CASE REPORT

Enteric adenocarcinoma lung: a rare presentation in an Omani woman

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SUMMARY

Pulmonary adenocarcinoma is a common neoplasm, yet the one with enteric or intestinal differentiation poses a diagnostic challenge to pathologists as it shares a common immunohistochemical profile with metastatic colorectal carcinoma. We report a case of a 61-year-old woman. She was on surveillance when incidentally she was discovered to have multiple bilateral lung nodules on imaging; the largest was surgically removed for histological examination. Morphology was consistent with a moderately differentiated adenocarcinoma. The tumour cells were positive for cytokeratin (CK) 7, CDX2, CK20 and were negative for thyroid transcription factor 1. The morphology and immune histochemical profile raised the differential diagnosis of a metastatic colorectal carcinoma and a primary lung adenocarcinoma with enteric differentiation. On the basis of morphology and CK7 positivity we established the diagnosis of enteric-type adenocarcinoma of primary lung origin. She has completed planned courses of palliative chemotherapy and remains on surveillance.

BACKGROUND

Adenocarcinoma of the lung is the leading cause of cancer death worldwide. Overall prognosis of lung carcinoma is dismal. Smoking in addition to environmental carcinogens are the main contributory factors leading to the development of adenocarcinoma.¹ There is an increase in the incidence of adenocarcinoma in women including those who are non-smokers.²

There is a lot of overlap between the enteric-type adenocarcinoma and metastatic colorectal cancer.³ Clinical history, disease distribution and routine histological examination can resolve the differential diagnosis in majority of the cases. Immunohistochemical studies using a small panel of antibodies have emerged as a powerful tool in more difficult cases which include thyroid transcription factor 1 (TTF1), cytokeratin (CK) 7, CK20 and CDX2 9.³ CDX-2 is a sensitive and specific marker for primary and metastatic colorectal adenocarcinomas, although it has been reported in 13% of lung adenocarcinomas, and occasionally in other non-gastrointestinal adenocarcinomas.⁴ A combination of histology, panel of immunohistochemical markers, imaging and negative colonoscopy helps to establish definitive diagnosis.

CASE PRESENTATION

A 61-year-old morbid obese, ex-nurse walks into the oncology outpatients of Sultan Qaboos University Hospital, Muscat, Oman. She had a

recent h/o left mini-thoracotomy and is known to have systemic lupus erythematosus and lupus arthritis on prednisone and azothioprine, hypothyroidism on thyroxine replacement, type 2 diabetes mellitus on metformin and mixtard insulin, dyslipidemia on statins, hypertension on carvedilol and amlodipine, ischaemic heart disease, allergic rhinitis, atopic bronchial asthma, interstitial lung disease, pelvic inflammatory disease C5–6, osteoporosis on elandronate, bilateral knee osteoarthritis, antral gastritis, gastroesophageal reflux disease and mini-hiatus hernia and h/o postpartum haemorrhage with each delivery necessitating dilation and curettage. There was significant surgical history, including; mini-laprotomy for bilateral tubal ligation (1982), laproscopic appendectomy (1990), balloon angioplasty—vessel rupture and open heart surgery (1993), umbilical herniorrhaphy (1995), Manchester repair for anteverted uterus (2000), vaginal repairs and recent h/o cystoscopic urethral dilation for incontinence and intra-aortic balloon pump with coronary stenting in April 2012 on dual antiplatelets.

INVESTIGATIONS

She was undergoing surveillance high-resolution CT which revealed bilateral multilobar lung nodules. A positron emission tomography CT was consistent with fluorodeoxyglucose avid bilateral pulmonary and subpleural nodules (SUVmax 2.2), largest 1.7×1.1 cm in the left lower lobe, which underwent wedge resection in April 2012 abroad. There was a 1.6×1.5 cm nodule in left adrenal gland (SUVmax 4.2), incidental uterine fibroids, granulomas in right basal ganglia, spleen and bilateral gluteal regions. The histology on H&E from lung nodule was consistent with bronchioalveolar carcinoma lung, carrying wild-type epidermal growth factor receptor (EGFR) and no evidence of activating somatic mutations.

The paraffin blocks and slides were brought to Sultan Qaboos university Hospital pathology department for second opinion.

