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Parotid gland metastasis of lung adenocarcinoma identified on surveillance ^{18}F-FDG PET/CT

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SUMMARY

A 79-year-old man with a previous history of primary bilateral pulmonary adenocarcinomas was found to have a new parotid lesion on oncological surveillance imaging, raising the possibility of metastatic disease. Biopsy of the lesion confirmed metastatic deposit from primary lung adenocarcinoma. Following multidisciplinary discussions, the patient underwent a left parotidectomy where clear resection margins and preservation of facial nerve function were achieved.

BACKGROUND

The routine use of ^{18}F-FDG PET/CT as part of oncological surveillance has allowed for early detection of locoregional or metastatic tumour recurrence. The parotid gland is not a common site of metastatic tumour deposits, and when these do occur, they usually originate from primary head and neck malignancies. A better understanding of the prognosis associated with the treatment of non-head and neck primary metastatic deposits to the parotid gland is crucial to aid treatment decision making.

We report a case which highlights the work-up and management of an incidental solitary left parotid metastatic pulmonary adenocarcinoma on surveillance imaging.

CASE PRESENTATION

A 79-year-old man was initially diagnosed with synchronous T1N0 right upper and lower lobe lung adenocarcinoma, treated with 48 Gy radiotherapy in four fractions with complete resolution on subsequent imaging. Two years later, he was diagnosed with a T1N0 left lower lobe adenocarcinoma that was treated with 54 Gy radiotherapy in three fractions. A surveillance ^{18}F-FDG PET/CT 8 months later identified a left posterior lung nodule with right hilar and subcarinal nodal involvements. Subsequent subcarinal endobronchial ultrasound biopsy confirmed T1N2 adenocarcinoma, which was treated with 60 Gy in 30 fractions. This was on a background of prior occupational asbestos exposure and a 60 pack-year smoking history.

One month following completion of radiotherapy, an incidental 15 mm, low-grade avid (SUV_{max} 3.7) mass in the left superficial parotid lobe was identified on routine ^{18}F-FDG PET/CT. There were no other fluorodeoxyglucose (FDG) avid lung parenchymal lesions reflective of tumour recurrence (figure 1). He was then referred to the Head and Neck Team for consideration of treatment for this isolated parotid lesion, for which no prior chemotherapy was initiated.

Clinical examination identified a painless mobile 20 mm left parotid mass that was not adherent to the underlying sternocleidomastoid muscle and not involving the overlying skin. Facial nerve function was intact (House-Brackmann grade I).

INVESTIGATIONS

He proceeded to have an ultrasound-guided core biopsy of the left parotid lesion. The histopathological result showed CK5/6 (–), CK7 (+), CK20 (–), CDX2 (–), p40 (–), S100 (–) and TTF1 (+) poorly differentiated adenocarcinoma with programmed death-ligand 1 (PDL-1) expression, likely of pulmonary origin.

TREATMENT

Following multidisciplinary team review, a decision for surgical excision was made. The patient underwent a left total parotidectomy with facial nerve preservation. The patient tolerated the procedure and was discharged home 2 days later. Facial nerve function remained intact postoperatively (House-Brackmann grade I).

Histology from the excision showed a 12 mm well-to-moderately differentiated adenocarcinoma, staining positive for CK7 and TTF1 and negative for CK20 on immunohistochemistry, features consistent with metastatic lung adenocarcinoma (figure 2). Clear margins were obtained with closest being the 1 mm margins from superior and deep margins.

His case was rediscussed in the multidisciplinary team meeting with a consensus to continue active surveillance considering no other metastatic deposit was identified at the time of his surgery.

OUTCOME AND FOLLOW-UP

The patient attended his routine postoperative review 10 days after where he continued to demonstrate uncomplicated recovery course with intact facial nerve function. Unfortunately, 2 months following surgery, the patient presented to the Emergency Department (ED) in respiratory distress, with elevated inflammatory markers and radiological evidence of multiple subpleural nodules predominantly affecting the left upper and lower lobes, right hilar lymphadenopathy just inferior to the right pulmonary trunk and a left pleural effusion likely indicating disease recurrence (figure 3). Due to suspicion of superimposed infection, he was also commenced on intravenous antibiotics. A long-term pleural drainage catheter was inserted to aid drainage of the malignant effusion and he was referred to the palliative care team for symptom management.

