Case Report

Bronchiolitis Obliterans Organizing Pneumonia after Radiotherapy: A Case Report of Post-Esophagectomy Diagnosis

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Abstract

Bronchiolitis obliterans organizing pneumonia (BOOP) is a diffuse, infiltrative lung disease. BOOP is mostly idiopathic, and possible causes are pulmonary infections, drugs, collagen vascular disease, thyroiditis, or radiotherapy. Radiation injury to the lung is a common event after radiotherapy. This article presents a case report of BOOP occurrence after minimally invasive esophagectomy that was possibly associated with radiotherapy. The patient, a 66-year-old woman, was diagnosed with middle third esophageal squamous cell carcinoma. The patient received neoadjuvant chemoradiotherapy. Nine months after neoadjuvant therapy, the patient underwent a minimally invasive thoraco-laparoscopic esophagectomy. During the post-operative (PO) period, the patient complained of dyspnea and presented hypoxemic findings in arterial gasometry. We made the diagnosis of BOOP by a lung biopsy using right thoracotomy and histopathological findings. Based on this diagnosis, we initiated the administration of methylprednisolone. The patient showed clinical improvement after the initiation of corticotherapy. This is the first case of BOOP diagnosed during the early post-operative period of an esophagectomy. This case report serves to increase the awareness of interstitial lung disease in the differential diagnosis of patients presenting with lung infiltrates after radiotherapy. Thus, patients who do not have quick resolution of infiltrates should receive additional investigation.

ABBREVIATIONS

BOOP: Bronchiolitis Obliterans Organizing Pneumonia; CT: Computed Tomography; CR: Chest Radiograph; DVH: Dose-Volume Histogram; IMRT: Intensity-Modulated Radiotherapy

INTRODUCTION

Bronchiolitis obliterans organizing pneumonia (BOOP) is a diffuse, infiltrative lung disease predominantly found in the alveolar ducts and alveoli. This condition often impairs the bronchioles. It is characterized by clinical symptoms of a flu-like illness: cough, fever, dyspnea, and crackles [1-4]. BOOP is mostly idiopathic, and possibly caused by pulmonary infections, drugs, collagen vascular disease, thyroiditis, or radiotherapy [1,4]. The lung biopsy is the standard diagnostic method, with an accuracy of 90% [5]. The histopathologic findings are organizing granulation tissue plugging within the alveolar space and small airways [2-4]. Radiation injury to the lung is common after radiotherapy for thoracic cancer and occurs within the radiation field [3]. However, it is important to be aware of the risk of the less common post-radiotherapy BOOP. All reported interstitial lung diseases in patients after radiotherapy, irrespective of the precise diagnosis, based on histological examination of the primary BOOP lesion and initiation of corticosteroid therapy, are described to respond dramatically well to steroids [6,7]. However, some patients may relapse when the glucocorticoic dose is reduced and some cases may show rapid progression and a poor prognosis [8].

The aim of this article is to present a case report of BOOP after minimally invasive esophagectomy that is possibly related with radiotherapy.

CASE PRESENTATION

A 66-year old Caucasian, non-smoker woman with no previous history of collagen vascular disease was diagnosed with middle third esophageal squamous cell carcinoma, clinical stage T3N2M0. The patient received radiotherapy with concurrent neoadjuvant chemoradiotherapy with administration
of carboplatin and paclitaxel for 5 weeks. Two-dimensional treatment planning for radiation therapy, using four isocentric fields (anterior, posterior, right, and left lateral) was delivered to the esophageal lesion and regional lymph nodes. Dose prescribed was 45 Gy in 25 fractions and the photon energy was 6 MV.

A routine follow-up computed tomography scan (CT) after chemoradiotherapy was normal. Furthermore, the patient complained of intermittent non-productive cough and dyspnea. The physical examination and laboratory data showed normal results and the pulmonary function tests revealed a mild obstructive ventilatory defect. The patient showed no history of recent infection, asthma, use of systemic or inhaled drugs, or recent travels. Eight weeks after neoadjuvant therapy, the patient was subjected to minimally invasive thoraco-laparoscopic esophagectomy. During the thoracoscopy, the macroscopic lung appearance was normal; however, an intense fibrosis process was observed in the mediastinum (Figure 1). During the postoperative (PO) period, the patient complained of dyspnea and arterial gasometry analysis showed hypoxemic findings. Although the laboratory tests revealed normal results, the physical examination revealed bilateral crackles. Blood and urine cultures were negative. The chest radiograph (CR) showed bilateral patchy infiltrates and the CT examination revealed ground-glass opacities, bilateral disease, nodular opacities, air bronchograms, and pleural effusion (Figure 2). The patient required invasive ventilation support. Based on these findings, a diagnosis of BOOP was made; the patient was administered methylprednisolone 120 mg/day. To confirm the diagnosis, on the eighth day post-operation, a lung biopsy via right thoracotomy was performed. The histopathological findings confirmed the BOOP diagnosis (Figure 3). The patient showed clinical improvement with the initiation of corticotherapy and mechanical ventilation was withdrawn on the 10th day post-operation. She was discharged on the 28th day post-operation. The patient was advised to continue treatment with prednisone at 80 mg/day.

