

LETTERS TO THE EDITOR

Colonic polyp harboring lung cancer metastasis: An unpleasant surprise

Dear Editor,

Lung cancer is a most frequent malignancy, however diagnosis of lung cancer from an endoscopically resected metastatic colonic polyp is very unusual.

A 55-year-old male with positive family history for colon cancer and personal history of heavy smoking, hypertension and mild depression, underwent a surveillance colonoscopy. Three years earlier, on his first colonoscopy, a small tubular adenoma was removed from the sigmoid colon, and a 1-cm tubulovillous adenoma was found and also resected from the rectum. This time, colonoscopy revealed a 1.5-cm sessile polyp in the ascending colon, which was removed endoscopically uneventfully and sent for histopathological examination. The latter showed large pleomorphic cells with hyperchromasia, prominent nucleoli, and high mitotic counts encompassing a polypoid colon fragment (Figure 1a). Due to the difficult differential diagnosis, an extensive immunohistochemical study was carried out. Neoplastic cells were strongly immunoreactive to cytokeratin AE1/AE3, cytokeratin 7, cytokeratin 19 and thyroid transcription factor-1 (TTF-1), with Ki-67 also briskly positive (Figure 1a,b). On the other hand, cytokeratin 20, CDX-2, Ca 19-9, S-100, melan-A, HMB-45, CD-68, carletinin, renal cell carcinoma antigen and CD10 were negative. Finally, the diagnosis of metastatic non-small cell lung cancer in a colonic adenoma was set. The patient underwent a chest computed tomography (CT) scan, which showed a large right lower lobe primary tumor, with concomitant enlarged mediastinal lymph nodes. He was staged as stage IV, due to proven distant metastatic disease and treated with palliative chemotherapy. Unfortunately, the patient died five months later due to pulmonary embolism.

Primary lung cancer is the second most common cancer-related cause of death among both sexes. Metastasis from lung cancer may occur to regional lymph nodes, brain, bones, adrenals and even heart [1]. It is rare for metastatic deposits to arise in the gastrointestinal (GI) tract, and even more seldom to be found in the colon. From the GI tract, the small intestine is mostly reported as the site of lung cancer metastasis, and especially the jejunum compared to duodenum or ileum. Hematogenous or lymphatic spread of the neoplastic cells is the prevailing pathogenetic mechanism [2]. Esophageal involvement due to direct tumor extension has been reported before as well as a handful of cases of gastric metastasis from pulmonary adenocarcinoma [3]. To the best of our knowledge, previous reports of colon metastasis from lung cancer presented as obstruction or perforation, or as fistulas with other organs in patients with disseminated disease [4]. In our case a solitary small hyperplastic polyp on first impres-

sion was removed and led to the diagnosis of primary lung cancer, which is extremely rare.

Polyps harboring metastasis from extracolonic cancers have been reported in patients with breast, ovarian, skin (melanoma), gastric, esophageal and renal cancer [5].

This case demonstrates the importance of histopathological examination and proper immunohistochemical work-up in the assessment of unusual findings in common lesions.

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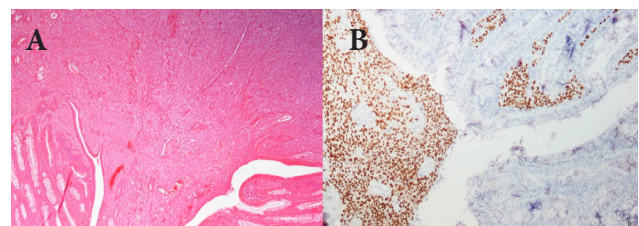


Figure 1. A: Large pleomorphic cells with hyperchromasia, prominent nucleoli and high mitotic counts embedded in a polypoid colon fragment (H & E x400). **B:** Immunohistochemical section indicating neoplastic cells positive for TTF-1 (nuclear stain) (TTF-1 x400).

Peri-operative maintenance of dual antiplatelet therapy is safe in patients requiring laser cordectomy for laryngeal cancer

Dear Editor,

We had recently come across the case of a 72-year old male patient with hoarseness of two-month duration, who had undergone drug-eluting coronary artery stent (DES) placement 2 days prior to his laryngological examination, and was under dual antiplatelet therapy with clopidogrel 75 mg and aspirin 100 mg. Moreover, the patient demonstrated severe left ventricular dysfunction with an ejection fraction of 35%, and consequent arrhythmia.

The endoscopic view of the patient's larynx is shown in Figure 1a. The vocal cord movement appeared normal, whereas no cervical lymph nodes were palpated. A CT scan of the neck and chest was unremarkable. The patient was informed that a microlaryngoscopy and biopsy under general anaesthesia was necessary for diagnosis, and consequent treatment planning.

DES are thought to reduce the rate of restenosis observed with bare-metal stents. However, the implementation of dual antiplatelet therapy with aspirin and thienopyridine for a minimum of six months is recommended in patients with DES to prevent stent thrombosis [1]. Premature cessation of dual antiplatelet therapy has been shown to be the single most important predictor in the latter process [2], which represents a sudden and potentially catastrophic complication of stent placement, with a high mortality rate. Therefore, the risk of withdrawing antiplatelet therapy in patients with DES must be weighed against the risk of retaining them, and elective surgical procedures are best delayed by at least six months after DES placement.