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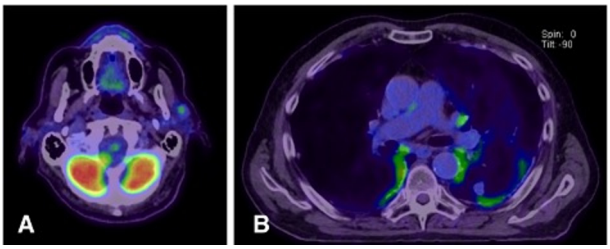

Figure 1 (A) Left parotid lesion of low-grade ^{18}F-FDG PET avidity (SUV_{max} 3.7). (B) Mild metabolic activity in bilateral pulmonary hilum with no ^{18}F-FDG PET avid mediastinal lymphadenopathy.

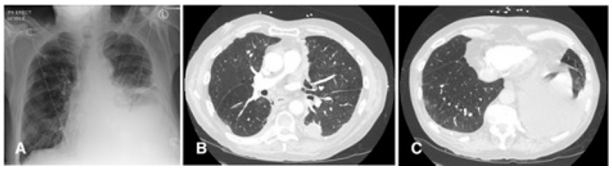

Figure 3 (A) Chest X-ray image highlighting new left pleural effusion contributing to patient's presentation to the Emergency Department 2 months following his parotidectomy; (B) CT image slice demonstrating left upper lobe nodule, potentially representing metastatic recurrence; (C) CT image slice showing a moderate volume left pleural effusion.

DISCUSSION

Parotid gland is an uncommon metastatic site for non-head and neck primary tumours. Metastatic tumours found in the parotid gland more commonly originate from primary head and neck cancers, while those originating from non-head and neck sites constitute 13% of metastatic lesions found in the parotid.[1–4] Of the various non-head and neck primary tumours, lung cancer is the most common site of origin with other previously reported sites include renal, breast, colon and gynaecological carcinomas, as well as lymphomas.[2 5] It is postulated that these infraclavicular tumours usually affect the parotid parenchyma by means of haematogenous spread, while primary head and neck malignancies tend to spread to the parotid lymph nodes via the lymphatics. Oncologically, however, there remains no distinction between metastatic deposits found in the parenchyma and the lymph nodes.[2]

Parotid involvement is rarely encountered in oligometastatic lung cancer. There are 12 previously reported cases of metastatic lung cancer affecting the parotid (table 1), all involving males with a median age of 60 years (range 40–74 years).[6–17]

Unlike other features of parotid malignancies typically associated with facial nerve deficits and fixation to deeper tissues,[4] it was found that the most common clinical presentation of metastatic lung cancer reported in the literature was a painless parotid mass without evidence of facial nerve palsy. All of the parotid lesions appeared to have been found on the ipsilateral side of the primary lung cancer, including two patients with bilateral parotid involvement. The pathophysiology of these metastatic spread to the parotid on the ipsilateral side is still poorly understood, possibly due to involvement of the thoracic duct or Batson's venous plexus.[5] Small cell carcinoma was the most common histological subtype, followed by adenocarcinoma and squamous cell carcinoma. The parotid lesions were frequently encountered along with other distant metastatic sites, such as to the mediastinum, cervical lymph nodes, liver, brain, adrenal gland, kidney, cranium and other bony metastases, hence the presence of parotid involvement may indicate disseminated disease with a poor prognosis.

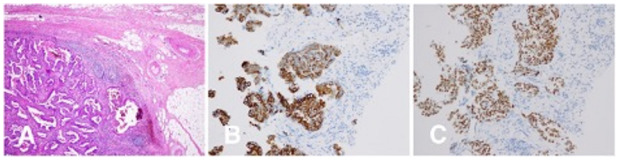

Figure 2 (A) H&E stain of the resected left parotid lesion demonstrating fibrous stroma with numerous glands lined by large pleomorphic cells with large nuclei and prominent nucleoli, with features consistent with moderately differentiated lung adenocarcinoma (×200). (B–C) Immunoperoxidase staining positive for CK7 (B) and TTF1 (C), as consistent with metastatic lung adenocarcinoma.

