

## Isolated bilateral abducens nerve palsy secondary to clivus metastasis of prostate adenocarcinoma undetected by magnetic resonance imaging<sup>☆</sup>



### Paresia del nervio abducens bilateral aislada secundaria a metástasis en clivus de adenocarcinoma de próstata inadvertida en resonancia magnética

Dear Editor:

Bilateral abducens nerve palsy has numerous causes, including cerebrovascular diseases, intracranial hypertension, carotid-cavernous fistulas, infection, trauma, Guillain–Barré syndrome, Wernicke–Korsakoff syndrome, and tumours. The condition rarely presents in isolation; when it does, presence of a tumour in the clivus should be ruled out. We present a case of bilateral abducens nerve palsy secondary to clival metastasis of prostate cancer.

Our patient was a 72-year-old man with 6-year history of prostate adenocarcinoma and bone metastases who visited our emergency department in March 2018 due to diplopia of 2 months' progression; he was receiving sixth-line treatment with radium-223 and had already completed 4 cycles, showing good tolerance. He initially reported difficulty with left eye abduction, developing difficulty with right eye abduction 2 weeks later.

The most recent imaging studies available, performed a month previously, were bone scintigraphy, which revealed bone lesions in multiple sites, including the skull and the left superior maxillary bone (see online supplementary material), and a chest and abdominal axial CT scan, which revealed no visceral anomalies. A week previously, the patient had undergone a brain MRI study, which was initially interpreted as normal; however, a later evaluation of MR images detected contrast uptake in the left abducens nerve (Fig. 1). An electromyography study conducted the previous day had yielded normal results.

The neurological examination detected isolated bilateral abducens nerve palsy (Fig. 2). A blood analysis detected no abnormalities; acute-phase reactants were within normal ranges. A head CT bone window study revealed diffuse hyperdensities in the clivus and sphenoid bones, suggestive of bone metastases (Fig. 1).

We started outpatient treatment with dexamethasone dosed at 4 mg/24 h, which was later down-titrated, and skull base radiation therapy (total dose of 30 Gy); given the progression of the cancer, treatment was switched to a new line of chemotherapy with cabazitaxel. Diplopia resolved within 4 weeks, and has not reappeared after 6 months of follow-up. No follow-up neuroimages are available.

The abducens nerve innervates the lateral rectus muscle, responsible for eye abduction. Its trajectory is subdivided into 5 segments<sup>1,2</sup>:

- 1 Intra-axial: the abducens nucleus is located in the posterior, caudal portion of the pons. It projects axons anteriorly through the medial lemniscus, which is medial to the fascicles of the facial nerve.
- 2 Cisternal: the abducens nerve emerges at the pontomedullary sulcus, lateral to the bundles of the corticospinal tract, and courses upwards along the prepontine cistern until reaching the posterior, dural surface of the clivus.
- 3 Dorello canal: after perforating the clival dura mater, the abducens nerve enters the Dorello canal to reach the cavernous sinus.
- 4 Cavernous sinus: the abducens nerve runs immediately lateral to the internal carotid artery.
- 5 Extracranial: the abducens nerve enters the orbit through the superior orbital fissure and reaches the lateral rectus muscle.

A clival lesion may therefore damage the abducens nerve bilaterally at the level of the Dorello canal.

The literature includes only 12 cases of isolated bilateral abducens nerve palsy secondary to tumours of varying aetiology. In 7 patients (3 with primary tumours and 4 with metastases), the clivus was the main structure involved: clivus chordoma (2),<sup>3,4</sup> multiple myeloma of the clivus (1),<sup>5</sup> clivus diffuse large B cell lymphoma (1),<sup>6</sup> clivus metastasis of Ewing's sarcoma (1),<sup>7</sup> clivus metastasis of small-cell lung carcinoma (1),<sup>8</sup> and clivus metastasis of lung adenocarcinoma (1).<sup>9</sup> The remaining 5 patients had pituitary adenoma (3),<sup>10–12</sup> primary non-Hodgkin's lymphoma of the sphenoid sinus (1),<sup>13</sup> and nasopharyngeal carcinoma (1).<sup>14</sup> The primary tumour was previously unknown in only one of the 3 patients presenting metastasis.<sup>9</sup> In some patients, abducens nerve palsy was bilateral from diagnosis, whereas other patients initially presented unilateral symptoms, with bilateral palsy developing over the course of several days or weeks.

Our case shows that bone metastases may go undetected in contrast brain MRI scans; head CT scans, particularly bone window images, may be extremely helpful for diagnosis.

To our knowledge, this is the first reported case of isolated bilateral abducens nerve palsy secondary to clival metastasis of prostate adenocarcinoma. Clivus tumours should be included in the differential diagnosis of bilateral abducens nerve palsy.

