Metastatic ampullary adenocarcinoma in exfoliative sputum cytology: A rare presentation

Sir,

The ampulla of Vater is a complex structure formed by the sphincter of Oddi muscle surrounding the confluence of the distal common bile duct (CBD) and main pancreatic duct that opens at the papilla of Vater on the medial wall of the duodenum. Ampullary carcinomas are defined as those that arise from structures within the ampullary complex.[1] These are rare tumors constituting approximately 0.5% of all gastrointestinal (GI) tract malignancies and encountered commonly in the sixth to eighth decades of life with a slight male preponderance.[2]

Ampullary carcinoma tends to manifest early with jaundice due to biliary outflow obstruction, thereby making it amenable for surgical resection in most cases and overall better survival compared with pancreatic neoplasms that are often advanced when diagnosed.[2] Ampullary carcinoma most often metastasizes to abdominal lymph nodes, peritoneum, and the liver. Metastasis to lungs, bones, and rarely brain, ovaries are also documented.[3]

Sputum examination for exfoliated malignant cells is fast losing its relevance in modern-day cytology practice, mostly replaced by sophisticated techniques such as bronchoscopy, broncholaveolar lavage (BAL), or fine-needle aspiration cytology (FNAC). Although its role in the diagnosis of primary lung carcinoma has been validated time and again in various studies, in metastatic lesions, sputum cytology has been reported to have a poorer yield.[4,5]

We diagnosed a case of metastatic adenocarcinoma to the lung in a patient with ampullary primary in exfoliative sputum cytology.

A 55-year-old man underwent pancreaticoduodenectomy in April, 2013, in a private hospital for carcinoma of the ampulla of Vater. The discharge summary mentioned a moderately differentiated adenocarcinoma [Figure 1a] invading the pancreas with resection margins free of tumor, no nodal involvement or clinicoradiological evidence of distant metastasis. The tumor was characterized as pT3, pN0, M0, and bracketed in stage IIA disease. He did not receive any adjuvant chemotherapy.

On routine follow up, he has been asymptomatic until August 2014 when he presented to the Department of Pulmonary Medicine at our hospital with complaints of progressively increasing dyspnea, productive cough expectorating blood-streaked sputum, bilateral basal lung crepitations on auscultation, and a markedly elevated CA 19.9 level of 950 U/mL (reference range: 0–5 U/mL). A routine chest radiograph showed multiple nodular lesions in both the lung fields. A PET-CT further highlighted left supraclavicular nodes, retrocrural and portacaval nodes [Figure 1b].

Sputum samples collected on two consecutive days were submitted for cytological evaluation. Papanicolaou-stained smears revealed three-dimensional clusters of malignant cells with central to eccentrically placed vesicular nuclei, anisonucleosis, prominent nucleoli, moderate to abundant eosinophilic and focally vacuolated cytoplasm, consistent with an adenocarcinoma [Figure 1c and d]. The original slides from the ampullary tumor were reviewed in our hospital and the cytological findings were consistent with metastasis from the ampullary adenocarcinoma.

The CA 19.9 level nearly tripled in one week. The patient expired within two weeks of the diagnosis of metastatic disease.

Ampullary carcinoma is a relatively uncommon GI malignancy but with an ominous trend of rising incidence since 1973 at an annual percentage rate of 0.9%. Adenocarcinoma, not otherwise specified (NOS) (65%) is the commonest histologic type with either an intestinal or pancreaticobiliary type of differentiation.[1]

The survival scenario of ampullary carcinoma after pancreaticoduodenectomy has been improving attributable largely to early presentation at a surgically resectable stage and lately to improved surgical technique with decreased operative mortality and morbidity. The 5-year survival observed in various studies even with nodal metastasis ranged from 16% to 50%; a maximum survival of 81% reported by a Japanese series in patients with no nodal metastases.[2]

Almost any cancer has the ability to spread to the lungs, but the tumors that most commonly do so include bladder, colon, breast, prostate cancers, sarcoma, melanoma, Wilms tumor, and neuroblastoma. Chest radiography has poor overall sensitivity in the detection of lung metastasis. Newer advanced imaging techniques such as computed tomography

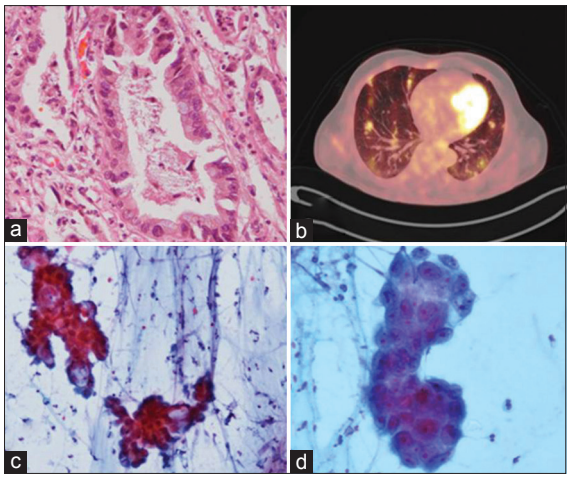

Figure 1: (a) Adenocarcinoma of the ampulla of Vater (hematoxylin and eosin, ×10), (b) Positron emission tomography (PET) scan showing bilateral hypermetabolic lung nodules, (c and d) Sputum cytology showing clusters of malignant cells from metastatic adenocarcinoma (Papanicolaou stain, ×10 and ×40, respectively)

with superior sensitivity and resolution is routinely used for diagnosis of lung metastasis. More recently, metabolic imaging using positron emission tomography scan is widely employed for metastatic work up.[6]

The role of sputum cytology is well established in the diagnosis of primary lung carcinoma. In a study published way back in 1971 by Oswald *et al.*, evaluation of one or more satisfactory sputum specimens from 2035 patients gave a pathological proof of primary lung carcinoma in 59% of patients and positivity rate escalated to 69% and 85% when three and four or more specimens were tested, respectively.[4] Agustí *et al.,* reported a higher diagnostic yield of induced sputum compared with spontaneous sputum in patients with peripheral lung tumors who had normal bronchoscopic evaluation.[5] Sing *et al.,* observed an overall comparable sensitivity of sputum and brush cytology in the diagnosis of lung carcinomas. Sputum cytology was more useful in early and peripheral carcinomas, whereas brushing ranked superior in the diagnosis of advanced and centrally located malignancies.[7] Choi *et al.,* proposed that the sensitivity rate of sputum cytology can be further enhanced using automated ThinPrep cytopreparatory method.[8] Researchers have also attempted using sputum as an easily obtainable noninvasive sample for early diagnosis and screening by molecular methods.[9]

However, when dealing with metastatic tumors, sputum cytology is touted to have a poorer diagnostic yield. Ali *et al.,* retrospectively reviewed the positive sputum samples of 35 patients with metastatic tumors involving the lung and observed intact tumor architecture in the exfoliated cells in 75% of patients. Metastatic colonic adenocarcinoma was the commonest primary site.[10] Radford *et al.,* evaluated the sputum samples of 22 patients with pulmonary metastases from colorectal adenocarcinoma with a positive or atypical result in 65%

of cases. The authors observed that the positivity rate increases if three samples are collected.[11] To the best of our knowledge, no case of metastatic ampullary carcinoma to the lung with the pathological diagnosis established on sputum cytology has been reported so far.

Sputum cytology for malignant cells in suspected lung metastasis has largely been shelved and replaced by more invasive cytological techniques such as FNAC, bronchoscopic washings and BAL. The newer modalities, besides having a higher sensitivity, also provide a platform for immunocytochemistry on cell block preparation.[12]

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