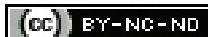


Metastasis of Head and Neck Malignancies to Liver: A Report of Two Cases

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ABSTRACT

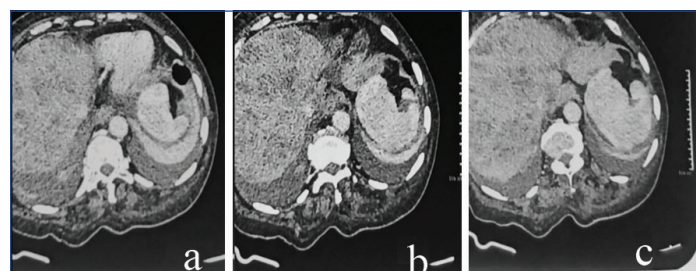
The liver is a premetastatic niche due to its high vascularity and dual blood supply and metastasis to the liver is associated with a poor prognosis. It is a common organ for metastasis, second only to lymph nodes, for malignancies like gastrointestinal cancers, breast and prostate carcinomas, uveal melanoma, neuroendocrine tumours and sarcomas. Distant metastasis from head and neck squamous cell carcinomas and Adenoid Cystic Carcinoma (ACC) is infrequent and also associated with poor prognosis. The common sites of distant metastasis from head and neck cancers are the lungs, followed by bone and then the liver. Secondary metastases to the liver from Oral Squamous Cell Carcinoma (OSCC) and ACC are extremely rare. This report presents a case of a 53-year-old male who was operated on for left submandibular gland ACC. Seven months later, he presented with icterus, generalised weakness and loss of appetite, along with increased levels of Alkaline Phosphatase and Gamma-Glutamyl Transferase. Another case involved a 61-year-old female who was diagnosed with SCC of the buccal mucosa and presented with elevated levels of Alkaline Phosphatase and Gamma-Glutamyl Transferase. Fine Needle Aspiration Cytology (FNAC) was performed on both cases, and metastasis of ACC and SCC was confirmed, respectively, by FNAC. Although the liver is a common site of metastasis, it is rare for uncommon malignant cells to be aspirated during FNAC, demonstrating its utility as a minimally invasive and rapid diagnostic tool in the management of head and neck cancers. Early detection of distant metastasis plays a significant role in the prognosis and management of affected individuals.

Keywords: Adenoid cystic carcinoma, Liver, Squamous cell carcinoma

CASE REPORT

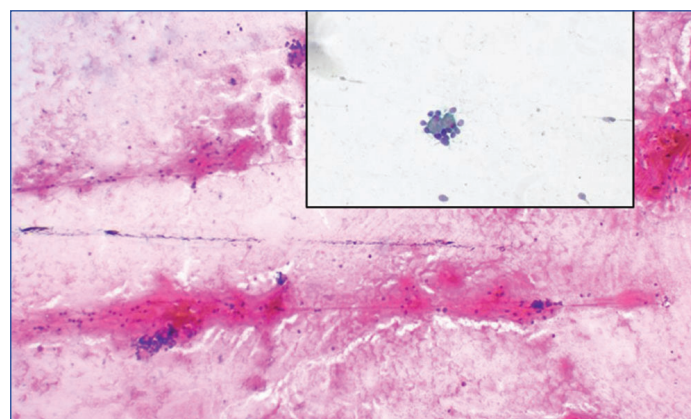
Case 1

A 53-year-old male presented with a small swelling beneath the left ear of five months' duration. The swelling measured 3×2 cm. Fine needle aspiration was performed and the diagnosis was reported as left submandibular salivary gland ACC. The patient underwent left total parotidectomy along with left modified radical neck dissection and the histopathological diagnosis confirmed ACC. Seven months later, he presented with icterus, generalised weakness and loss of appetite that had persisted for two weeks. The surgical site appeared normal and there was no ascites. The patient exhibited an increased Alkaline Phosphatase level of 263 U/L (normal range: 38 U/L-126 U/L), a Gamma-Glutamyl Transferase level of 266 U/L (normal range: 15 U/L-73 U/L), and a total bilirubin level of 10.3 mg/dL (normal range: 0.2 mg/dL-1.3 mg/dL). An abdomino-pelvic ultrasound revealed multiple well-defined, variable-sized lesions, with the largest measuring 2.6×2.5 cm, demonstrating peripheral and internal vascularity, as well as heterogeneously hypoechoic lesions in both lobes of the liver, suggestive of hepatic metastasis. Contrast Enhanced Computed Tomography (CECT) of the abdomen and pelvis showed innumerable ill-defined hypodense lesions, with the largest measuring 3.2×2.5×2.1 cm, and no significant postcontrast enhancement [Table/Fig-1].