Interestingly, all 12 cases above describe parotid deposits that were identified at the initial time of diagnosis of lung cancer, in patients with no previous history of lung cancer. Our case was distinct as it was identified in a routine surveillance ^{18}FDG-PET/CT scan for known primary recurrent lung cancers, while still asymptomatic. ^{18}FDG-PET/CT itself has now been adopted as a good tool for staging and surveillance with one of the aims being for early detection of metastatic disease.[18–20] Despite some variance, increased uptake in ^{18}FDG-PET/CT can be described for those with an SUV_{max} of >3.[21] In the parotid, these lesions have been labelled as parotid incidentaloma or focal parotid findings (FPF). It was estimated that the prevalence of these lesions range between 0.3% and 1.73%.[18 19 21] Considering the wide use of ^{18}FDG-PET/CT as a surveillance modality in lung cancer, it is not surprising that FPF is more frequently detected in patients with lung cancers. In a study involving 604 lung cancer patients, Davidson *et al* detected an incidence of FPF in 3.8% with a mean SUV_{max} of 7.7±3.7 (range 2.5–17.8).[2] Prior study by Wang *et al* also reported similar findings with 23 of 58 FPFs found in lung cancer patients.[21] These FPFs can be identified in all histological subtypes and stages of lung cancer and hence, no significant correlation was found between the subtypes and stages of the primary lung cancer with the prevalence of FPF.[19]

It was estimated that the risk of malignancy for FPFs can be as high as 30%, with the risk being higher in the setting of known concurrent malignancy.[20 22 23] Unfortunately, not all FPFs were subjected to further work-up including subsequent histopathological correlations. Despite the arbitrary cut-off on ^{18}FDG-PET for FPF, establishing the benign or malignant nature of the lesion based solely on SUV_{max} can be quite challenging. Although higher SUV_{max} was often encountered in malignant lesions, benign lesions, such as pleomorphic adenoma and Warthin's tumour, may also present with similarly high SUV_{max}. This was demonstrated by Wang *et al*, which did not find any statistically significant differences between benign and malignant lesions (mean SUV_{max} 8.46±4.59 in benign vs 9.98±6.04 in malignant lesions, p=0.695).[21] However, when compared with benign lesions with a mean FDG uptake of 3.65±2.59, malignant lesions, pleomorphic adenomas and Warthin's tumours all had significantly higher mean FDG uptake, with mean scores of 9.98±6.04 (p=0.043), 9.55±4.18 (p=0.019) and 10.67±5.15 (p=0.028), respectively.[21] Due to these challenges, clinicians might need to consider other techniques or parameters to assist in stratifying the risk of malignancy of these lesions. The use of combined ^{18}FDG-PET/CT as commonly utilised nowadays may provide benefit by allowing additional features that may point towards malignancy, such as ill-defined margins and lesion heterogeneity, to be visualised.[18] Wang *et al* highlighted that the inclusion of CT improved diagnostic accuracy and specificity from 19.1%

Table 1 Previously reported cases of metastatic lung cancer involving the parotid gland

