Multifocal metastases to choroid plexus from papillary thyroid carcinoma: illustrative case

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BACKGROUND Choroid plexus metastases are extremely rare from all types of malignancy, with only 42 cases reported in the literature thus far. Most of these originate from renal cell carcinoma and present as a solitary choroid plexus lesion; only two cases of multifocal choroid plexus metastases have been reported to date.

OBSERVATIONS The authors report the third case of multifocal metastases to the choroid plexus, that of a 75-year-old man who developed three measurable choroid plexus lesions approximately 3.5 years after undergoing total thyroidectomy and chemotherapy for papillary thyroid carcinoma. He underwent intraventricular biopsy of the largest lesion and subsequently died of hydrocephalus after opting for comfort care only.

LESSONS This is the third case of multifocal choroid plexus metastasis in the literature and the second case of multifocal metastasis from thyroid carcinoma. As such, the natural disease course is not well characterized. This case is compared with the previous eight reports of choroid plexus metastases from thyroid carcinoma, seven of which involved solitary lesions. The eight prior cases are evaluated with attention to treatment modalities used and factors potentially influencing prognosis, specifically those that might contribute to hydrocephalus, a reported complication for this pathology.

BACKGROUND Choroid plexus (CP) is an uncommon location for metastases from central nervous system (CNS) and non-CNS malignancies, with only 42 cases reported in the literature.1–4 Eight cases of CP metastases from thyroid carcinoma have been reported previously, with only two confirmed cases of multifocal CP metastases known to date.5–11 All eight cases involved differentiated thyroid carcinoma (DTC), namely papillary or follicular subtypes. Only two known cases of multifocal metastasis to the CP from any malignancy exist in the literature, originating from papillary thyroid carcinoma and renal cell carcinoma, respectively.1,12

Brain metastasis from differentiated thyroid carcinoma suggests a poor prognosis. Differentiated thyroid carcinoma without brain metastasis has a 90% 10-year survival rate, whereas the presence of any brain metastases from DTC is associated with a 67% mortality rate and a median survival rate of 12.4 months from diagnosis.13,14 Review of nine cases of CP metastasis from DTC suggests that this entity likely bears an even poorer prognosis than that of overall brain metastases from DTC. Hydrocephalus was present in at least three of the nine cases—those with the worst outcomes, suggesting the presence of hydrocephalus as another poor prognostic indicator. We present the ninth case of CP metastasis from thyroid carcinoma, which is also unique in being the second of these presenting with multifocal CP lesions, a likely marker of poor prognosis.1

Illustrative Case

The patient was a 75-year-old man with a history of papillary thyroid carcinoma (PTC), tall cell variant, metastatic to the neck and lung, who presented with altered mental status, severe headache, low back pain, and urinary retention. He had been diagnosed with PTC 4 years prior and was treated with total thyroidectomy,
cervical lymph node excision, and lenvatinib therapy. He later developed further metastasis to the C5 vertebral body and was treated with radiation and continued lenvatinib.

The patient had undergone brain magnetic resonance imaging (MRI) 1 month before presentation after seeing his primary oncologist for several days of headache, urinary frequency, and low back pain. This imaging revealed several CP abnormalities, including a 1.6 × 0.9-cm nodule in the temporal horn of the left lateral ventricle and avidly enhancing nodularity and thickening of CP in both lateral ventricles and the fourth ventricle (Fig. 1). There were also trace dependent blood products in the occipital horns of both lateral ventricles and a slight rightward midline shift. These findings were concerning for intraventricular metastatic disease with mild associated intraventricular hemorrhage (IVH).

When the patient presented to the emergency department about 1 month later, his neurological examination was characterized by inattention, perseveration, and difficulty with multistep commands. He also had a postvoid residual of 578 mL and mild hyponatremia. MRI with contrast demonstrated numerous enhancing CP lesions in the body and temporal horn of the left lateral ventricle and nodular enhancement along the CP in the fourth ventricle (Fig. 2). A small enhancing lesion was seen in the third ventricle along the superior aspect of the cerebral aqueduct. The lateral and third ventricles had...
| Characteristic | Zhang et al., 2009<sup>5</sup> | Wasita et al., 2010<sup>6</sup> | Heery et al., 2012<sup>7</sup> | Kitagawa et al., 2013<sup>8</sup> | Manzil et al., 2014<sup>9</sup> | Healy et al., 2014<sup>10</sup> | Sharifi et al., 2015<sup>1</sup> | Umehara et al., 2015<sup>11</sup> | Present Case |
|---------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------|
| Age, sex      | 62, M                         | 75, M                         | 88, M                         | 74, F                         | 62, M                         | 70, F                         | 52, F                         | 58, M           | 75, M        |
| DTC type, subtype | Follicular, papillary†        | Papillary                    | Papillary                    | Follicular                    | Papillary                    | Papillary                    | Papillary                    | Follicular, papillary†     |
| Presenting symptoms | Progressive short-term memory loss | Severe headache, nausea, vomiting | Confusion, ataxia, dysartria, urinary incontinence | Vertigo, memory loss, left hand clumsiness | Incidental finding | Enlarging cervical mass | Severe headache, nausea and vomiting, right hemiparesis, speech disturbance | Severe headache, gait disturbance, confusion |
| Hydrocephalus | N.R.                          | Yes                           | Yes                           | N.R.                          | N.R.                          | N.R.                          | N.R.                          | N.R.                          | Yes                       |
| IVH           | No                            | Yes                           | No                            | No                            | No                            | No                            | Yes                           | Yes                            | Yes                       |
| Intraventricular location | Right trigone                | Right trigone                | Left occipital horn           | Right trigone                | Left trigone                | Left trigone                | Both lateral ventricles        | Roof of third ventricle     | Right temporal horn, both lateral ventricles, fourth ventricle |
| Intervention  | Frameless stereotactic craniotomy for subtotal excision, transcortical approach | Occipital transcrical approach, total resection | Parieto-occipital craniotomy with resection | Open biopsy (parietal transcortical approach) | Gamma Knife stereotactic radiosurgery | Gamma Knife radiosurgery, X<sup>2</sup>‡ | Left ventricular tumor resection, posterior parietal parasagittal approach | Endoscopic hematoma evacuation with biopsy, septostomy | Biopsy with microcauterization |
| CSF diversion | No                            | VP shunt                      | VP shunt                      | N.R.                          | No                            | No                            | EVD                           | EVD                           | EVD                       |
| Ultimate outcome | Reduced tumor size, stable 18 mos postoperatively | Survived at least 2 yrs after initial presentation | Neurologically stable 14 mos postoperatively | Radiographic evidence of improvement—further detail N.R. | At least 6 yrs from time of initial diagnosis | No recurrence at 6-mo follow-up | Alive at time of publication (8 mos after Mets. found) | Death 2 mos after initial presentation |

