CASE REPORT

Concurrent metastases of papillary thyroid carcinoma to the scalp and Meckel's cave

Patrick S Phelan,¹ Jamie L Mull,² Mohamed Z Rajput,³ Amy C Musiek²

¹Washington University in Saint Louis School of Medicine, Saint Louis, Missouri, USA

²Division of Dermatology, Washington University in Saint Louis School of Medicine, Saint Louis, Missouri, USA

³Washington University in Saint Louis School of Medicine, Mallinckrodt Institute of Radiology, Saint Louis, Missouri, USA

Correspondence to
Dr Jamie L Mull,
jamie.l.mull@gmail.com

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SUMMARY

We present the case of a 65-year-old man with severe headaches and unilateral facial weakness, seen in consultation by the dermatology service to rule out primary cutaneous melanoma after brain imaging identified an enlarging mass within the right trigeminal (Meckel's) cave. Examination revealed only a pair of erythematous papules on the scalp, for which biopsy demonstrated metastatic papillary thyroid carcinoma. Further evaluation and subsequent thyroidectomy confirmed the origin of widespread internal disease, followed by definitive excision of scalp lesions and multimodal management of systemic involvement. Whereas presentation of metastasis to the skin is highly variable, a low threshold for biopsy may allow for histological identification of internal disease not otherwise considered in the clinical differential.

BACKGROUND

The prevalence of cutaneous involvement in the setting of metastatic malignancy has been estimated as high as 10%,¹ with primary internal malignancies most commonly originating from breast, lung and gastrointestinal tissues.² Previous reports of cutaneous metastases of papillary thyroid carcinoma (PTC) have described variable features, ranging from conspicuous violaceous nodules mimicking primary neoplasms and cysts to subtle patches and plaques mimicking cutaneous infections.^{3,4} In the present case, non-specific clinical features presented difficulty in diagnosis, and our outcome highlights both the need for consideration of cutaneous metastases in clinical evaluation and the value of dermatological assessment and cutaneous biopsy in diagnosis of metastatic disease.

Figure 1 Clinical appearance of scalp lesions at initial examination.

Figure 2 Initial imaging at time of diagnosis. Brain MRI with and without intravenous contrast: postcontrast T1-weighted sequence (top) demonstrating a hyperintense lesion within the right trigeminal cave extending into the prepontine cistern. PET (middle) and MRI-fused series (bottom) demonstrating lack of metabolic activity, attributed to intralesional haemorrhage.

CASE PRESENTATION

A 65-year-old Caucasian man with a history of significant sun exposure and former smoking presented to an outside hospital for initial evaluation of recent-onset severe headaches and right-sided facial weakness. Following unsuccessful carbamazepine therapy for presumed trigeminal neuralgia, brain MRI at our institution revealed a growing mass in the right trigeminal (Meckel's) cave, suspicious for metastatic melanoma. A dermatology consult was requested for evaluation of a possible cutaneous primary tumour, and physical examination revealed two erythematous, eroded papules on the posterior scalp, each approximately 7 mm in diameter, which the patient reported to have been present for the past year (figure 1).

INVESTIGATIONS

Initial brain MRI without and with intravenous contrast revealed an enhancing T1-hyperintense and T2-hyperintense lesion in the right trigeminal cave, which had significantly increased in size in comparison with MRI 3 months earlier (when it was first identified) and was concerning for interval haemorrhage (figure 2). Subsequent CT of the chest, abdomen and pelvis and whole-body ¹⁸F-fludeoxyglucose Positron emission tomography, PET-CT demonstrated the intracranial lesion to be hypometabolic and also

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Figure 3 Histopathology of scalp biopsy, revealing tubular formations of mucinous cells within a fibromyxoid stroma (H&E 5×, 20× and 40×).

revealed additional hypermetabolic lesions within the lingula, left submandibular space, right anterior buccal space and T1 vertebral spinous process. Same-day dermatology consult resulted in shave biopsy of the posterior scalp lesions, which revealed tubular arrangements of atypical, mucinous epithelial cells and a fibromyxoid stroma within the dermis (figure 3). Initial immunohistochemistry found lesional cells positive for cytokeratin-7 and negative for MART-1 (Melan-A), S-100 and cytokeratin-20, yielding a preliminary assessment of metastatic adenocarcinoma of unknown primary origin (figure 4).