She was essentially asymptomatic, with a performance status of 2, bradycardia, with thoracotomy scars at the anterior median and left postero-lateral skin. There was minimal pitting oedema and protuberant (fat) abdomen. She was admitted for work-up including and revealing baseline bloods and biochemistry (urea and electrolytes, liver function tests, coagulation parameters, hepatitis viral serology, HIV, thyroid function test, quantitative immunoglobulin's, complement and inflammatory markers were within normal, but her

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Figure 1 H&E photo micrograph.

CD4 counts were $0.335 \times 10^9/l$, trace proteinurea and glycosylated haemoglobin 7.6%), bone mineral density with mild osteopaenia and low risk of fracture, ECHO (left ventricular ejection fraction 59%, mild left ventricular hypertrophy, minimal pericardial effusion and degenerative valvular disease including mild MV stenoses and trivial TR), Upper gastrointestinal endoscopy (consistent with mild active chronic gastritis). H&E stained sections revealed lung parenchyma infiltrated by neoplastic cells arranged in glands. Individual cells showed nuclear atypia and focal mucin production figure 1. Periphery of the lesion showed lipaedic growth pattern of tumour cells figure 1 (inset). The tumour cells showed immunoreactivity for CK7, CK20 and CDX2 and were negative for TTF1 composite figure 2. A villin stain was also performed which was also negative.

DIFFERENTIAL DIAGNOSIS

The histological impression was enteric-type adenocarcinoma lung versus primary colorectal adenocarcinoma. This differential was raised because the morphological pattern showed neoplastic glands lined by mucinous type of epithelium this morphology is seen in both types of cancer. The immunohistochemical features

for the types is similar except for the fact that colorectal cancer is usually negative for CK7 stain. However, subsequent colonoscopy till caecum was normal. Biopsies were also taken and they were reported as negative, thereby excluding the possibility of colorectal cancer metastases.

TREATMENT

Patient was consented to be treated with pemetrexed carboplatin and she has completed four cycles with stable lung nodules, marked reduction in adrenal and liver deposits. She is tolerating the planned courses of chemotherapy quiet well with minimal fatigue and grade 1 thrombocytopaenia, grade 2 neutropaenia but without grade 3 or 4 toxicity. Our plan is to complete six cycles (last two with pemetrexed alone) followed by surveillance and restart chemotherapy at first clinical or radiological evidence of disease progression.

DISCUSSION

WHO classification of lung cancers 2004 remained a gold standard for some time, but there was an increasing need to use multidisciplinary approach keeping in view the recent advances in imaging techniques, molecular pathology and anticancer therapies.⁵ A new classification of lung cancer was proposed in 2011.⁶ The distinction of pulmonary adenocarcinoma with intestinal differentiation from metastatic colorectal carcinoma is important because of critical differences in therapeutic strategies and prognosis.

Other recommendations included in the document are recognition of the enteric pattern of adenocarcinoma as a variant, and assimilation of what once was referred to as mucinous bronchioloalveolar carcinoma into the variant category of invasive mucinous adenocarcinoma. The former needs to be distinguished from metastatic colorectal cancer, whereas the latter frequently harbours k ras mutation. Clear cell and signet ring cell variants have been removed but are still recognised as legitimate descriptions; signet ring cell adenocarcinoma remains important due to EML4 ALK fusion gene alterations.⁷

This new classification strategy is based on a multidisciplinary approach to the diagnosis of lung adenocarcinoma that

Figure 2 Immunohistochemical stains.

incorporates clinical features, molecular profiling, imaging and surgical findings yet pivotally based on histology. This classification is intended to support clinical practice and clinical trials. As EGFR mutation is a validated predictive marker for response and enhanced progression-free survival with EGFR tyrosine kinase inhibitors in advanced lung cancers therefore EGFR mutational testing remains obligatory in modern day practice. This classification also has implications for strategic management of tissue, particularly for small biopsies and cytology samples, to maximise high-quality tissue availability for molecular studies. Impact factor calculation depends on the size of invasive component (T), number of lymph nodes involved (N) and metastases (M)^{8 9} and by radiologically measuring the size of the solid component.¹⁰

Learning points

- The distinction of pulmonary adenocarcinoma with intestinal differentiation from metastatic colorectal carcinoma is important because of obvious differences in therapeutic strategies and prognosis.
- Clinical history, disease distribution and routine histological examination can resolve the differential diagnosis in most cases.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

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