Case report

Reminder of an important clinical lesson: breast cancer metastasis to the parotid gland

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SUMMARY

A 59-year-old woman presented to an otolaryngology clinic with an 8-week history of a painless lump over her left parotid gland. Her medical history included an invasive ductal carcinoma (33 mm) and a ductal carcinoma in situ (70 mm) of the right breast, for which she had a mastectomy and various adjuvant therapies. The primary tumour presented 8 years prior to the metachronous metastasis. This patient was a non-smoker and had no significant family history. Post-superficial parotidectomy pathology revealed the parotid gland tumour to be oestrogen receptor-positive and HER2 receptor-positive, thus ruling out the initial differential diagnosis of a pleomorphic adenoma. A consequential total parotidectomy with a posterolateral neck dissection was performed with sparing of the facial nerve. The patient recovered well having only encountered a self-resolving salivary fistula. She portrayed no signs of facial nerve palsy and subsequent imaging scans showed no abnormalities.

BACKGROUND

While invasive ductal carcinomas (IDCs) are the most common breast cancer, metachronous metastases from the breast to the parotid gland are extremely rare. Both haematogenous and lymphatic routes of transmission have been reported, thus emphasising our limited knowledge of this disease.¹ The importance of this case is evident when considering the rarity of the diagnosis and how easily it can be misdiagnosed. Further awareness of this metastasis may allow for improvements in understanding the physiology of this disease and thus, in turn, improve treatment too. Treatment of this metastasis varies depending on the staging, but generally includes a combination of an excision of the tumour, chemotherapy, hormone therapy and radiotherapy. Fine-needle aspiration cytology (FNAC) of the parotid neoplasm has been perceived as vital in diagnosing the tumour as primary or secondary.² When a patient presents with a parotid gland lump and a history of breast cancer, the parotid lump ought to be presumed to be a secondary tumour from the breast until proven otherwise.

CASE PRESENTATION

A 59-year-old woman presented to an otolaryngology (ear, nose and throat) clinic with an 8-week history of a 15 mm × 20 mm painless lump behind the angle of the mandible on the left side. Initial assessment of her upper airway using flexible

nasendoscopy found symmetrical hypertrophy of the tongue base tissue and a mobile, hard, flat mass behind the mandible. Palpation of the posterior area of the mass was not possible and did not appear to be attached to the parotid. The patient denied a change in size of the mass over this 8-week period and had no dysphagia, dyspnoea or dysphonia.

This otherwise fit and well non-smoker had no significant family history but had undergone treatment for breast cancer 8 years earlier. Following a prior 9-year diagnosis of fibrocystic disease of both breasts, although predominantly the right, she presented with a lump on the right breast which was not alleviated through aspiration. Further investigations found this patient to have a 33 mm grade III (modified Bloom and Richardson criteria), partly cystic IDC and microinvasion of an extensive ductal carcinoma in situ (DCIS). The total size of the tumour with the DCIS was 103 mm. A staging CT placed the breast cancer at T2N0M0 (tumour, node, metastases). Following this diagnosis, the patient underwent a right mastectomy. The tumour was completely excised with negative margins. The sentinel nodes were also negative. As the tumour was HER2-positive and oestrogen receptor-positive, the patient was provided with adjuvant therapies. Chemotherapy consisted of six cycles of FEC-75 (600 mg/m² fluorouracil, 75 g/m² epirubicin and 600 mg/m² cyclophosphamide), followed by 3 weeks of intense radiotherapy (50 gray, 25 fractions) to the chest wall. Herceptin was prescribed for 12 months (18 cycles) and anastrozole for 10 years. Subsequent annual mammograms detected no metastases.

Following her mastectomy and a successive dual-energy X-ray absorptiometry scan diagnosing her as osteopaenic, the patient was taking anastrozole (25 mg once a day), risedronate sodium (5 mg once a day) and Cacit D₃ (500 mg once a day).

INVESTIGATIONS AND TREATMENT

As the mass was initially thought to be a pleomorphic adenoma and given the history of breast cancer, it was excised. Histopathological studies showed metastatic cells which were oestrogen receptor-positive and HER2 receptor-positive, thus identifying the mass to be a metastasis of the breast cancer. **Figure 1** shows oestrogen receptor staining—80% of the nuclei showed moderate positivity. **Figure 2** shows progesterone receptor (PR) staining—the tumour was PR-negative. **Figure 3** shows HER2 staining—the tumour was HER2-positive (intense

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Figure 1 Oestrogen receptor staining of metastatic parotid tumour cells.

and circumferential membranous staining was scored as 3+). [Figure 4](#) shows the metastatic tumour with normal parotid tissue in the lower right corner, and [figure 5](#) shows the metastasis at $\times 20$ magnification. The cancer antigen 15-3 blood test, which is used for breast cancer monitoring,³ was within the normal range. Additionally, no distant metastases were found on staging CT, therefore identifying this as an isolated metastasis.

As the margins of the excision were positive, a resection was required. The patient therefore underwent a left parotidectomy at levels 2–3 with a selective (posterolateral) neck dissection. Of the 32 lymph nodes removed, none showed signs of macrometastases or micrometastases.

Prior to surgery, the patient was still taking anastrozole, and was then changed to exemestane. While anastrozole and exemestane have been shown to be equally effective as adjuvant therapy for postmenopausal breast cancer, exemestane is less toxic to the bone,⁴ a desirable benefit in this patient who had osteopaenia and experienced frequent joint pain. Furthermore, anastrozole reversibly binds to the aromatase enzyme, whereas exemestane acts via irreversible binding, thereby suppressing

Figure 2 Progesterone receptor staining of metastatic parotid tumour cells.

