CASE REPORT

Dilemma in Managing Carcinoid Crisis Secondary to a Metastatic Well-differentiated Neuroendocrine Tumor of the Lung

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Abstract

Background: Well-differentiated neuroendocrine tumors (NET) of the lung account for 2% of all primary lung neoplasms. Less than 2% of the lung NET present with the carcinoid syndrome manifested as facial flushing, diarrhea, palpitation, and bronchospasm, as a result of a hypersecretion of hormones and peptides from the tumor. Carcinoid crisis is a life-threatening complication of the carcinoid syndrome and its manifestation as coronary vasospasm is rare. Octreotide is a gold-standard treatment to control the symptoms; however, octreotide as a triggering factor for coronary vasospasm has never been reported.

Case description: A 62-year-old man presented with multiple episodes of carcinoid symptoms is referred to our hospital. A series of investigations were carried out and he was diagnosed with the lung NET with a liver and bone metastasis. He developed coronary vasospasm, which could be due to the carcinoid crisis itself or the treating agent octreotide, after initiation of octreotide for carcinoid syndromes. After intense perioperative management by multidisciplinary teams, he underwent successful symptom control by perioperative octreotide and surgery.

Conclusion: Surgery is the mainstay treatment to control carcinoid syndromes or crisis. Multidisciplinary therapy in perioperative care is paramount to ensure an optimal surgical outcome.

Keywords: Carcinoid syndromes, Carcinoid tumors, Neuroendocrine tumors.

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Background

Well-differentiated lung NET or lung carcinoid account for 2% of primary lung neoplasms.[1] Only less than 2% of lung carcinoids are functional, exhibiting the carcinoid syndrome: facial flushing, diarrhea, palpitation, and bronchospasm due to a hyper secretion of hormones and peptides, such as serotonin from the tumor.[2] Carcinoid crisis is a life-threatening complication of the carcinoid syndrome causing a severe hypertension or hypotension, which can be precipitated by general anesthesia, tumor manipulation, and diagnostic or therapeutic intervention. Coronary vasospasm is a rare manifestation of the carcinoid crisis.[3]

Octreotide is a somatostatin analog (SSA) that binds to a somatostatin receptor, inhibiting the release of peptides and amines and thus help controlling symptoms.[4] Octreotide is a gold-standard treatment to control both the carcinoid syndrome and crisis, and is also recommended as prophylaxis against the carcinoid crisis when these patients undergo a surgery.[5] The side effects of octreotide are minimal,[5] and octreotide as a trigger to coronary vasospasm has never been reported.

Lung NET with the carcinoid syndrome or crisis is a rare tumor with limited published literature to date. There is no standard treatment available especially for metastatic lung carcinoids, but primary tumor removal is recommended with multidisciplinary team involvement.[6] Optimum perioperative management to minimize the risk of crisis is imperative to improve surgical outcomes.

Case Description

A 62-year-old man presented with multiple episodes of carcinoid syndrome manifested as profuse diarrhea, vomiting, and facial flushing for 3 months is referred to our hospital. A series of investigations did revealed raised urine 5-HIAA (3677 mg, normal range 2–7) and serum chromogranin (67,320 ng/mL, normal range 27–94). Contrast enhanced computerized tomography (CECT) showed a left lung mass with multiple metastatic bilobar lesions in the liver and bone. An ultrasound-guided biopsy of the liver lesion showed a well-differentiated neuroendocrine tumor positive for TTF-1, which indicated a lung or thyroid origin. A Ga-68 DOTANOC PET scan showed a somatostatin receptor (SSRT) expressed in the left lung mass, liver, and bones (Fig. 1). He was treated for lung NET with a liver and bone metastasis.

He received the first subcutaneous dose of 30-mg long-acting octreotide after the diagnosis. He developed the carcinoid

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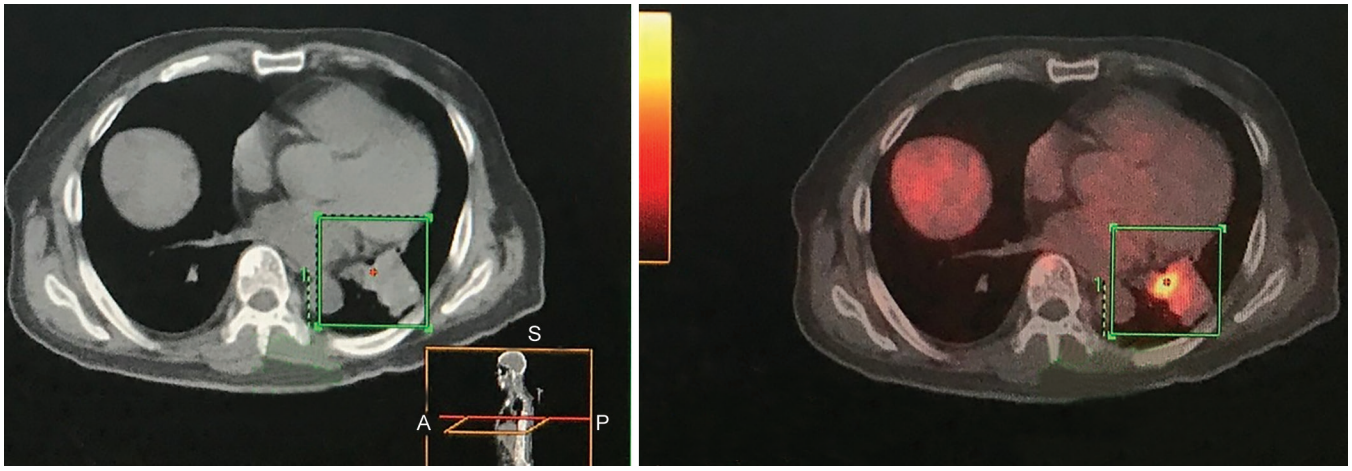

Fig. 1: CT/PET Ga-68 showing an irregular mass at the left lower lobe of the lung with Ga-68 DOTANOC uptake

syndrome one week later and was started intravenous (IV) octreotide infusion for the first time and this was when he first experienced chest pain. The symptoms resolved with the cessation of the infusion. A series of echocardiogram showed transient ST elevation. The ECHO revealed ejection fraction (55%) and mild tricuspid regurgitation. Coronary angiography revealed mild disease (50%) at the distal left anterior descending coronary artery. We treated him for coronary vasospasm secondary to the octreotide or carcinoid crisis.

