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CASE REPORT

Epinephrine use during chemotherapy to treat severe tracheal stenosis secondary to advanced esophageal cancer: A case report and review of the literature

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Abstract

Dyspnea from tracheal stenosis due to compression by a tumor is an emergency that complicates therapy in oncology. We report a case of advanced esophageal cancer in a 56-year-old male who developed severe dyspnea due to airway compression by mediastinal lymph node enlargement. We used epinephrine by subcutaneous injection and aerosol inhalation to temporarily relieve dyspnea while the patient received bevacizumab and chemotherapy. The dyspnea had subsided considerably after 5 days, and the mediastinal lymph nodes were significantly reduced after 2 cycles of chemotherapy. However, the patient died of massive tracheal hemorrhage 2 months later.

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Dyspnea occurs mainly in patients with tracheal obstruction or external compression by either a foreign object or neoplasm, and can be difficult to treat. Stenting is widely used for palliation of airway stenosis in patients with metastatic disease [1–5]. However, tracheal hemorrhage and other complications are more common in patients who have not received radiation therapy before, because tissues are very fragile after radiotherapy.

Case report

A 56-year-old male with a history of esophageal cancer was admitted to our hospital (The Affiliated Hospital of Jiangsu University, Yixing People's Hospital, Wuxi, China) on November 23, 2013. He was diagnosed with esophageal cancer and underwent radical surgery on February 26, 2010 in our hospital. The postoperative pathology report found moderately differentiated esophageal squamous cell carcinoma, with invasion of the submucosa; some squamous cells with atypical hyperplasia in the upper margin; no carcinoma in the lower margin; 1 of 6 lymph nodes was found to have cancer cells. The patient was treated with 4 cycles of postoperative adjuvant chemotherapy, using TP (paclitaxel 120 mg on day 1 and 90 mg on day 8, and nedaplatin 50 mg on days 1 and 8), from March 27, 2010 to July 3, 2010. Computed tomography (CT) revealed mediastinal lymph node enlargement on January 3, 2013 (Fig. 1). The patient subsequently received 2 cycles of GP (gemcitabine 1.4 g on day 1 and 1.2 g on day 8, and cisplatin 20 mg on days 1 to 4) on January 14, 2013 and February 16, 2013. CT on March 20, 2013 showed no obvious changes in the mediastinal lymph node enlargement after 2 cycles of chemotherapy (Fig. 2). Following palliative chemotherapy, gamma-knife treatment was administered to the patient's enlarged mediastinal lymph nodes in April, 2013, followed by rest at home. The patient had no awareness of hoarseness as of June, 2013, but developed dyspnea as the disease gradually progressed.

He came to our hospital on November 23, 2013, when the symptoms were severe, and a three-concave sign was observed. CT showed that the mediastinal lymph nodes had enlarged significantly between March 20, 2013 and November 25, 2013 (Fig. 3). Anti-inflammatory drugs and asthma treatment had no apparent effect. By November 30, 2013, the patient could not lie down because of dyspnea, even with large doses of aerosol inhalation, and other conventional treatment methods. The dyspnea worsened on December 2, 2013; electrocardiography monitoring showed a heart rate up to 120 beats per minute and blood oxygen saturation decreased to 80%, but

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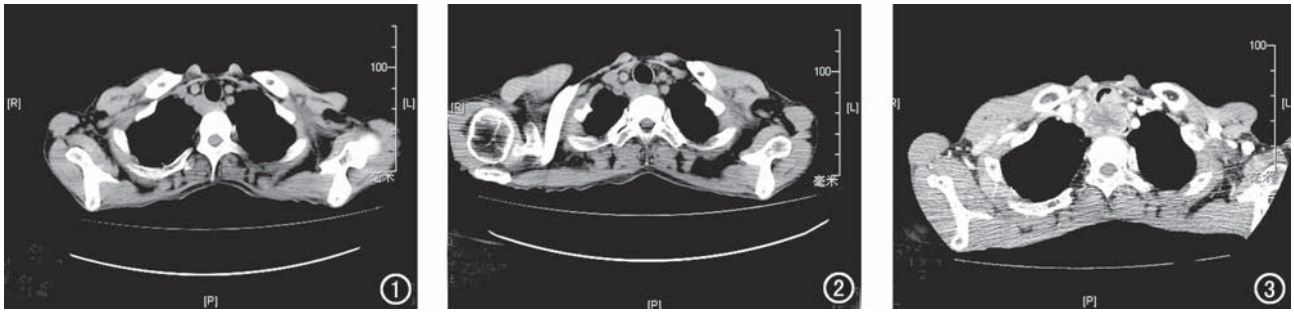

