CASE REPORT

Metastatic Papillary Thyroid Carcinoma Presenting as Abducens Palsy Complicated by Ocular Neuromyotonia

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ABSTRACT

Papillary thyroid carcinoma (PTC) is a type of well-differentiated thyroid cancer that accounts for the majority of thyroid malignancies. The prognosis of PTC is very good and distant metastases are rare, especially to the skull base. The authors report the case of a 47-year-old woman with biopsy-proven PTC treated with surgery and radiation therapy who presented with headache and diplopia after 5 years and was found to have clivus and cavernous sinus metastasis. Following radiation therapy for her skull base and cavernous sinus lesion, she subsequently developed sixth nerve ocular neuromyotonia. Possible causes and treatments are reviewed.

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Introduction

The incidence of thyroid cancer has been on the rise in recent years, with increased frequency seen in both genders and across ethnic backgrounds.¹ This increase could be explained in part by increased ultrasound screening and earlier diagnosis.² Papillary thyroid carcinoma (PTC) is a type of well-differentiated thyroid cancer that accounts for the majority of thyroid malignancies.¹ The prognosis of PTC is very good and distant metastases are rare, especially to the skull base.^{2,3} We report the case of a 47-year-old woman with biopsy-proven PTC treated with surgery and radiation therapy who presented with headache and diplopia after 5 years and was found to have clivus and cavernous sinus metastasis. She subsequently developed ocular neuromyotonia involving the sixth nerve.

Case report

A 47-year-old African American woman presented 5 years prior with a thyroid lesion initially diagnosed as goitre. Biopsy, however, revealed papillary thyroid carcinoma (PTC), and she underwent a total

thyroidectomy with subsequent radioiodine (RAI) therapy for 6 weeks. Levothyroxine was initiated for thyroid hormone replacement and thyroid-stimulating hormone (TSH) suppression, and the patient was stable for the next 2 years.

Three years prior to presentation to our clinic, however, she experienced an acute episode of binocular horizontal diplopia lasting 2 weeks with spontaneous resolution. An isolated abducens nerve palsy was suspected, but no imaging was performed at that time. She was again stable for 2 years until she presented with new-onset worsening headache as well as binocular horizontal diplopia. Magnetic resonance imaging (MRI) and computed tomography (CT) of the head showed a large (2.9 cm anteroposterior × 3.3 cm transverse × 2.7 cm craniocaudal) lobulated heterogeneously enhancing skull base mass (Figure 1). The lesion extended into the bilateral cavernous sinuses and minimally protruded in the prepontine cistern with no significant mass effect on the brainstem. Although craniopharyngioma was suspected initially, endoscopic transphenoidal biopsy revealed metastatic papillary carcinoma of the thyroid. She underwent debulking

Figure 1. Imaging of the metastasis. MRI T1 post-contrast axial (A), coronal (B), and sagittal (C) images demonstrate the heterogeneously enhancing lesion involving the clivus, suprasellar space, and cavernous sinuses. (D) Destruction of the clivus.

and definitive hypofractionated intensity modulated stereotactic radiotherapy (IMRT) for the skull base metastasis. A lung nodule was also found by chest CT, and treatment with RAI under thyrotropin stimulation was initiated for presumed metastasis. She was referred to our neuro-ophthalmology clinic for further evaluation.

On examination, best-corrected visual acuity was 20/25 in each eye. External examination showed no ptosis or proptosis. The pupils measured 4 mm in the dark and 2 mm in the light without relative afferent pupillary defect. She had a -2 underaction of abduction in the right eye with a 30-prism dioptre (PD) esotropia (ET) in primary position which increased to >35 PD ET on right gaze. Slit-lamp examination was normal. Ophthalmoscopy showed no disc oedema or optic atrophy. There was no evidence of radiation retinopathy. In addition, cranial nerves V and VII were normal. She reported improvement of her diplopia since the surgery, and a patch was recommended for symptomatic relief.

At her next clinic appointment 3 months later, a transient exotropia involving the abducting eye was noted following prolonged lateral gaze in both directions (Figure 2). She was diagnosed

with ocular neuromyotonia (ONM) attributed to the IMRT. She was observed without treatment, and was stable after 6 months with no changes in her condition.

Informed consent was sought and granted by the patient.

Discussion

PTC is a type of well-differentiated thyroid cancer that accounts for the majority of thyroid malignancies.¹ PTC can be divided into the following subtypes: conventional PTC, follicular-variant PTC (FVPTC), and tall-cell PTC.² Our patient had FVPTC, which constitutes about 6.6% of PTC and has rarer lymph node and soft tissue invasion than patients with conventional PTC.⁴

PTC generally has an excellent prognosis, and distant metastatic disease is rare. A large prospective study of patients with PTC and follicular thyroid cancer (FTC) found a 76% survival rate, with a recurrence rate of 30% and an 8% cancer death rate after 30 years of follow-up.⁵ The most common site of metastasis is local lymph nodes, followed by lung and bone.⁶ Metastasis to the skull