He underwent a left uniportal video-assisted thoracoscopic surgery (VATS), a lower lobectomy, and a lymph node dissection within one month from the last episode of the crisis. For medical control, an IV octreotide infusion was initiated 12 hours before surgery at a slow tapering dose: 25 mcg/hour for the first 2 hours, then 50 mcg/hour for 2 hours, and subsequently maintained at 100 mcg/hour till surgery. The aim was to keep the intensity of an anticipated crisis to the minimum during surgery and watch out for coronary vasospasm complication. Despite continuous octreotide infusion (100 mcg/hour) and a frequent intermittent high dose of bolus octreotide (50–100 mcg) intraoperatively, he developed a carcinoid crisis evident by a persistent hypotension, which was supported by vasopressin and phenylepinephrine without evidence of an acute coronary event. The surgical aim to control the crisis was by first identifying and ligating the left inferior pulmonary vein, followed by the common basal and superior segmental artery, then bronchus of the lower lobe, and finally lymph node dissection (Fig. 2). Postoperatively he was infused with octreotide at a tapering dose for a day. His postoperative recovery was uneventful and was discharged home on day 7.

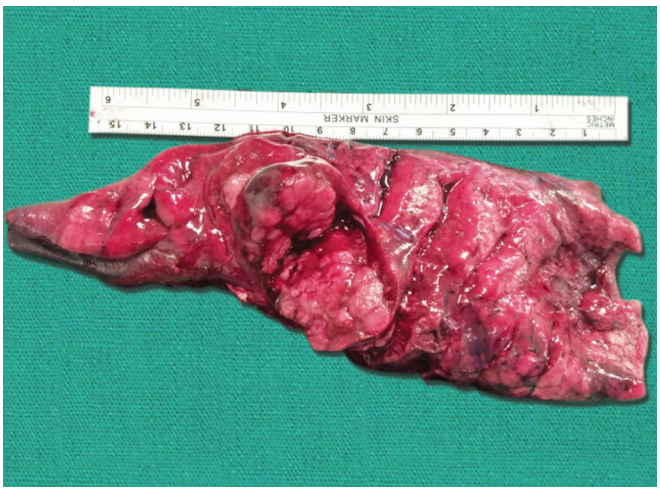

Fig. 2: A centrally located solid tumor measuring 3 × 4 cm

Discussion

The patient was subjected for a left lower lobectomy to reduce the tumor burden and his frequency of developing the carcinoid syndrome and crisis. The dilemma was whether to initiate octreotide preoperatively in consideration of his previous history of developing coronary vasospasm possible secondary to either the octreotide or carcinoid crisis. About 40% of patients with the carcinoid syndrome have the manifestation of cardiac complications where 95% of the cases showed a right valvular dysfunction.[3] The phenomenon of coronary vasospasm secondary to the carcinoid crisis has only scarcely been reported.[3] Mediators secreted by the carcinoid tumor such as serotonin and histamine have been suggested to be involved in the pathogenesis of coronary vasospasm.[7] In contrast, coronary vasospasm complicated by octreotide has never been reported. Fenning reported a case of coronary vasospasm, after the first peptide receptor radionuclide therapy (PRRT) treatment for the carcinoid syndrome secondary to a metastatic NET.[3] This shows that the treating modality can be an iatrogenic trigger for coronary vasospasm, as in this case, octreotide. The demonstrated spasm was temporary and reversible, and the same treatment was resumed without complication subsequently.

Though most literature agreed to pre-medicate patient undergoing a procedure or surgery with octreotide to reduce the risk of carcinoid crisis,[8] there is no standard guideline describing the dose and duration for the administration of octreotide. The ENET consensus guidelines recommended IV octreotide infusion at a starting dose of 50–100 mcg/hour as prophylaxis 12 hours before surgery and continued 48 hours after surgery with dose titration as required.[9] Owing to previous coronary vasospasm, in which octreotide could be one of the possible causes, we started octreotide pre-operatively at a lower dose of 25 mcg/hour and titrate accordingly with a close cardiac monitor. We tapered

off his octreotide one day after surgery, all without any acute cardiac event.

Surgical resection is the treatment of choice for the lung NET.[2] The National Comprehensive Cancer Network (NCCN) guidelines advocate a minimally invasive surgery to be considered for all patients requiring a lung resection for malignancy.[10] VATS lobectomy has gained international acceptance and popularity because of benefits such as shorter hospital stay, less tissue trauma, and less postoperative pain.[10] Nodal involvement affects survival[11] and it is present in up to 25% of well-differentiated lung NET.[6] Therefore, a complete lymph node dissection should be carried out at the time of resection.

Conclusion

Lung NET with the carcinoid syndrome or crisis are a unique and heterogeneous group of tumors requiring a multidisciplinary team approach for optimal care. The carcinoid syndrome needs to be controlled by octreotide prior to a surgical intervention, and the management can be challenging when dealing with a life-threatening coronary vasospasm when its root cause is not well-established. Surgery is the mainstay of treatment and the minimally-invasive approach is favored.

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