A multidisciplinary team consisting of an ENT Surgeon, Anaesthetist, Cardiologist and Haematologist reviewed the case and suggested that the patient be operated four weeks following his initial examination [3], whilst on aspirin and having stopped the clopidogrel on the previous day. The patient would resume his medication four and eight hours postoperatively, regarding the aspirin and clopidogrel, respectively. One unit of packed red blood cells and two bags of pooled platelets were also available if needed, whereas intravenous tranexamic acid was also ready to be administered upon request.

Nonetheless, the procedure was uneventful. No significant bleeding was encountered, and haemostasis was achieved with adrenaline-soaked neuro-patties. The patient was discharged the next day. Histology showed that the anterior commissure was free of disease, the anterior third of the left vocal cord had highly differentiated squamous-cell carcinoma, whereas an area of leucoplacia in the posterior third proved to be *in situ* carcinoma.

The patient was given two options for definitive treatment; laser cordectomy or external irradiation, and chose the former. He underwent an endoscopic laser cordectomy of his left vocal cord (2.5 watts continuous emission) three weeks later (Figure 1b), under the same medical precautions. The operation was again uneventful and the patient was discharged the next day. Histology showed complete

tumor removal within healthy margins.

In conclusion, dual antiplatelet therapy with aspirin and thienopyridines can be safely maintained in patients requiring laser cordectomy for laryngeal cancer within the first six months of DES placement to minimize the risk of peri- or postoperative stent thrombosis, as the associated bleeding tendency is minimal, and a potential airway compromise not likely to occur.

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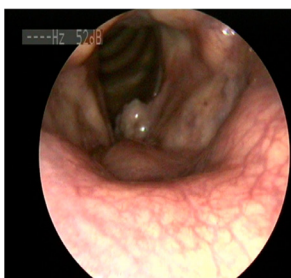


Figure 1a

Pre-operative endoscopic view of the patient's left vocal cord.

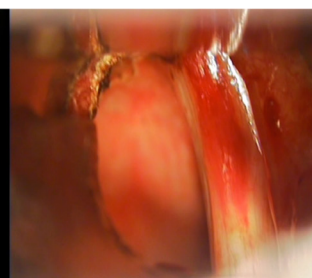


Figure 1b

Postoperative microscopic view of the patient's larynx.

Can aromatase inhibitors cause forgetfulness in women with breast cancer ?

Dear Editor,

Forgetfulness is a common complaint among breast cancer patients with an estimated incidence of 70%. This complaint is more frequent particularly in patients using aromatase inhibitors such as letrozole, anastrozole or exemestane. Breast cancer is primarily a postmenopausal disease and more common in patients over the age of 50. Incidence of forgetfulness exhibits an increasing frequency as a result of the natural physiology of aging, especially after the 5th decade. Indeed, forgetfulness and dementia are more frequent in postmenopausal patients when compared with premenopausal women. A general consensus of the researchers on the cause of forgetfulness is that it is most likely secondary to the vascular and/or neurotransmitters' damage in brain parenchyma [1]. The most prominent neurotransmitters relevant to such damage are gamma-aminobutyric acid (GABA) and acetylcholine. It has been shown that the decrease or deficiency of the amount of acetylcholine in the central nervous system (CNS) is directly associated with Alzheimer's disease. Today, forgetfulness is known as the first emerged symptom in Alzheimer disease and the severity of forgetfulness is directly correlated with the severity of Alzheimer's disease. Moreover, the therapies which increase the levels of acetylcholine in CNS decelerate disease progression significantly and reduce the complaints of forgetfulness [2].

In women, it has been shown that estrogens protect from cardiovascular thromboembolic events with their direct protective effect or with indirect effect due to their positive influence on lipid profile. Furthermore, the increased estrogen levels in the CNS has been found to be antiapoptotic for brain tissue, protective against neural damage and has also been found to act as direct vasodilator and vasoprotective by increasing the nitric oxide levels in the CNS [3]. In addition, the estrogens reduce B-amyloid and neurotransmitter levels which lead to impairment of the brain parenchyma. Based on these findings, it was suggested that low estrogen levels might be associated with decreased cognitive changes in postmenopausal women, however there is no certain data to prove this statement.

Estrogen increases the levels of glutamate, serotonin, noradrenaline and acetylcholine which act as excitatory in the CNS. The effect of estrogens on acetylcholine levels may be of particular importance on forgetfulness. Dementia other than Alzheimer's disease may also develop due to increased prothrombotic events which are in parallel with the decrease in estrogen levels. On the other hand, the relationship between estrogen levels and temporary memory loss in middle-aged women has never been demonstrated. Additionally, no significant difference was observed in the estrogen replacement group compared with placebo in

terms of forgetfulness levels and cognitive changes after a 4-month course of estrogen [4]. Depending on that study, it was suggested that estrogen therapy had no proven benefit in patients with memory impairment.

It is still unclear if aromatase inhibitors have negative effect on memory due to vascular events secondary to diminished estrogen levels or that these inhibitors may affect the brain tissue directly independent of acetylcholine levels [5]. Besides, there is no clear data on the safety and efficacy of aromatase inhibitors in Alzheimer's disease and in early-age dementia syndromes. Complaints of forgetfulness which developed during the use of aromatase inhibitors remains a clinical problem whether this should lead to treatment discontinuation and it is also not clear how an optimal clinical approach should have been to establish patients in this condition. Furthermore, complaints of forgetfulness, even if it is likely to be associated with the direct effects of aromatase inhibitors, it is yet not clear whether such an effect will be permanent.

Therefore, more randomized controlled trials are required to explain if aromatase inhibitors may cause forgetfulness affecting directly the CNS and independent from dementia induced by vascular and neurological structural disorders.

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