[Table/Fig-1]: CECT images (a-c) showed several ill-defined and non enhancing hypodense areas.

A differential diagnosis of cholangiocarcinoma with satellite lesions and hypovascular metastasis was considered. Ultrasound-guided FNAC of the liver was performed, yielding 0.5 mL of blood-tinged material. The smear examination showed moderate cellularity, with tumour cells arranged in an acinar pattern, in clusters and singly. Individual tumour cells were monomorphic, round in shape, with hyperchromatic and pleomorphic angulated nuclei and scant cytoplasm. Tumour cells surrounding hyaline globules were also observed [Table/Fig-2]. There was no evidence of bile pigments, transgressing blood vessels, or endothelial wrapping in the studied smear. The features were consistent with metastatic carcinoma in the liver—diagnosed as ACC. Further biopsy was conducted, confirming the metastasis. The patient underwent chemotherapy and radiotherapy and died a month later.



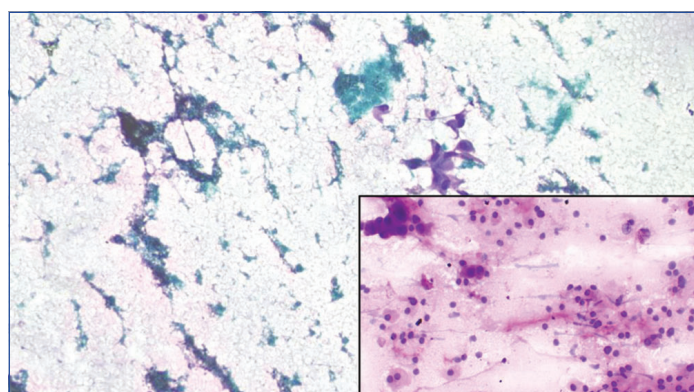
[Table/Fig-2]: Moderately cellular area showing the arrangement of tumour cells in acinar pattern, clusters and individually (H&E, 100x). The inset shows hyaline globules surrounded by tumour cells (PAP, 400x).

Case 2

A 61-year-old female presented with complaints of cough with expectoration lasting for two months. Laboratory investigations revealed elevated liver enzyme levels. A chest radiograph returned

normal results. The Alkaline Phosphatase level was 171 U/L (normal range: 38 U/L-126 U/L) and the Gamma-Glutamyl Transferase level was 111 U/L (normal range: 15 U/L-73 U/L). An ultrasound of the abdomino-pelvic region was performed, which identified two ill-defined, variably sized, heterogeneously hyperechoic lesions in both lobes of the liver, the largest measuring 1.2×1.0 cm in the left lobe, suggestive of either hepatic haemangioma or hepatic metastasis.

Further, an ultrasound-guided FNAC of liver was conducted, resulting in the aspiration of 0.5 mL of blood-tinged material. The smear examination was highly cellular, consisting of tumour cells arranged in clusters and sheets. Individual tumour cells were round to polygonal, with enlarged pleomorphic, hyperchromatic nuclei and a moderate amount of eosinophilic cytoplasm. Some cells exhibited prominent nucleoli and a few binucleate cells, tumour giant cells, and benign hepatocytes were also noted. The background exhibited haemorrhage and necrosis [Table/Fig-3]. The features were reported as deposits of SCC in the liver.



