specific involvement of basal ganglia structures, particularly the subthalamic nucleus or regions functionally connected to the posterolateral putamen.[5] Most brain metastases are located at the cortico-subcortical junction of the cerebral hemispheres, following the distribution of cerebral blood flow, with a lower frequency of deep basal ganglia involvement.[2,9]

Urothelial carcinoma seldom metastasizes to the central nervous system (3%-7%), with brain metastases generally being a late manifestation of the disease.[5,10,11] Presentation with movement disorders is even rarer, with no reported cases of HCA found in the literature. The prognosis of patients with brain metastases from urothelial carcinoma is generally poor, with median survival ranging from 2 to 3 months.[10,11,12]

The acute presentation of HCA is also unexpected, as brain metastases usually present with subacute neurologic symptoms due to tumor growth. In this case, we propose a role for the surrounding subthalamic edema, although less exuberant than in other metastases.

Treatment of HCA in the context of brain metastases is multifaceted, including therapy directed at the brain lesions and symptomatic control of the movement disorder. The approach to brain metastases depends on the number of lesions, location, patient functional status, control of systemic disease, and available therapeutic options.[2,7] In the present case, given the presence of multiple metastases and advanced systemic disease, conservative treatment with corticosteroid therapy was chosen.

Corticosteroids constitute first-line treatment for vasogenic edema associated with brain metastases and should be used at the minimum effective dose for the shortest possible time.[7] Dexamethasone is the corticosteroid of choice, with a typical initial dose of 4-10 mg, which can be increased in cases of extensive edema or severe symptoms.[7]

For symptomatic control of HCA, antidopaminergic agents, including typical and atypical neuroleptics, constitute first-line therapy.[3,13,14] Haloperidol, used in this case, has demonstrated efficacy in controlling chorea and ballismus.[13] Alternatively, risperidone and other atypical antipsychotics have been used successfully.[13] Tetrabenazine, a dopamine-depleting agent, is considered by some authors as the preferred option because it does not cause tardive dyskinesia. However, it is not available in all countries and is not readily available in the emergency setting.[3]

In cases refractory to pharmacological treatment, neurosurgical options may be considered, including deep brain stimulation of the internal globus pallidus or ventral intermediate thalamus, with favorable results reported in case series.[15,16] However, these approaches are generally reserved for cases of persistent and disabling HCA in patients with favorable prognosis, not being applicable in the context of advanced metastatic disease.

The prognosis of patients with brain metastases manifesting with movement disorders is generally poor, reflecting advanced systemic disease. ■

Contributorship Statement / Declaração de Contribuição

MM and NF: Conception, design and writing.

RV, JB and PF: Critical review of an important part of its intellectual content.

All authors approved the final version of the manuscript for publication and assume responsibility for all aspects of the work, ensuring the accuracy and integrity of the data presented.

MM e NF: Conceção, desenho e redação.

RV, JB e PF: Revisão crítica de parte importante do seu conteúdo intelectual.

Todos os autores aprovaram a versão final do manuscrito para publicação e assumem responsabilidade por todos os aspetos do trabalho, garantindo a exatidão e a integridade dos dados apresentados.

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Consentimento: Consentimento do doente para publicação obtido.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

Ethical Disclosures

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Patient Consent: Consent for publication was obtained.

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

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