Dissemination of Prostate Adenocarcinoma to the Skull Base Mimicking Giant Trigeminal Schwannoma: Anatomic Relevance of the Extradural Neural Axis Component

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ABSTRACT

We report an unusual case of a large metastatic lesion from prostate adenocarcinoma with its epicenter located in Meckel's cave. The patient presented with acute neurological deterioration due to pontomesencephalic, cranial nerve, and temporal lobe compression. This lesion radiologically mimicked a giant trigeminal schwannoma. Complete surgical resection was achieved with improvement in the performance status of the patient. The anatomic relevance the extradural neural axis component in the process of dissemination of prostate adenocarcinoma to the skull base is highlighted.

KEYWORDS: Prostate, brain metastases, EDNAC, Meckel's cave, schwannoma

Intracranial deposits of metastatic prostate carcinoma are unusual and mostly reported in autopsy series.^{1,2} Confusion, headache, and memory deficits are the most common symptoms at presentation.³ Knowledge of prostatic disease usually precedes dissemination to the neuraxis with a median interval from diagnosis of 35 months for patients with prostate adenocarcinoma.³ This delay

in diagnosis may be partially due to late, nonspecific neurological symptoms and signs along with normal levels of serum prostate-specific antigen.⁴ Simultaneous presence of combined supratentorial and infratentorial metastatic deposits is exceedingly rare, representing 0.6% of all metastases of prostate adenocarcinoma and 3% of all brain parenchyma metastases.³

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CASE REPORT

This 66-year-old, right-handed African-American man with past medical history significant for long-standing untreated depression presented to our institution with a 3-week history of worsening gait and left facial weakness and numbness. Transient, self-limited episodes of confusion and disorientation lasting ~10 to 20 minutes, highly suggestive of complex partial seizures, had been observed over the 1-year period prior to presentation. In addition, a 30-pound weight loss occurred over a 6-month period.

On initial neurological assessment, the patient was alert, oriented to place only, and unable to cooperate for most components of the examination. Speech was limited and dysarthric; the patient was able to answer only some simple questions. A partial

left oculomotor ophthalmoplegia with an afferent pupillary defect and eyelid ptosis was evident. The response to testing of all three divisions of the trigeminal nerve was markedly depressed with lack of grimace to pinprick. In addition, a left facial and right hemibody paresis was present. Gag reflex was intact.

Laboratory workup was significant for elevated prostatic-specific antigen at 354 ng/dL, an elevated erythrocyte sedimentation rate at 92 mg/L, and alkaline phosphatase at 657 IU/L. Magnetic resonance imaging of the brain revealed an isointense complex skull base dumbbell-shaped mass lesion, involving the left cerebellopontine angle (3 cm) and ipsilateral middle cranial fossa and temporal lobe (3.4×4 cm), with its epicenter located in a completely obliterated Meckel's cave (Fig. 1A to C). There was significant mass effect

Figure 1 Preoperative magnetic resonance imaging (MRI) evaluation. Note how the lesion appears to arise from the dorsal root entry zone of the trigeminal nerve and Meckel's cave. (A) T1 weighted imaging (T1WI) postgadolinium MRI, sagittal view. (B) T2 weighted imaging postgadolinium, axial view. (C) T1WI postgadolinium MRI, coronal view. (D) Preoperative computerized tomography in bone window revealing absence of left petrous bone invasion. (E, F) Postoperative axial fluid attenuation inversion recovery (FLAIR) and coronal T1WI MRI postgadolinium enhancement showing gross total resection of the lesion.

from the tumor mass onto the left pons and ipsilateral medial temporal lobe with a surrounding rim of edema and hemosiderin. Diffusion weighted imaging (DWI) sequences were negative for acute ischemia. Intratumoral subacute to chronic methemoglobin was present on gradient echo sequence. The tumor did not appear to invade the petrous bone (Fig. 1D).