Figure 4 Representative immunohistochemical stains of scalp biopsy for CK-7 (5×) and PAX8 (5×, similar to TTF-1). PAX8, paired box gene 8; TTF-1, thyroid transcription factor 1.

In the course of our patient's rapid multidisciplinary workup, CT-guided biopsy of the T1 spinous process lesion was also obtained the following day per medical oncology evaluation. One week later, final dermatopathology results became available for the scalp lesions, showing lesional cells diffusely positive for thyroid transcription factor and paired box gene 8 and negative for napsin A, GATA 3, synaptophysin and chromogranin, most consistent with thyroid origin (figure 4). Pathology results of the vertebral lesion were reported 2 days later and demonstrated similar papillary adenocarcinoma with an identical immunophenotype (and additionally positive for thyroglobulin (Tg)), consistent with a diagnosis of metastatic PTC (mPTC) (figure 5). Several days later, on evaluation by radiation oncology, the patient was referred for neck ultrasound and fine-needle aspiration (FNA), as well as surgical evaluation for total thyroidectomy. Ultrasound-guided FNA of the right thyroid lobe and a cervical level III lymph node revealed 'atypia of undetermined significance' and mPTC, respectively.

Right-sided neck dissection (lateral levels 2a–4, central level 6) and total thyroidectomy were performed, revealing bilateral subcentimetre tumours in the thyroid lobes, with extrathyroidal extension and 3/40 lymph nodes involved. Tumour pathology described infiltrative follicular variant and classical PTC (figure 6), and the patient was staged T3/N1B/M1 (stage IVC).

DIFFERENTIAL DIAGNOSIS

The clinical appearance of the scalp lesions evoked consideration of folliculitis, inflamed cysts and adnexal neoplasms. Although not strongly favoured, a diagnosis of amelanotic melanoma was also considered, given the patient's suspected Central nervous system (CNS) malignancy.

TREATMENT

Definitive treatment of the scalp lesions was accomplished via local excision with clear margins (figure 7). During investigation for primary tumour origin, initial serum tumour marker measurements were obtained, finding normal serum Tg (3.3 ng/mL, intact thyroid reference <33 ng/mL) and elevated antithyroglobulin (anti-Tg) antibody (21 IU/mL, reference <4 IU/mL). Immediately following, radiosurgical ablation of 18 Gy to the trigeminal cave lesion was performed, with marked improvement in the patient's headaches. Following diagnosis of metastatic PTC, at 7.5 weeks since last iodinated contrast exposure (of 75 mL ioversol 74%), the patient underwent iodine-131 whole-body scintigraphy (5 mCi dose), revealing no abnormal uptake within the brain, scalp or other sites of putative metastases per previous PET (figure 8). Subsequent definitive radioactive iodine-131 (RAI) therapy was attempted the following day with 250 mCi. Four days later, iodine avidity was not observed

Figure 5 Histopathology of T1 spinous process core biopsy. (A and B) Elongated tubular and papillary structures lined by tall columnar epithelial cells, some with clear or lightly eosinophilic cytoplasm (H&E 4× and 10×). (C and D) Immunohistochemical stains for CK-7 (figure part C: 4×) and TTF-1 (figure part D: 4×). TTF-1, thyroid transcription factor 1.

on post-RAI whole-body scan despite sufficient pretreatment iodine-free interval,^{5 6} consistent with RAI-resistant disease.

