Which “P” Came First? The Parotid or the Pancreas? A Diagnostic Dilemma

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ABSTRACT

Neoplasm of the salivary glands is rare and accounts for 3% to 6% of all head and neck tumors, and about 85% occurs in the parotid glands. Metastatic disease to the salivary gland, in particular the parotid gland, is noted to be uncommon among solid tumors and has not been well described before. We report a patient who presented with an initial parotid swelling, only to ascertain, it was a metastatic lesion arising from an adenocarcinoma of the pancreas.

Key Words: Salivary glands, parotid gland, adenocarcinoma, metastatic

INTRODUCTION

Tumors of the salivary glands account for 3% to 6% of all head and neck neoplasm in adults. Their clinical and histological appearances vary markedly. The World Health Organization describes 24 distinct malignant epithelial tumors of salivary origin (1).

About 85% of salivary gland tumors occur in the parotid glands, followed by the submandibular and minor salivary glands, and about 1% occurs in the sublingual glands. 75 to 80% are benign, slow-growing, movable, painless, usually solitary nodules beneath normal skin or mucosa (2). Malignant tumors of salivary glands are less common and can be characterized by rapid growth or a sudden growth spurt. Mucoepidermoid carcinoma, adenoid cystic carcinoma, and adenocarcinoma account for over 75% of all salivary gland carcinomas (3). Mucoepidermoid carcinoma is the most common malignant tumor of the parotid gland, accounting for 30% of parotid malignancies. Adenocarcinoma of the parotid develops from the secretory element of the gland. Histological appearances varying between low-grade well-differentiated papillary or mucinous patterns to high-grade, undifferentiated lesions (4). This is an aggressive lesion with potential for both local lymphatic and distant metastases. Approximately 33% of patients have nodal or distant metastasis present at the time of initial diagnosis.

The most common solid tumors to metastasize to the pancreas include carcinomas of the kidney, lung, breast, colon, stomach, esophagus, and melanoma (5). However, this case reveals an initial presentation of a metastatic lesion of the parotid gland, with a late detection of its primary, the adenocarcinoma of the pancreas.

CASE REPORT

A 63 year old gentleman, ex-smoker, with no known medical illness, presented with a painless left parotid swelling for 2 weeks which had increased in size. He denied other systemic symptoms at early presentation except for occasional pluritic chest pain. A thorough otorhinolaryngological (ORL) examination was performed which revealed a left parotid swelling, measuring 3cm x 3cm and firm in consistency. Other physical examinations were unremarkable. Fine Needle Aspiration Cytology (FNAC) of the parotid swelling was performed, which revealed the possibility of adenocarcinoma.

Subsequently, the patient underwent a Computed Tomography (CT) scan of the neck, thorax and abdomen, which showed a left parotid mass (Figure 1), and right lung mass (Figure 2a) with mediastinal lymphadenopathy. Rim-enhancing hypodense lesions were noted in the paravertebral (Figure 2b) and anterior chest wall muscles, suggestive of metastases. The pancreatic head was bulky, with multiple rim-enhancing hypodense intrapancreatic lesions. (Figure 3a and 3b).

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doi:http://dx.doi.org/10.12996/gmj.2019.77
Figure 1: Axial CT scan image showing an ill defined, heterogeneously enhancing mass in the superficial lobe of the left parotid gland (arrow).

Figure 2a: Axial CT image in the lung window showing the mass in the right lung (arrow), with small cavitation within.

Figure 2b: Axial CT image in the mediastinal window showing right hilar mass (yellow arrow) and rim-enhancing lesion in the left erector spinae muscle (white arrow)

Referrals to the respiratory team were made in view of the lung lesion to determine metastasis to the lungs. Furthermore, a CT guided biopsy of the right lung lesion was performed, and results showed non-small cell type of carcinoma.

Fluorine-18-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (F-18-FDG –PET/CT) scan was done and showed widespread malignancy involving the right lung, left parotid, left adrenal, pancreas, peritoneal nodules, nodes (cervical, supraclavicular, mediastinal and abdominal), bones and muscles. At this time, the primary malignancy was suspected to be originating from the right lung. (Figure 4a-c).
Figure 3a and 3b: Axial CT image showing bulky head of pancreas, with rim-enhancing hypodense lesions within the head and tail of pancreas (arrows)

Figure 4a: FDG uptake at the left parotid (yellow arrow) and right hilar region (white arrow)

Figure 4b: FDG uptake at the right hilar mass (box)

Figure 4c: FDG uptake at the pancreas (box)
Survival rates are reported to be poorer for high-grade tumours (10). Grade 3 (high-grade) tumours are more solid with a greater mitotic rate. Grade 1 (low-grade) tumours are circumscribed and minimally invasive. Grade 2 lymph node involvement (9). Other features of malignancy include local infiltration to the parapharyngeal often ill defined, with heterogeneous enhancement, as seen in this patient. Tumours. On the other hand, malignant or metastatic parotid tumours are benignity. Cystic or haemorrhagic components may be found in larger benign usually have poorly defined margins and enhance inhomogeneously (9). Other evidence in regards to adenocarcinoma tumours in particular.

**DISCUSSION**

This clinical case shows a dilemma between the primary source of the adenocarcinoma, as the initial presentation did not complement the origin of the cancer. Carcinomas most commonly metastasize via the lymphatic system; first to the regional lymph nodes and then into the general circulation. Dependent upon the primary site of the tumour, metastases from carcinomas commonly occur to the lungs, liver and bones. It is important to be able to distinguish the origin of the mass as the management will depend significantly on the histological type and staging of the disease. It is rare for soft-tissue metastases to be a presenting sign of an occult cancer as by the time these appear, the patient has commonly developed symptoms pertaining to the primary tumour (6).