Fig. 1 CT showed mediastinal lymph node enlargement on January 03, 2013
Fig. 2 CT on March 20, 2013, showed no obvious change in mediastinal lymph node enlargement after 2 cycles of chemotherapy
Fig. 3 CT showed a significant increase in mediastinal lymph nodes between March 20, 2013 and November 25, 2013, and the primary bronchi were severely compromised by the enlarged lymph nodes

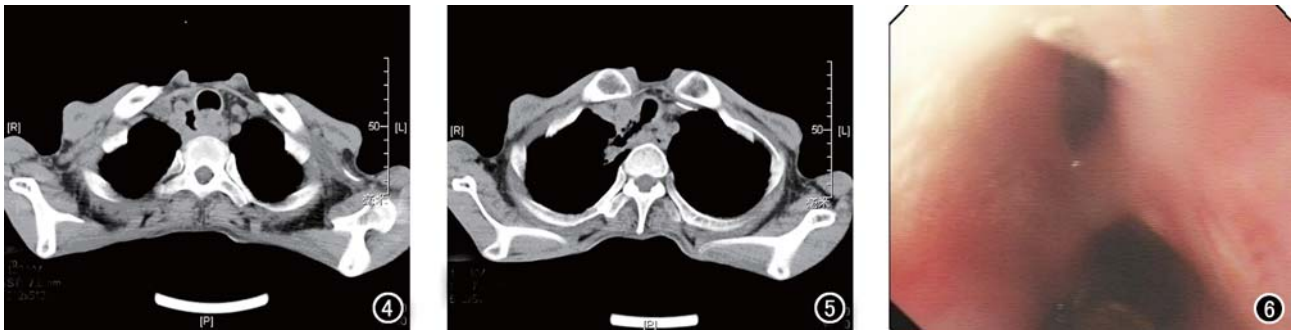

Fig. 4–5 CT showed a significant decrease in the mediastinal lymph nodes between November 25, 2013 and January 12, 2014, but a tracheoesophageal fistula appeared to have developed
Fig. 6 Gastroscopy showed a fistula in the esophagus, 20 cm distance from the incisors

the blood pressure was normal. We administered large doses of methylprednisolone immediately, with no apparent effect. As the patient was critical, we administered 0.5 mg of epinephrine by subcutaneous injection. To our surprise, the patient's dyspnea eased slightly after about 5 minutes; the heart rate decreased to 100 beats per minute, the blood oxygen saturation increased to 95%, and the blood pressure increased slightly. Subsequently, aerosol inhalation of budesonide, ambroxol, and epinephrine was administered every 4 to 6 hours. The patient's dyspnea eased slightly after each inhalation or epinephrine subcutaneous injection, but he still could not lie down. Bevacizumab combined with TP chemotherapy was administered on December 3, 2013 (bevacizumab 200 mg on day 1 and paclitaxel 120 mg on day 1, and cisplatin 20 mg on days 1 to 3). The patient's dyspnea had subsided by December 5, 2013. He was obviously in much better health by December 7, 2013, and could again lie down. Therefore, we discontinued aerosol inhalation of epinephrine on December 7, 2013. Third-degree bone marrow suppression subsequently developed. We again gave bevacizumab combined with TP chemotherapy on December 30, 2013 (bevacizumab 200 mg on day 1 and paclitaxel 120 mg on day 1, and cisplatin 20 mg on days 1 to 4). The patient's condition was stable, and he was hospitalized for additional treatment. Respiratory difficulty occurred after eating on January 12, 2014, but CT revealed a significant decrease in the mediastinal lymph nodes between November 25, 2013 and January 12, 2014 (Fig. 4). However, there was evidence of a tracheoesophageal fistula (Fig. 5), which was confirmed by gastroscopy (Fig. 6). Nasal feeding and peripheral parenteral nutrition were started. The patient died of a massive tracheal hemorrhage on February 16, 2014.