OUTCOME AND FOLLOW-UP

Unfortunately, PET-CT at 1-month follow-up revealed new vertebral and iliac lesions, and the patient was referred to medical oncology for management, at which time, sorafenib therapy was initiated in accordance with current treatment guidelines.⁷ Follow-up MRI in the fourth month following radiosurgery showed stable intracranial disease with no change in lesion size. Monitoring of serum tumour markers found initial elevation of serum Tg (to 25 ng/mL, athyrotic reference 0–0.5 ng/mL) and normalisation of anti-Tg (to <1.8 IU/mL) postoperatively, though following subsequent radioiodine treatment, continued surveillance showed near-normalisation of serum Tg (to 0.7 ng/mL) and rebound elevation of anti-Tg (to peak 23 IU/mL) by 6 months post-treatment (all measurements obtained at basal conditions via consistent analytic methods). Serum thyrotropin (TSH) and free thyroxine (fT₄) measurements were first obtained 1 week after thyroidectomy, initially consistent with postoperative hypothyroidism (TSH: 22 mIU/mL, fT₄: 0.48 ng/dL) and peaking at 3 weeks (TSH: 75 mIU/mL, fT₄: 0.14 ng/dL; all in the setting of thyroid hormone withdrawal). Levothyroxine therapy was begun immediately following RAI treatment, and suppression of endogenous TSH was achieved to 0.02 mIU/mL by the 6-month mark (monitoring levothyroxine dosing; all measurements obtained via consistent analytic methods), at which point surveillance PET-CT and brain MRI demonstrated the intracranial metastasis to be metabolically unchanged with modest decrease in size (figure 9). Although the patient experienced persistence of facial numbness, all interventions were well tolerated, and treatment with sorafenib is ongoing.

DISCUSSION

Correction for surface area reveals strong selectivity for particular sites of cutaneous metastasis, notably the scalp, and potential assortment based on tissue of origin.⁸ In the case of well-differentiated

Figure 6 Histopathology of thyroidectomy specimen. (A and B) Left thyroid lobe, papillary thyroid carcinoma, classical type (4× and 10×). (C) Right thyroid lobe, infiltrative papillary thyroid carcinoma, follicular variant (10×).

malignancies of the thyroid, metastatic spread towards lung, bone and lymphatic tissues is typical, though the brain and skin (particularly the scalp) are the most prominent sites of atypical metastasis and are associated with advanced disease^{6 9}; both were involved in the present case. It is not uncommon for cutaneous metastasis to be the initial manifestation of advanced disease, as in our case, and has been previously documented for PTC.^{7 10}

Figure 7 Histopathology of definitive scalp excision, demonstrating typical characteristics of papillary thyroid carcinoma, follicular variant (H&E 2× and 10×).

Figure 8 Diagnostic iodine-131 whole-body scan, anterior (left) and posterior (right) views, demonstrating no iodine avidity within the intracranial or other identified metastases. Iodine uptake within the thyroglossal duct is seen, consistent with residual native thyroid tissue.

Figure 9 Surveillance imaging at 6 months following radiosurgery. Brain MRI with and without intravenous contrast: postcontrast T1-weighted sequence (top) demonstrating interval decrease in size of the right trigeminal cave lesion, most notably in the prepontine portion. PET (middle) and MRI-fused series (bottom) demonstrating persistent lack of metabolic activity within the lesion.

Previous reports of malignancies metastatic to the trigeminal cave have included carcinoma of the lung, breast, colon and thyroid, as well as cutaneous melanoma.¹¹ Distant metastasis to the cranial cavity occurs via haematogenous spread, as does metastasis of internal malignancy to the skin. It should not be surprising that the two sites may thus be affected simultaneously.¹² In consideration of suspected skull base malignancies like ours, it has been argued that well-differentiated thyroid carcinomas should be included in the differential.¹³ Taken in conjunction with the logistic difficulty of histological assessment of these deep lesions,¹³ the possibility of concurrent cutaneous metastasis by thyroid carcinoma makes a strong argument for the utility of dermatological evaluation with a low threshold for exclusionary biopsy.

In the present case, directed examination for potential cutaneous sources of CNS metastasis warranted biopsy of the scalp lesions despite low clinical suspicion for malignancy; in the absence of such a mission, threshold to biopsy would need to be quite low to exclude similar subtle metastases. This is especially relevant where diverse malignancies beyond the thyroid may produce great variability in metastatic morphology.¹⁴ However, dermatological examination in the setting of metastatic

Learning points

- ▶ Cutaneous metastasis may be the presenting sign of advanced malignant disease of diverse tissue origin.
- ▶ Such lesions may mimic benign neoplasms or appear otherwise atypical.
- ▶ In patients with internal metastatic malignancy of unknown origin, dermatological exam with a low threshold for biopsy may be a valuable tool for diagnosis.

malignancy offers advantages beyond the search for primary cutaneous disease. In similar cases of presentation with unknown primary source, it offers the potential to identify subtle cutaneous metastases as well as provide histopathological evidence for tissue of origin via biopsy. Given the low morbidity, cost, and difficulty of skin biopsy, this represents an attractive adjunct approach in the diagnostic workup.

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