Mets. = metastasis; N.R. = not reported; VP = ventriculoperitoneal.

* In Sharifi et al., eight cases of choroid plexus metastases from thyroid carcinoma are reported. However, one of these cases was reported incorrectly—that of Ferrer Garcia et al. This latter article is available only in Spanish, but it reports a case of thyroid carcinoma metastatic to the choroid layer of the eye and not the intraventricular choroid plexus.

† Follicular variant found in CP.

‡ Due to patient refusal of surgery.
increased in size from the previous MRI with associated small IVH. Due to concern for metastatic disease and developing hydrocephalus, the patient underwent left frontal endoscopic tumor biopsy and placement of an external ventricular drain (EVD).

During the operation, a hemorrhagic-appearing mass was found nearly occluding the foramen of Monro (Fig. 2D). A left frontal endoscopic approach was chosen, the hemorrhagic mass was biopsied, and associated hematoma was removed, with the goal of removing the obstructive blood products to improve cerebrospinal fluid (CSF) drainage. The mass bled at the time of biopsy and was extensively cauterized, but visualization was partially obscured due to new and old blood products in the CSF. Underneath the hemorrhagic mass, the CP was abnormally hyperemic and enlarged. The left lateral ventricle was irrigated extensively to remove blood products, and an EVD was placed in the left lateral ventricle.

Follow-up computed tomography (CT) on postoperative day 1 revealed expected postoperative changes and decreased size of the CP lesion in the left lateral ventricle (Fig. 3). The surgical pathology returned as metastatic papillary thyroid cancer, tall cell variant, and molecular testing later demonstrated a v-raf murine sarcoma viral oncogene homolog B V600E mutation (Fig. 4). The patient's EVD was clamped with serial CT showing stable ventricular size until its removal on postoperative day 7. His neurological status at first fluctuated between full orientation and confusion, but it soon progressively declined. A repeat head CT revealed interval increase in ventricular size with persistent IVH.

Continued urinary retention and back pain prompted a full spine MRI, which revealed numerous thoracic spine lesions, a new L1 vertebral body lesion, and an increased C5 vertebral body lesion. Given the severe burden of disease, the patient was transitioning to a comfort-directed plan of care on postoperative day 15. He was discharged to a hospice and died about 1 week later.

Discussion

Observations

Metastatic disease to the CP is uncommon, with only 42 reports in the literature from any solid tumor primary malignancy. Thyroid carcinomas are rare as well, representing 1% of all malignancies. Thyroid carcinoma metastasizes to the brain in only 0.9%–1.5% of cases and has been reported in the CP in eight prior cases. Patients in the cases with the two worst outcomes had clinical and radiographic evidence of hydrocephalus, one of which was complicated by IVH. Overall, IVH was present in four of the cases, with hydrocephalus present in at least three.

CSF diversion procedures (EVD or ventriculoperitoneal shunt) were employed in at least five of the nine cases, suggesting the presence of hydrocephalus in more than three of these cases.

There is no treatment protocol for DTC metastases to CP due to the limited number of cases, but options have included resection, whole-brain radiation, Gamma Knife stereotactic radiosurgery, and radiodine therapy (as an adjunctive therapy). Radiosurgery has not been used as a standalone approach in cases of CP metastasis from DTC; it has been used only as an adjunctive therapy after surgical intervention. In all types of thyroid carcinoma presenting with solitary brain metastasis, there is a positive association between resection and increased survival time: 3–10 months, on average, with no surgical intervention compared with 17–54 months after resection. The one known reported case of multifocal brain metastasis from thyroid carcinoma was also treated with resection, but the outcome after 6 months was not reported. Surgery may be complicated by IVH due to the hyperemic nature of CP metastases, which neurosurgeons should be prepared to manage intraoperatively using irrigation, cautery, and CSF diversion procedures. Hydrocephalus, a likely factor in the majority of these cases, can be worsened by IVH, a complication that should be anticipated.

Conclusions

Thyroid carcinoma metastatic to the CP is exceedingly rare and typically presents as a solitary lesion. This is the second known reported case of multifocal CP metastasis from thyroid carcinoma specifically. Multifocal CP metastases are likely the manifestation of a more aggressive malignancy; if there is suspicion for the diagnosis, an endoscopic intraventricular biopsy with EVD placement may be performed to confirm the diagnosis. Resection can be considered for solitary and obstructive lesions, but because the entity is rare, further evidence is necessary to make stronger recommendations. This case expands the limited documentation of metastatic thyroid carcinoma to the choroid plexus and, along with previous reports, suggests an association with hydrocephalus that should be managed by CSF diversion.

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Disclosures
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