CASE REPORTS

Third Nerve Palsy as the Presenting Sign of Metastatic Endometrial Carcinoma with Lymphovascular Space Invasion

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ABSTRACT

We present a case of endometrial carcinoma (EC) presenting with a third cranial nerve palsy due to metastasis to the cavernous sinus. Although the tumour was only stage 1B, histopathologic features including higher grade and lymphovascular space invasion (LVSI) increase the risk of recurrent and metastatic disease. To our knowledge, this is the first case of EC presenting as a third cranial nerve palsy in the English-language ophthalmic literature. Clinicians should be aware that the risk of metastatic EC including neuro-ophthalmic presentations depends upon not only stage and grade but also the presence of unique histopathological findings such as LVSI.

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Case

A 63-year-old female presented with subacute onset over 6 days of progressive, painful double vision and ptosis in the left eye. Past medical history included hypertension, prediabetes, and hyperlipidaemia. Endometrial carcinoma (EC) had been diagnosed 17 months prior to presentation, and she had undergone total abdominal hysterectomy (TAH), bilateral salphingo-oophorectomy (SBO), and sentinel lymph node mapping which was negative. She received pelvic external radiation and vaginal cuff brachytherapy. Serum tumour marker CA-125 was initially elevated at 90.7 U/ml (normal <35) but was normal at 19.5 U/ml on serial testing following treatment.

On examination, she was found to have an almost complete ptosis of the left eye (OS). Visual acuity was 20/20 in both eyes (OU), and pupils were symmetric and reactive, with no anisocoria and no relative afferent pupillary defect. Slit lamp, external, intraocular pressure, and fundus examinations were normal OU. Extraocular movements were normal in the right eye (OD). There was underaction of adduction (−2),

infraduction (−1 to −2), and supraduction (−1) OS (Figure 1). Abduction, however, was normal OS, and intorsion was present in attempted downgaze, suggesting an intact fourth cranial nerve function. In primary gaze, there was a 20 prism dioptre exotropia (XT) and small left hypotropia. Fifth cranial nerve testing was normal. A diagnosis of third cranial nerve palsy OS was made.

An initial computed tomography (CT) of the head without contrast was negative. Magnetic resonance imaging (MRI) of the brain with contrast revealed an enhancing mass in the left aspect of the sella measuring 1.6 cm × 1 cm × 1.2 cm, with extension into the left cavernous sinus (Figure 2A, B). Serum CA-125 remained normal at 20 U/ml. Serum angiotensin-converting enzyme, lysozyme, interferon gamma release assay, anti-neutrophilic cytoplasm antibody panel, erythrocyte sedimentation rate, and C-reactive protein were negative. Biopsy of the tissue from transsphenoidal resection showed solid sheets of highly atypical cells without gland formation. Few cells showed intracytoplasmic mucin. Mitotic figures were readily identified. The tumour cells were immunoreactive for

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Figure 1. Extraocular motility examination showed that the right eye moved normally. The left eye had a -2 underaction of adduction and -1 to -2 underaction of infraduction and a -1 underaction of supraduction with an exotropia of approximately 20 prism dioptres with a small left hypotropia. The abduction was normal, and there was intorsion in downgaze consistent with an intact fourth cranial nerve function.

Figure 2. (A) Sagittal view and (B) axial view of MRI brain with contrast, showing enhancing mass in the left aspect of the sella measuring approximately $1.6 \times 1 \times 1.2$ cm extending into left cavernous sinus. The mass elevates the normal-appearing enhancing pituitary tissue superiorly and to the right.

Pax8 and oestrogen receptor. WT1, progesterone receptor, p53, and p16 showed patchy positivity. The overall features were consistent with metastatic high-grade endometrial adenocarcinoma (Figure 3).

A whole-body positron emission tomography-CT showed suspicious osseous metastatic disease in the skull base but no other lesions. Upon discharge, the patient noted partial improvement of ptosis and double vision. At last follow-up with oncology one week after discharge, the patient had only mild ptosis and diplopia with downgaze. She was referred for radiation therapy for residual metastatic disease in the skull base.

Discussion

Solitary brain metastases of distant gynaecologic cancer are rare, and EC metastases in particular occur in only 0.5–0.86% of all EC patients.^{1–3} In fact, EC has been previously referred to as a “neurophobic” cancer for its general lack of spread to the brain.⁴ In a systematic review of the literature, Uccella et al. identified only 51 total reported cases of solitary brain metastasis from endometrial cancer and only 76 in which a brain metastasis (usually in association with other disseminated metastatic sites) was the indication of relapse.¹

Figure 3. Biopsy of the mass revealed sheets of atypical, poorly differentiated cells with mitotic figures and few intracytoplasmic mucin, consistent with high-grade endometrial adenocarcinoma. Magnification 40X, stained with H&E.

The majority were located in the supratentorial cerebrum (88.9%) and presented commonly with headache or limb weakness.¹

In our case of a low-stage (IB) and grade III EC, the histopathologic finding of lymphovascular space invasion (LVSI) was essential towards indicating the risk of metastasis. LVSI is a pathologic finding of tumour cells within the endothelium-lined channels of the specimen, outside of the borders of the tumour, reported in about 8–10% of patients with EC.⁵ LVSI is noted to be a negative prognostic factor even in low-stage and low-grade carcinomas, indicating higher independent risk for recurrence (hazard ratio of 4.9) and lower overall survival (73–82.7% compared with 91–97.2%).^{5–7} Although adjuvant radiotherapy has been recommended in addition to complete surgical resection (TAH and SBO) for low-stage cancers with LVSI, risk of recurrence does not appear to be affected by treatment of LVSI, and recurrence is more likely to be noted at distant sites such as the brain than at the local pelvic lymph nodes.⁸

To our knowledge, this is the first case in the English-language ophthalmic literature of a neurologically isolated, third cranial nerve palsy as the presenting and the only sign of metastatic EC to the cavernous sinus. Clinicians should be aware of the importance of consideration of histopathologic findings such as LVSI in EC as they relate with

prognostic indicators for recurrence and metastasis of cancer regardless of stage or grade.

Consent

Images have been de-identified, and this patient has provided written informed consent for the publication of these figures.

Declaration of interest

The authors have no conflicts of interest to disclose.

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