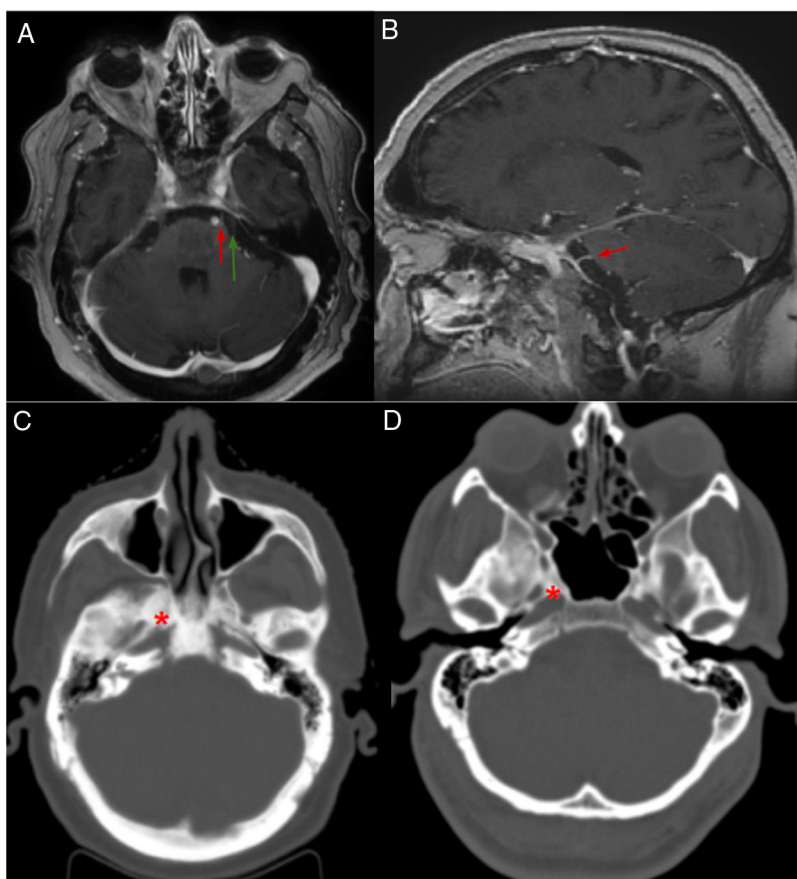
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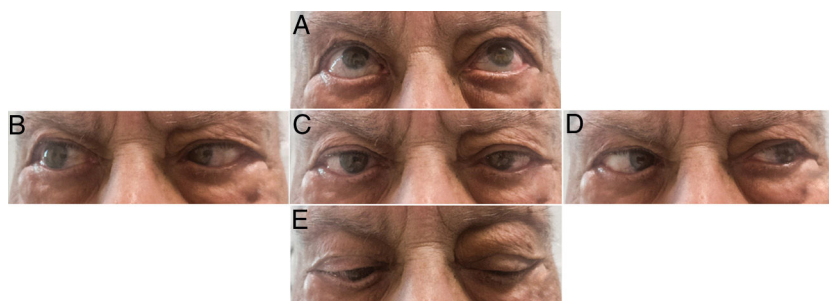
### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:  
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**Figure 1** A and B) Brain MRI. Contrast T1-weighted sequences: A) axial plane; B) sagittal plane. Red arrow: the left abducens nerve, emerging from the prepontine cistern, shows increased contrast uptake, probably due to involvement of the Dorello canal. Green arrow: trigeminal nerve, with no contrast uptake. C and D) Head CT scan (bone window), axial plane. C) Diffuse hyperdensities in the clivus and sphenoid bone (red asterisk), suggesting bone metastases. D) Image from a control, showing no hyperdensities at the base of the skull.



**Figure 2** A) Upward gaze with no alterations. B) Rightward gaze, with partial abduction of the right eye. C) Primary position, with bilateral esotropia. D) Leftward gaze, with mildly impaired abduction of the left eye. E) Downward gaze, with mild right eye esotropia. Preserved convergence (not shown). Examination performed after 14 days of treatment, with partial improvement, mainly of the left abducens nerve (increased contrast uptake on MRI). Diplopia persisted.

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## De novo *KAT6B* mutation, Say-Barber-Biesecker-Young-Simpson syndrome, and specific language impairment<sup>☆</sup>



### Mutación *de novo* en *KAT6B*, síndrome Say-Barber-Biesecker-Young-Simpson y trastorno específico del lenguaje

Dear Editor:

The histone acetyltransferase *KAT6B* is a component of the MOZ/MORF protein complex of epigenetic readers. The protein participates in both transcriptional activation and repression, and is involved in the development of the cerebral cortex.<sup>1,2</sup> As with other genes responsible for chromatin regulation, *KAT6B* dysfunction causes a multisystem developmental disorder.<sup>1</sup>

Some of the disorders known to be linked to the *KAT6B* gene include genitopatellar syndrome and Say-Barber-Biesecker-Young-Simpson syndrome (SBBYSS), also known as the Say-Barber-Biesecker-Young-Simpson variant of Ohdo syndrome.<sup>1,3–8</sup>

We describe the case of a boy with a *de novo KAT6B* mutation presenting a phenotype compatible with SBBYSS, without intellectual disability but with specific language impairment and severe attentional disorder.

The patient was an 8.5-year-old boy, an only child born to healthy parents of Spanish origin. The patient was brought to our centre due to severe learning difficulties, language problems, and attentional disorder; he did not present restricted interests or stereotypes, and displayed marked social interest. The patient displayed poor vocabulary, and made significant grammatical errors. He had no relevant family history. He was born after a normal pregnancy and delivery, with a birth weight of 2970 g (10th percentile) and a birth length of 49 cm (25th percentile). The patient had undergone surgery due to hypospadias and cryptorchidism. He presented severe language delay, using very few words at the age of 3 years. Motor development was normal, and the patient had started walking at 14 months of age. At the age of 6 years, a neuropsychological evaluation (WPPSI-III) revealed a verbal intelligence quotient (IQ) of 58 (percentile 0.3) (comprehension subtest, with a typical score of 1), and a manipulative IQ of 93 (33rd percentile); total IQ could not be calculated due to the difference between scales.

The physical examination detected no focal neurological signs, although the patient displayed severe language impairment (poor vocabulary and comprehension). He weighed 38 kg and was 140 cm tall (97th percentile). He also presented several dysmorphic features: blepharophimosis, ptosis, hypertelorism, bulbous nose, mild retrognathia, limited ability to separate the fingers in both hands, mild limitations on complete extension of the knees, and long toes on both feet (Fig. 1).

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