The differential diagnosis in this location included schwannoma of the trigeminal nerve, meningioma, and metastatic lesion. Systemic workup with computed tomography of chest, abdomen, and pelvis demonstrated an enlarged prostate measuring 7.7×6.2 cm with enlarged bilateral common iliac lymph nodes and several nodules in both lung parenchymae. Positron emission tomography scan showed extensive axial and appendicular skeletal involvement. Transrectal needle biopsy revealed a Gleason 9 (4 + 5) adenocarcinoma of the prostate, and hormone therapy with leuprolide was initiated. Despite therapy with intravenous dexamethasone and anticonvulsants, the patient's neurological status deteriorated rapidly over a week, progressing to a dense right-sided hemiplegia and ultimately requiring intubation for airway protection. Given the large size and the complexity of this skull base tumor, a cerebral angiogram was performed with intention of tumor devascularization via endovascular therapy followed by anterior petrosal tumor resection. Angiography did not reveal tumor hypervascularity; hence no embolization was performed. Surgical intervention was performed through a petrosal approach, combining suboccipital craniotomy for cerebellopontine angle exposure and temporal craniotomy for middle cranial exposure. The middle fossa tumor component was approached first using extradural dissection technique. The foramen spinosum was encountered, and the middle meningeal artery was carefully coagulated and divided. With this, the lateral margin of the trigeminal nerve was exposed; however, most of the tumor appeared to be intradural. Careful dissection and devascularization were performed, and the temporal lobe and middle cranial fossa tumor extension were removed en bloc. Frozen section

revealed diagnosis of metastatic carcinoma. The approach was modified to standard retromastoid suboccipital corridor for cerebellopontine angle tumor removal and brain stem decompression. A good dissection plane was developed, and the tumor was removed via gross total resection. Intraoperatively, the tumor extension into Meckel's cave was identified, and it was resected as well (Fig. 1E and F).

Hematoxylin and eosin staining of frozen and permanent sections revealed sheets of monomorphic tumor cells with prominent nucleoli forming many acinar structures and glands (Fig. 2A and B). Solid as well as cribriform patterns were also noted. In some areas, a papillary configuration of tall columnar tumor cells was seen, with scattered mitotic figures. Focal areas of hemorrhage with hemosiderin deposition were noted. Immunohistochemical stains showed diffuse and strong positivity for pan cytokeratin (OSCAR) and prostatic-specific antigen in the tumor cells (Fig. 2C and D), which were negative for TTF-1 and S-100 protein. These histological features, as well as immunohistochemical profile, were diagnostic of a metastatic adenocarcinoma of prostatic origin.

Two-month postoperative follow-up revealed a significantly improved level of consciousness, speech, left facial paralysis, and right-sided hemiplegia. The patient is currently able to ambulate with the assistance of a walker.

DISCUSSION

The extradural neuraxis compartment (EDNAC) has been described as an anatomic continuum between the orbit and the coccyx.^{5,6} It contains the so-called "cerebral spinal venous system" (CSVs), a system of valveless epidural veins with bidirectional flow from the periorbita and cavernous sinus that connect with the veins of Breschet at the clivus and basilar process of the occiput and further caudally with the spinal epidural veins of Batson.⁷ This route of metastatic spread to the leptomeninges through its connection to the prostate venous plexus was

Figure 2 (A) Touch prep. Hematoxylin and eosin (H&E) stain. (B) Frozen section H&E stain. (C) Immunostain for pan cytokeratin, proving the epithelial origin of the lesion. (D) Immunostain for prostate-specific antigen, proving the lesion originated in the prostate gland.