Discussion

Dyspnea caused by a neoplasm is not common in oncology, but is an emergency when it occurs. The consequences can be catastrophic, and the majority of patients die of hypoxia in a few days if tracheal stenosis is not corrected. Surgical resection is an option [6–7], but is not suitable in a critically ill patient. Airway stenting has been considered the "gold standard" for the treatment of benign and malignant airway stenosis in the past 20 years [4, 8]. Two patients with esophageal cancer received

chemoradiotherapy after airway stenting and survived for 24 months and 54 months, respectively. One patient with esophageal cancer died of airway bleeding 2 months after stent placement [9]. Some studies used airway stenting as a temporary measure, with removal after relief of tracheal stenosis [3, 5]. In this case, the patient's general status was very poor, and surgical resection would be difficult to implement; airway stenting was also ruled out because radiation therapy had been used for the enlarged mediastinal lymph nodes; moreover, the patient's family refused surgery. Chemotherapy seemed to be our only option, and the patient's family consented. With the family's full understanding, bevacizumab combined with chemotherapy was administered, but the dose was small because of the patient's poor condition. However, when he became critical, relief of dyspnea was essential, or death from hypoxia would occur within hours.

Epinephrine acts on α and β receptors, and is usually used to rescue patients with anaphylactic shock, sudden cardiac arrest, and severe dyspnea caused by bronchial spasm in emergencies, but it is seldom used to treat dyspnea caused by tumor compression. The side effects of epinephrine include elevation of blood pressure, palpitations, headache, and arrhythmia. We did not observe these side effects in this case, but some symptoms may have been concealed by severe dyspnea. In this case, epinephrine may have acted by alleviating edema in the compromised trachea and relaxing bronchial smooth muscles; the duration of effect was only 4–6 hours after each dose of epinephrine, which was consistent with the metabolism and pharmacokinetics of epinephrine.

We gave this patient a total of 24 mg of epinephrine, with 2 doses of 0.5 mg subcutaneously, and 23 mg by aerosol inhalation of 1 mg per dose. After each dose of epinephrine, the patient's dyspnea eased for about 4 to 6 hours. We simultaneously gave bevacizumab combined with TP chemotherapy. The general status of this patient was very poor, necessitating a relatively low chemotherapy dose. With these measures, the patient's dyspnea was relieved after 3 days, and he could lie down again after 5 days. Bevacizumab is a vascular endothelial growth factor-specific angiogenesis inhibitor indicated for the treatment of metastatic colorectal cancer, non-squamous non-small cell lung cancer, and metastatic breast cancer. It is not clear whether bevacizumab or chemotherapy, or possibly both, played a greater role in this case. We did not consider this in detail.

Airway stenting has only been performed in large medical centers. Most smaller hospitals do not have this technology. Our experience may be of use in the treatment of patients with dyspnea caused by tracheal stenosis in smaller hospitals, and possibly buy time until airway stenting can be performed at a large medical center. Airway stenting also has many complications, including cough, and massive tracheal hemorrhage due to stent irritation. One study showed that despite improvement in symptoms, the actual survival benefit was limited due to severe potential complications. Two patients with advanced lung cancer who underwent bronchial stenting for intractable dyspnea had dramatic improvement in symptoms and quality of life, but both died shortly after [10]. We prolonged the life of this patient more than 2 months, but he finally died of a massive tracheal hemorrhage on February 16, 2014. The patient's quality of life was clearly improved, however briefly. The experience from this case can also be of value for patients who do not want or cannot afford airway stenting. Moreover, radiotherapy may also be effective on a compressing neoplasm.

In conclusion, we present a case of using epinephrine combined with chemotherapy to relieve dyspnea caused by a neoplasm.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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