Figure 3 HER2 staining of metastatic parotid tumour cells.

plasma oestrogen.⁵ Thus, in a patient with an oestrogen receptor-positive metastasis, it is wise to inhibit production of steroid hormones.

Radiotherapy, chemotherapy and Herceptin were not advised by the oncology team as the tumorous gland was completely excised, and the facial nerve showed no sign of metastatic disease.

OUTCOME AND FOLLOW-UP

The patient recovered well having developed no complications aside from a small salivary fistula and paraesthesia across the left cheek (numbness). These risks were explained to her prior to the surgery. Other risks the patient was made aware of included damage to the facial nerve, Frey's syndrome and the risk of a numb ear.

The fistula was managed conservatively as it was likely to resolve by itself over time. Histology showed no evidence of malignancy, and facial function following the operation was normal. Positron emission tomography (PET)-CT at 1 month postoperatively, as advised by the oncology team, produced no significant findings.

DISCUSSION

Infiltrating ductal carcinomas are the most common and most classic type of breast cancer, making up 70% of cases.⁶ Of infiltrating ductal carcinomas, 40%–60% metastasise to the axillary

Figure 4 Metastatic tumour with normal parotid tissue in the lower right corner.

Figure 5 Metastatic tumour at $\times 20$ magnification.

lymph nodes. Sites of haematogenous metastatic spread from breast cancer include the lungs, liver, bone, adrenals and brain.⁶ Breast cancer metastases to the parotid gland are extremely rare with only 16 cases reported worldwide between 1982 and 2013.²

Involvement of the parotid gland by tumours other than those of primary origin is incredibly unusual, with most originating from the head or neck, predominantly from the scalp and the ear.⁷ Distinguishing between primary and metastatic salivary gland tumours is important for therapy and prognosis.⁸ Malignant salivary tumours account for 0.5%–1% of all cancers, and of these only 10% are metastatic.¹ Metastatic parotid gland neoplasms account for roughly 9%–14% of all parotid tumours.⁹

Parotid gland metastases are rarely from a distant source (any source outside of the head and neck).¹⁰ This is due to the difference in the number, anatomical relationships of the lymph nodes and their drainage.² Conversely, submandibular gland metastases tend to originate from the breast, kidney or pancreas.² The submandibular gland has no lymphoid tissue and thus is not susceptible to lymphatic spread, whereas the parotid gland has significant lymphatic tissue. With respect to this patient, it is interesting to note the common spread via the lymphatics as the patient's mastectomy included a negative-result sentinel node biopsy. Moreover, the parotid tumour presented on the contralateral side to the breast tumour, thus further highlighting the confounding nature of this metastasis.

Some studies theorise that a haematogenous route of metastasis is more feasible.¹ This is due to breast cancer metastases to ipsilateral and contralateral parotid tumours being equally reported. For this reason, haematogenous spread is likely in this patient. Due to the rarity of this metastatic variation, it is difficult to further research the exact metastatic route. Rather, research should aim to increase awareness of parotid gland metastases from breast cancer, even many years after the initial presentation of the primary cancer.

Presentation has also been reported to be extremely variable; while most patients present with a swelling over the parotid gland, others may have facial nerve palsy as their initial cause for concern. It has been suggested that those who experience nerve palsy are likely to have parotid malignancies.¹

Imaging is vital in determining the location and nature of the tumour (benign or malignant). However, to identify whether the tumour is primary or secondary, FNAC is the gold standard.² Unfortunately, FNAC can present diagnostic challenges with respect to metastases of breast cancers to salivary glands

as primary salivary duct carcinomas and metastatic ductal carcinomas are morphologically and immunocytochemically similar.² It is therefore vital to obtain a thorough clinical history and present the case to pathologists. PET-CT scanning is recommended to observe distant spread of the disease.¹

Treatment options of metastases to the parotid gland follow that of most malignancies—surgery, chemotherapy and radiotherapy. The exact regimen is dependent on the radiological staging. As this patient's tumour was oestrogen receptor-positive and HER2 receptor-positive, adjuvant hormone therapy was suitable, but radiotherapy was not as it was an isolated neoplasm. The patient was previously on anastrozole for hormone therapy; however, this was changed to exemestane at the point of the parotid metastasis diagnosis.

A review of published literature deduces treatment of a solitary parotid metastasis from the breast to be controversial.¹ This is likely due to the variation of receptors expressed by the mass and the route of metastatic transmission.¹¹ Nonetheless, a parotidectomy with negative margins and, ideally, preservation of the facial nerve is common practice where the nerve has shown no sign of disease.¹ As the transmission is or has the potential to be lymphatic, a neck dissection is also recommended. There are various types of neck dissections, which differ in what structures are preserved. In this patient, where spread was contralateral and thus likely haematogenous in nature, a parotidectomy with a selective neck dissection was most appropriate. Unfortunately, certain case reports suggest that parotidectomies do not improve life expectancy, but rather parotid metastasis management is palliative irrespective of the treatment method.¹² It is worth noting, however, that this proposition is for parotid gland metastases from all primary sites, not from the breast alone.

Learning points

- For patients who present with a parotid gland lump and have a history of breast cancer, the mass ought to be investigated as a breast cancer metastasis.
- Histopathological investigations, including fine-needle aspiration, alongside a thorough history, are imperative to ensure correct diagnosis of a breast cancer metastasis to the parotid gland.
- Positron emission tomography-CT scans are vital following breast cancer metastasis to evaluate disease spread.

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