Evaluating the origin of metastatic disease could be difficult and confusing in many cases because of the presence of concomitant sites of involvement. In our case, although the origin of metastatic disease preliminary diagnosis was considered to be of salivary gland origin, the chance of having a second malignancy or primary could not be completely ruled out.

The incidence of distant metastasis in head and neck cancer and especially in salivary gland cancer is relatively low in comparison to other malignancies. Furthermore, the presence of distant metastasis heralds a poor prognosis in head and neck cancer, with a median survival of 4.3-7.3 months (6).

A report in 2014, was the first case which showed presentation of acinic cell carcinoma of the parotid with metastatic spread to the pancreas even after years of treatment of the initial diagnosis. Overall, metastases to the parotid are uncommon in solid tumours, with autopsy studies showing pancreatic involvement as a diffuse metastatic disease in 3-12% of all patients (7).

However in this clinical case, it has shown to be vice versa. There is a similarity between the structure of the salivary glands and the pancreas. The duct system made up of acinar and duct cells ensconced in a sheet of myoepithelial cells. The acinar cells line the intercalated and striated ducts through which the saliva travels before it is expelled into the mouth. While the salivary glands themselves are mesodermal in origin, endocrine cells may be found within these glands, most likely derived from embryonic neural crest cells of the diffuse neuroendocrine system. It is likely that such cells give rise to neuroendocrine tumours in this location, although it has been proposed that pluripotential stem cells capable of dual epithelial and endocrine differentiation may be the source of the tumour (8). However, there has been no conclusive evidence in regards to adenocarcinoma tumours in particular.

With regards to imaging appearance, benign parotid tumours are generally well circumscribed, uniformly enhancing focal lesions while malignant tumours usually have poorly defined margins and enhance inhomogeneously (9). Lobulated appearance, and presence of vascularity within the tumour suggest benignity. Cystic or haemorrhagic components may be found in larger benign tumours, whereas calcifications are usually seen in long standing benign tumours. On the other hand, malignant or metastatic parotid tumours are often ill defined, with heterogeneous enhancement, as seen in this patient. Other features of malignancy include local infiltration to the parapharyngeal space, encasement of the carotid vessels, perineural spread, and bone and lymph node involvement (9).

Adenocarcinomas can be classified according to their histological findings: Grade 1 (low-grade) tumours are circumscribed and minimally invasive, Grade 2 (intermediate-grade) tumours are seen in between Grade 1 and Grade 3, whereas Grade 3 (high-grade) tumours are more solid with a greater mitotic rate. Survival rates are reported to be poorer for high-grade tumours (10).

Metastases to salivary glands are mainly observed in the parotid gland due to the presence of intraglandular lymph nodes, which drain the face, external ear, and scalp. Skin malignancies (melanoma, squamous cell carcinomas) are the most common primary tumours metastasizing to the salivary glands, therefore careful clinical examination has to be performed. In addition, other malignancies, such as renal cell carcinomas, lung, breast and gastrointestinal carcinomas can also metastasize to the parotid gland or periparotid lymph nodes (9-11).

The most common primary tumours which give rise to pancreatic metastases are lung cancer, breast cancer, renal cell carcinoma, malignant melanoma, carcinoma of gastrointestinal origin and prostate cancer. Less commonly metastases from osteosarcoma, leiomyosarcoma, chondrosarcoma, and Merkel cell carcinoma, have also been reported (12).

A review of resection for metastases to the parotid found renal cell carcinoma to be the most frequent primary histopathology (62%), followed by non-small-cell lung cancer, and melanoma (13). Moreover, metastatic from the parotid gland is extremely rare. In view of its rarity, other lesions that were reported in the CT scan were quickly addressed and sent for biopsy to assure the source of the primary lesion.

CT is an excellent modality for the detection and characterization of pancreatic lesions. However, differentiation of primary pancreatic neoplasm from metastases is often difficult. Pancreatic metastases are usually hypovascular, and this can appear similar to pancreatic ductal adenocarcinoma (PDAC). Unlike PDAC, most metastases are generally well circumscribed (14). Multiplicity of lesions is more commonly seen in metastases than in primary neoplasms. However, there are reported cases of multiple lesions in PDAC, possibly synchronous primary tumours or intra-glandular metastases (15). In this case, there were multiple rim-enhancing hypodense lesions in the pancreas with ill-defined margins, suggestive of primary neoplasms.

Metastatic spread to the lungs may be haematogenously, resulting in multiple lung nodules of varying sizes located peripherally, or via lymphatic drainage, resulting in diffuse interstitial thickening (16). These radiologic findings are best seen on CT. Radiologic features of adenocarcinoma metastases include air-space nodules, ground-glass opacities, consolidation, and nodules with CT halo signs (16). Cavitition is frequently present, as seen in this case.

**CONCLUSION**

Evaluating the origin of metastatic disease could be difficult in many cases because of the presence of concomitant sites of involvements. Although the possibility of a primary adenocarcinoma of the parotid gland should be considered, the management should include recognition of possibilities of metastatic spread to uncommon anatomical sites. This case demonstrated the importance of thorough investigations and radiological imaging which helped to solve the diagnostic dilemma.

**Conflict of interest**

No conflict of interest was declared by the authors.

**Acknowledgement**

The authors would like to thank the board of doctors of ORL Department of Hospital Ampang, Dr Shahrul Bin Hilmat (Head of the ORL Department of Hospital Ampang) and Dr Wan Zainab Hayati Wan Mokhtar (Head of the Radiology Department of Hospital Ampang) for their utmost contribution to conduct this report. Not forgetting the family members of the deceased in helping to gather information for this report.

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