[Table/Fig-3]: Tumour cells arranged in clusters and individually. Individual tumour cells are round to polygonal with enlarged pleomorphic, hyperchromatic nuclei and a moderate amount of eosinophilic cytoplasm (PAP, 400x). The inset shows a smear with moderate cellularity of normal hepatocytes (H&E, 400x).

Upon further evaluation, an ulceroproliferative growth measuring 6×5 cm was observed on the right buccal mucosa, which was confirmed as SCC on biopsy. The patient was planned for right hemi-mandibulectomy, along with chemotherapy and radiotherapy for the metastasis but patient died a week later.

DISCUSSION

The OSCC is one of the most prevalent cancers in Kolar, accounting for over 29.66% of total cancer incidence [1]. Distant metastasis occurs primarily through the lymphatic route, with the common sites being the lungs, liver and bone. The incidence of liver metastases from head and neck cancers is approximately 4.4% [2]. A combination of medical history, radiological findings, FNAC and histopathological examination can be used to accurately diagnose metastatic lesions. Liver metastasis is extremely rare and typically associated with poor prognosis. Isolated nodules in the liver observed on ultrasound, along with a history of head and neck cancer and increased Lactate Dehydrogenase (LDH) levels, could serve as indicators of liver metastasis [3].

The presence of distant metastasis at diagnosis in head and neck squamous cell carcinoma has been significantly linked to adverse tumour characteristics, like poor differentiation, advanced T stage and advanced N stage [4]. Present case involved a patient who was recently diagnosed with OSCC and metastatic disease, for which hemi-mandibulectomy was considered but ultimately not undertaken. In studies conducted by Marcy PY et al., the incidence of distant metastases from head and neck carcinomas to the liver was reported to be 0.9% of the studied population, while Merino E et al., reported liver metastasis at a rate of 0.7% among head and neck cancer patients [2,5]. Prognosis is generally very poor, with a median survival of only four months [2]. Daiko H et al., conducted a study indicating that after resection of head and neck carcinoma in

patients with lung metastases, the three-year survival rate was 43% [6]. The five-year survival rate was documented at 40%, with a distal metastasis rate of 25% [7]. Despite advancements in both diagnosis and treatment, the prognosis for OSCC remains poor. Radiotherapy has been used as a primary treatment for surgical contraindications and unresectable tumours, although no improvement in survival rates has been reported. However, the use of immune checkpoint inhibitors, like nivolumab and pembrolizumab, has shown promising survival outcomes [8].

The ACC is a slow-growing, aggressive tumour with a high frequency of distant metastases [9]. The most common site for distant metastasis is the lungs, occurring via haematogenous spread. Only a few studies of isolated metastatic liver disease have been reported in the literature. Diagnosing isolated metastasis of ACC can be elusive, as CT and MRI scans may be non specific. However, 18F-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography (18F-FDG PET-CT) scans have improved sensitivity, which can aid in histopathological findings [10]. The five-year survival rate for ACC patients is approximately 89% [11]. In index patient, liver metastasis developed despite receiving chemotherapy, which exhibited resistance. The patient died one month later.

Karatzas A et al., studied a case of ACC of the submandibular gland that metastasised to the liver, detected during a routine liver ultrasound following a history of large bowel polypectomies. The patient was asymptomatic and routine laboratory findings were normal. CT-guided fine needle aspiration was performed, which was positive for malignancy. Further biopsy confirmed metastasis from the primary disease of ACC of the salivary gland. The patient subsequently received chemoembolisation, radiofrequency ablation and radiofrequency-assisted surgical resection and after one year of follow-up, had no recurrence [12]. A study by Scuderi V et al., on recurrent liver metastasis indicated that surgical resection resulted in the patient being disease-free for a year [13]. Due to the slow growth rate of ACC, the role of chemotherapy in metastatic situations remains controversial [14]. Surgical excision with clear margins is currently the only definitive treatment option.

CONCLUSION(S)

Although the liver is a common site for metastasis, it can rarely be a site of metastasis for uncommon malignancies. When performing tumour staging, liver metastasis should be taken into consideration, as treatment and prognosis can vary according to the staging. Further studies are required to investigate the clinical and molecular factors that contribute to the development of distant metastasis in head and neck cancer.

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