**DISCUSSION**

BOOP is characterized by an inflammation of the distal small airways (bronchioles) and surrounding alveolar lung tissue [7]. It usually occurs in individuals between 50 and 70 years of age; it is not sex specific and most often occurs in non-smokers. The incidence and prevalence remain undefined and nearly 75% of patients are symptomatic [1,6,9]. BOOP is mostly idiopathic; however, it can be caused by pulmonary infections, drugs, collagen vascular disease, thyroiditis, or radiotherapy. The CR typically reveals bilateral patchy infiltrates and the CT reveals ground-glass opacities, nodular opacities, and air bronchograms [10,4]. The exact pathogenesis of radiation-induced BOOP is poorly understood; however, an immune-mediated mechanism of pathogenesis is plausible [11]. In this case, we hypothesized that the patient had subclinical symptoms of BOOP prior to the esophagectomy, because she complained of intermittent non-productive cough and dyspnea before surgery and the initial CT before the radiotherapy treatment was normal, while the CT scan after radiotherapy revealed ground-glass and nodular opacities. Once the disease has become established to cause an immune and inflammatory response, the surgery, although minimally invasive, could exacerbate this condition. Although the BOOP described in this case report was likely induced by radiotherapy, we purport that the trauma from the esophagectomy surgery triggered for full clinical development of BOOP [3]. Radiation therapy causes...
a lymphocyte-mediated hypersensitivity reaction [12]. Although the occurrence of lymphocytic alveolitis appears to be very common after radiation therapy to the breast, the occurrence of BOOP syndrome that we describe in this study appears to be infrequent. This suggests that radiation alone is not sufficient for the development of BOOP; other factors such as a genetically susceptible host and/or unrecognized triggering factor acting on “radiation-primed” lymphocytes to produce a pneumonitis are probably needed for the development of BOOP [13]. This suggests that in addition to the classic radiation pneumonitis localized in the irradiated area, unilateral lung irradiation may “prime” the development of a characteristic BOOP syndrome that is similar to idiopathic BOOP.

Environmental factors may also be important; In vivo studies have shown that tobacco smoke suppresses radiation-induced inflammation in the lungs of rats and humans [14]. However, it should be noted that this patient was not a current smoker. In the case described above, there are some concerning aspects of the radiation therapy. Two-dimensional field radiation therapy based on radiographic images has many limitations; it requires larger margins and more normal tissue irradiation and lacks dose-volume information on organs at risk, such as the lung. Use of four-field technique can lead to excessive radiation doses in the lungs and is not the usual field arrangement. Conformal radiation therapy based on three-dimensional (3D) computed tomography is the technique indicated for minimal side effects. It allows for proper volume delineation and predicting appropriate risk dose volume histograms (DVH) to minimize radiation related toxicities. Additionally, several researchers have recently reported that an intensity-modulated radiotherapy (IMRT) plan is superior to a 3D conformal radiotherapy plan for patients with lung cancer or upper esophageal cancer, because an IMRT plan can spare the lung and spinal cord and improve the target dose conformity [15]. Modern radiotherapy approaches based on recent technological advances such as positron emission tomography-based planning, image-guided radiotherapy, respiratory-gated radiotherapy, and IMRT minimize post-treatment complications by improving gross tumor volume definition, reducing interfraction and intrafraction motion, and delivering better dose delivery to the precisely defined planning target volume [16].

As there are only few reports suggesting a relationship between low-dose level of lung DVH and respiratory toxicities, further clinical investigation of this topic is needed. It is important to emphasize that in this case report, the diagnosis of pneumonia was not indicated by laboratory tests and cultures. In addition, the patient was not administered antibiotics. This fact, concurrent with the corticotherapy response, supported the possibility of BOOP. To confirm the diagnosis and exclude other causes, a standard diagnostic lung biopsy was performed; the test has an accuracy of 90% [5] We decided to perform a lung biopsy by right thoracotomy on the eighth day post-operation; the histopathological findings further confirmed the diagnosis. Although there is no consensus in the treatment of BOOP, most authors recommend the use of corticotherapy with the dose of 0.75 – 1.5 mg/kg/d for 1 to 3 months, then 40 mg/d for 3 months, then 10 to 20 mg/d for a total of 1 year [1,6]. Furthermore, early treatment helps in the prevention of relapses [1]. In this clinical case, a high methylprednisolone dose (1.5 mg/kg/d) was used for the treatment of early symptoms and the patient showed a good clinical response without severe side effects or relapses. She was discharged at the 28th day post-operation and advised to continue treatment with prednisone at a dose of 80 mg/day (1 mg/kg/d). In conclusion, this case report suggests the role of radiotherapy in the development of BOOP and highlights the importance of considering radiation-induced BOOP in the context of parenchymal shadowing following radiotherapy. It is important to be aware of BOOP as a potential complication for patients who have received radiation and complains of cough and dyspnea. Early diagnosis and initiation of corticotherapy might improve the overall prognosis and halt the progression of the disease in these patients. To the best of our knowledge, this is the first case of BOOP diagnosis during the early post-operative period of an esophagectomy.

This case report serves to increase the awareness regarding interstitial lung disease in the differential diagnosis of patients presenting with lung infiltrates after radiotherapy. Patients who do not show quick resolution of infiltrates should receive additional examinations as early diagnosis and corticosteroid therapy might improve survival in these patients.

REFERENCES
10. Epler GR, Kelly EM. Kelly. Systematic Review of Post Radiotherapy Bronchiolitis Obliterans Organizing Pneumonia in Women with...