Author, Year	Age	Gender	Side	Pain	Facial nerve palsy	Symptom duration	Surgery	Other treatments	Subtype	Primary lung sites	Other metastatic sites	Outcome
Cui *et al*,[8] 2019	64	M	R	N	Y	1 month	Parotidectomy + right neck dissection	Chemotherapy	Small cell	Right upper lobe Right middle lobe	Cervical lymph node	Disease free at 3 months
Lawande *et al*,[12] 2017	52	M	R	Y	N	6 weeks	No	Chemotherapy Radiotherapy	Small cell	Right upper lobe Right middle lobe	Mediastinum Subdiaphragmatic	N/A
Lenouvel *et al*,[13] 2015	59	M	R	N	N	3 weeks	No	N/A	Adenocarcinoma	Right	Renal bone	Died on day of discharge
Shi *et al*,[15] 2014	61	M	R	Y	N	1 month	Partial parotidectomy	Chemotherapy Radiotherapy	Small cell	Right upper lobe	Mediastinum	N/A
Yildiz *et al*,[16] 2011	50	M	L	N	Y	4 days	No	Chemotherapy	Small cell	Left upper lobe	Left spinal Right deep cervical nodes Left supraclavicular nodes	Died 4 months post-treatment
Ulubas *et al*,[17] 2010	59	M	R	N	N	>1 month	No	Chemotherapy	Small cell	Right main bronchus	Liver Cranium	Died 10 months post-treatment
Laco *et al*,[11] 2010	65	M	L	N	N	N/A	Parotidectomy	Chemotherapy	Adenocarcinoma	Left hilum	Right adrenal gland Hilar lymph nodes	Lost to follow-up
Borg,[6] 2004	72	M	L	N	N	2 months	No	Radiotherapy	Squamous cell	Left upper lobe	Nil	Disease free at 3 years
Imauchi,[10] 2001	74	M	L	Y	N	2 months	Parotidectomy	Radiotherapy	Adenocarcinoma	Left upper lobe	Nil	Died 6 months post-treatment
Hisa,[9] 1998	61	M	B/L	N	N	N/A	Superficial parotidectomy	Chemotherapy	Small cell	Right middle lobe	Brain	Died 17 months post-treatment
Canterra,[7] 1989	40	M	B/L	N	N	3 weeks	No	Chemotherapy	Undifferentiated	Left hilum	Cranium	Died 3 weeks post-treatment
Shalowitz,[14] 1988	54	M	L	N	Y	1 day	No	Chemotherapy	Small cell	Left lower lobe	Liver Left adrenal gland	Disease free at 3 months

Gender: M, male; Side: R, right; L, left, B/L, bilateral; Pain: Y, yes; N, no; Facial nerve palsy: Y, yes; N, No; N/A, information not available.

to 85.1%, although in expense of sensitivity, which was reduced from 90.9% to 54.5%.[21] Further evaluation by additional radiological imaging modality, such as ultrasound and MRI may also provide additional benefit in identifying abnormal and/or aggressive features that may warrant biopsy or surgical interventions.[20]

As mentioned above, tissue biopsies were not commonly obtained from FPFs. Davidson *et al* reported that of the 38 FPF cases, fine needle aspirate was only performed in four patients, of which all resulted in mixed acute and chronic inflammatory changes without any malignant features.[20] A later study by Barbara *et al* found a higher proportion with 23 of 70 patients received histopathological diagnosis through biopsy. Three metastatic deposits were identified from B-cell non-Hodgkin's lymphoma, colorectal carcinoma and melanoma with the remaining attributed to benign findings. Of these, Warthin's tumour and pleomorphic adenoma were the most common, representing 60% and 8.6% of the group, respectively.[20] The relatively high incidence of Warthin's tumour among the FPF cases identified in the setting of known malignancy might be attributed to shared risk factors, such as smoking.[20 21]

Based on the 12 previously reported cases, we identified that parotidectomies were only performed in 5 cases. Total parotidectomy with ipsilateral neck dissection was performed in one case, which identified one nodal metastasis in the neck. Resection margins were unfortunately not reported in any of the prior cases. Most of the other cases were subjected to chemotherapy with or without radiotherapy. The exception was one patient who passed away shortly after diagnosis secondary to pulmonary embolism.[13] As highlighted in table 1, 10 of the 12 prior cases reported parotid metastases in conjunction with other metastatic sites. With only two patients in previous reports surviving beyond 12 months, it is crucial that further treatment decisions in the event of an isolated, surgically resectable parotid metastasis be made in a multi-disciplinary setting. Treatment plans should be tailored to each individual patients, taking into account their comorbidities, functional status, other metastatic disease sites, prior treatments, as well as perioperative risks.

Learning points

- Parotid gland involvement in metastatic lung adenocarcinoma remains an uncommon finding and may be a poor prognostic indicator.
- The use of ^{18}F-FDG PET in assessing treatment response and surveillance of lung cancer allows for early recognition of distant metastatic disease.
- Difficulties in differentiating between benign and malignant parotid lesions based on ^{18}F-FDG PET features highlight the need for further investigations, especially in patients with strong clinical history of other known primary malignancies.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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