Figure 2. Extraocular movement exam at the second office visit. Versions were full when first tested during the visit (A–E). However, after prolonged levoversion, left exotropia became evident on attempted primary gaze, consistent with ocular neuromyotonia (F). Informed consent was obtained from the patient for the photograph.

base is rare, with only 15 cases of PTC with such metastasis reported in the literature.^{3,6–16} However, only two of the aforementioned cases featured metastasis to the clivus.^{3,16} Among those reported, the most common symptom from skull metastasis was cranial nerve dysfunction.²

Our patient had an isolated sixth cranial nerve palsy that could be explained by the clival extension of the skull base mass.¹⁷ In patients with vasculopathic risk factors (tobacco use, hypertension, coronary artery disease, or hypercholesterolaemia), the most commonly presumed aetiology of an isolated ocular motor cranial nerve palsy is microvascular ischaemia.¹⁸ However, in a prospective multicentre study of 109 patients with isolated cranial nerve III, IV, or VI, 16.5% of patients with vasculopathic risk factors had causes other than microvascular ischaemia found by MRI (such as neoplasm, demyelination, or aneurysm).¹⁸ Given our patient's history of cancer, there is a strong possibility that the transient diplopia the patient experienced 2 years prior to presentation was due to this same lesion.

The American Thyroid Association (ATA) recommends surgery (i.e., partial or total thyroidectomy) and post-surgical RAI therapy using iodine-131 (¹³¹I) for treatment of PTC.¹⁹ ¹³¹I is used for adjuvant ablation of residual thyroid tissue, and monitoring for, as well as treating, metastatic disease. Additionally, all patients should be

started on levothyroxine to prevent hypothyroidism and to suppress TSH, since it is a potent stimulus for thyroid tumour growth.¹⁹ For those patients who have undergone surgery and RAI therapy but present with metastatic disease or have unresectable tumours, the next step is external-beam radiation therapy (EBRT).¹⁹ A modern type of EBRT is hypofractionated intensity-modulated radiation therapy (IMRT). In IMRT, the intensity of the radiation beam can be modified for the different areas of the target lesion while decreasing radiation exposure to the surrounding tissue.²⁰ This is especially useful inside the skull, where many critical structures reside in a small space.

Our patient underwent total thyroidectomy and ¹³¹I therapy after initial diagnosis. She was well for 2 years until she presented with an episode of binocular horizontal diplopia that spontaneously resolved after 2 weeks. The spontaneous recovery of the nerve can be explained by either decompression of the nerve, improvement of the vascular insufficiency, or remyelination.¹⁷ Volpe and Lessell reported a series of seven patients with clival tumours, mostly chordomas, who also had spontaneous resolution of symptoms ranging from 1 week to 18 months after the initial deficit.¹⁷ Unfortunately, since our patient was thought to be in remission and metastatic PTC was not suspected, no imaging was performed at the time

she was symptomatic, and it is unknown whether those symptoms were sporadic or secondary to metastasis to the skull base. Although rare, new-onset neurological symptoms in a patient with a history of PTC should raise suspicion for metastatic disease. An appropriate imaging study should be sought (i.e., MRI brain with and without contrast), including a careful evaluation of the sixth cranial nerve pathway with isolated sixth nerve palsies potentially localizing to either the clivus or cavernous sinus.

Other PTC cases with metastasis to the skull base in the literature were either diagnosed at presentation³ or more than 8 years had elapsed between detection of primary tumour and metastatic tumour, whereas in this case the patient had transient esotropia and diplopia after 2 years—the same symptoms that eventually led to detection of the metastasis. Thus, physicians should consider the possibility of metastatic disease even years after diagnosing a usually indolent cancer such as PTC.

An unexpected and unusual complication of this case was ocular neuromyotonia (ONM). ONM is characterised by intermittent, paroxysmal spasms of the extraocular muscles, resulting in transient ocular misalignment and diplopia. Various aetiologies have been proposed to explain the mechanism of this disorder, such as partial demyelination leading to ephaptic transmission of the neurons, or disruption of voltage-gated potassium channels in the ocular muscles.^{21,22} ONM has been associated with cranial nerve III in 56% of the cases, cranial nerve VI in 39% of the cases, and cranial nerve IV in only 9% of the cases.²¹ ONM has been reported after radiation therapy in several cases (e.g., Much et al.,²² Kau and Tsai,²³ Jacob et al.²⁴), but to the authors' knowledge, it has not occurred after a case of metastatic PTC to the clivus. Currently, the most common treatment is carbamazepine with one meta-analysis showing a success rate of 87.8%.²¹ Other medications have also been tried, such as phenytoin, clonazepam, and gabapentin, with variable degrees of success.^{23–25}

In conclusion, new neurological deficits should raise concern for recurrent and/or metastatic disease in a patient with a history of cancer, even if the deficit spontaneously resolves. In our case, the

patient had one transient episode of binocular horizontal diplopia and was diagnosed with isolated sixth nerve palsy. Early neuro-imaging can help distinguish among the different aetiologies of ocular motor nerve palsy and improve outcome.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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