initially described by Batson in 1967.⁸ The fifth cranial nerve enters this extradural compartment from the posterior fossa via the sleeve encountered at the Meckel's cave. The cerebrospinal fluid portal by which the trigeminal nerve travels from the prepontine cistern to the Meckel's cave is the porus trigeminus, the posterior margin of Meckel's cave, described elsewhere.⁹ In this case of a dumbbell-shaped metastatic deposit mimicking a trigeminal nerve schwannoma, it is not possible to identify the exact anatomic layer in which the metastasis originated. Because of its apparent epicenter in Meckel's cave, a potential connection between the veins of Breschet (CSVS) and the porus trigeminus via cerebrospinal fluid dissemination could have occurred (Fig. 3). If hematogenous spread were the mechanism, then one might expect skull invasion or metastatic deposits, but none was seen. This route, however, could be possible in other scenarios and should be taken into consideration. In particular, the valveless venous system connecting to the cavernous sinus can act as a bidirectional pathway through

which spread may occur. In this case, no centrifugal spread was evident, but the possibility remains.

Although the capability of metastatic prostatic neoplasms to mimic meningiomas has been well described,^{10–15} we have not encountered reports with radiographic and clinical similarities resembling trigeminal nerve schwannomas. In patients with proper clinical suspicion, this condition should be entertained as an option on differential diagnosis. A reciprocal relationship was reported by Wang et al, describing a series of vestibular nerve schwannomas that expressed prostate-specific membrane antigen. This finding highlights the fact that schwannomas should be considered in the differential diagnosis of positive lesions on prostate-specific membrane antigen radioimmuno-scintigraphy studies performed during metastatic and recurrence workup for prostatic adenocarcinoma and is intriguing in terms of how this might influence tumor biology of schwannomas.¹⁶

The interrelation of the EDNAC, CSVS, and the cave of Meckel plays a common role in

Figure 3 Postulated pathway of prostatic adenocarcinoma metastatic dissemination to Meckel's cave. (1) Venous dissemination via prostatic venous plexus to the cerebral spinal venous system via (2) Batson's epidural venous plexus and (3) veins of Breschet. Extension to the extradural neural axis component at Meckel's cave, via the cerebrospinal fluid (CSF) portal constituted by the porus trigeminus (4).

the dissemination of metastatic deposits of prostate adenocarcinoma that mimic primary intra-axial dumbbell-shaped lesions of more benign nature. This route of metastatic spread is both retrograde (cranial) or anterograde (caudal) in direction, and examples of either have been described in the literature.^{17,18} In addition, through this route, prostate metastasis can simultaneously spread to the anterior fossa (periorbita), middle (cavernous sinus/parasellar region), and posterior fossa (Meckel's cave and petroclival region) via the anatomic continuum provided by the CSVS, closely interrelated with the cavernous sinus. This would explain how metastatic lesions from prostate adenocarcinoma can span the three skull base fossae, mimicking a large skull base meningioma, as reported by Kwee et al.¹⁹ Although dural metastasis is a common occurrence in prostatic adenocarcinoma to the brain, location in the trigeminal fossae, parasellar region, or orbit is rare, thus making these areas more prone to misinterpretation, favoring more common primary

central nervous system lesions during the preoperative presumptive diagnosis. Transdural invasion, bone infiltration or erosion, and parenchymal invasion of the tumor mass into the temporal lobe may serve as diagnostic clues for tumors of more aggressive tumor, potentially assisting in the differential diagnosis.

We hope the anatomic concepts explained will remind practicing and in-training skull base surgeons about this potential but not exclusive route of metastatic spread of prostate cancer and assist in the differential diagnosis and management of these lesions.

CONCLUSION

Metastatic adenocarcinoma of the prostate can present mimicking dumbbell-shaped skull base lesions encasing the gasserian ganglion at Meckel's

cave in a similar fashion to that encountered with giant schwannomas of the trigeminal nerve. The EDNAC, CSVS, porus trigeminus, and Meckel's cave play an important anatomic role in the dissemination of metastatic deposits to the skull base responsible of the imaging characteristics typical of trigeminal nerve schwannomas and meningiomas. Gross total surgical resection of giant skull base metastatic lesions can relieve life-threatening neuroaxial compression and improve the performance status of a patient despite a scenario of widespread prostate cancer.

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