Bronchiolitis obliterans organizing pneumonia after adjuvant radiotherapy for breast carcinoma

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Introduction

External radiotherapy following surgery for breast carcinoma may induce radiation injury to the lungs in a number of patients. Two types of injury are recognized that are temporally related to radiotherapy; an acute pneumonitis-like illness and fibrosis, with abnormalities confined to the radiation port (1). However, the spectrum of radiotherapy-induced sequelae may be more diverse. Two patients developed a syndrome of idiopathic bronchiolitis obliterans organizing pneumonia (BOOP; synonym: cryptogenic organizing pneumonitis) after surgical intervention for breast carcinoma and treatment with external radiotherapy. As a distinctive feature, the syndrome was associated with migratory, recurrent infiltrates.

Case 1

A 53-year-old woman with carcinoma of the left breast (T1N0M0) underwent lumpectomy and lymph node dissection on 13 April 1994, followed by external radiotherapy on the left axilla and left breast (50 Gy each with a booster dose of 16 Gy on the tumour site). In October 1994, the patient developed a non-productive cough, weight loss and fever, with a chest radiograph showing alveolar consolidations in the left upper lobe. As treatment with amoxicillin did not alleviate her symptoms, the patient was admitted for further analysis. At physical examination, a healthy-appearing non-dyspnoeic woman was seen with normal pulse, blood pressure and temperature. Percussion of the left lung was dull over the area of the upper lobe, while on auscultation, bronchial breath sounds were heard.

Laboratory results were all normal except for an elevated erythrocyte sedimentation rate (ESR) (85 mm h⁻¹). Arterial blood gas analysis with the patient breathing room air was normal. Pulmonary function tests revealed restriction; vital capacity 2·64 l and total lung capacity 3·81 l (79 and 70% of predicted, respectively). Fibrebronchoscopy including microbiological analysis of the bronchoalveolar lavage (BAL) was negative, whereas microscopic examination of transbronchial biopsies showed interstitial and intra-alveolar fibrosis as well as interstitial inflammation with prominent type II pneumocytes. On follow-up chest radiographs, new nodular abnormalities were noticed in the right lung that were confirmed with a high-resolution computed tomographic scan (HRCT). An open lung biopsy from the lesion in the right lower lobe was performed. Pathological examination revealed patchy areas with intra-alveolar and interstitial proliferation of fibroblasts, and lymphocytic destruction of bronchioli, typical of BOOP (Plate 1). As physical, radiological and laboratory investigations improved spontaneously, it was decided not to institute any therapy. In March 1995, however, the patient began to complain of a dry cough and malaise while the chest radiogram showed infiltrations in both lower lobes, presumed to be due to
re-activation of BOOP. Prompt treatment with prednisone 60 mg daily led to rapid clinical improvement coinciding with normalization of ESR, radiological abnormalities and pulmonary function tests. Prednisone was gradually tapered uneventfully.

Case 2

A 58-year-old woman with carcinoma of the left breast (T1N1M0) underwent lumpectomy and lymph node dissection on 11 August 1994, followed by external radiotherapy on the left axilla and left breast (50 Gy each with a boost of 16 Gy on the tumour site). In December 1994, the patient began to suffer from dyspnoea, a non-productive cough, fever, malaise and left-sided pleuritic pain. A chest radiograph showed an airspace consolidation in the left upper lobe and in the apical segment of the lower lobe, as well as a pleural adhesion with the left hemidiaphragm. As therapy with erythromycin did not affect her complaints or the radiological abnormalities, the patient was referred to the authors' hospital for further analysis. On physical investigation, a healthy-appearing non-dyspnoeic woman was seen with normal pulse and blood pressure, and a temperature of 38.5°C. Except for auscultatory crackles over the left lung, no abnormalities were found. Laboratory investigations showed increased ESR (45 mm h⁻¹), normochromic anaemia (6.7 mmol 1⁻¹), mild leucocytosis (8.9 x 10⁹ 1⁻¹ with normal differentiation) and thrombocytosis (458 x 10⁹ 1⁻¹), but were otherwise completely normal. Arterial blood gas with the patient breathing room air was indicative of hypoxaemia (PO₂ 9.1 kPa). Pulmonary function tests pointed towards minor restriction (vital capacity 3.11 l and total lung capacity 5.24 l; 86 and 88% of predicted, respectively) and abnormal diffusion (carbon monoxide transfer capacity 1.5 1 mmol⁻¹ min⁻¹ kPa⁻¹ 1⁻¹; 75% of predicted). The results of fibrebronchoscopy including microbiological examination of transbronchial biopsies and of the BAL from the lingula were negative. The BAL contained predominantly alveolar macrophages (42%) and lymphocytes (30%). Pathological examination of the transbronchial biopsies revealed broadened alveolar septa with fibroblasts and deposition of excess collagen, and reactive pneumocytes lining the alveoli. Due to persistent fever, a new chest radiograph was made showing improvement of the airspace consolidation in the left upper lobe but new abnormalities in the right lung (Plate 2).
On HRCT, the presence of consolidations in both lungs was confirmed. An open lung biopsy was then taken from the apex of the left lower lobe. At microscopical examination, patchy areas of abnormal tissue consisting of interstitial fibrosis, prominence of pneumocytes, intra-alveolar granulation tissue and bronchiolitis obliterans were observed (BOOP). Subsequent treatment with prednisone 60 mg daily resulted in a dramatic improvement of symptoms and clearance of infiltrative abnormalities. Prednisone was gradually withdrawn and no relapse has occurred since.

Discussion

The cases described above suggest a role for radiotherapy in the development of migratory BOOP. Bronchiolitis obliterans organizing pneumonia is a restrictive lung disease characterized pathologically by destruction of the small airways, accompanied by excessive proliferation of granulation tissue extending in the alveoli (2). Although it may be associated with various stimuli, it is often idiopathic (3). The clinical presentation of patients with idiopathic BOOP may include fever, non-productive cough, dyspnoea and malaise, developing subacutely, and typically affecting 50-60-year-old patients (4). The spectrum of radiological abnormalities encompasses both patchy unilateral or bilateral airspace consolidations and nodular opacities or irregular reticular opacities (5). To establish the diagnosis, both HRCT and an open lung biopsy are required. High-resolution computed tomography is a valuable adjunct to examine the extent of the disease, and is recommended as a guide to determine the optimal site for open lung biopsy (6). Open lung biopsy is preferred over transbronchial biopsy, as the latter may yield insufficient tissue. Bronchiolitis obliterans organizing pneumonia can be effectively treated with corticosteroids.

Recently, three cases were described with migratory BOOP following post-operative radiotherapy for breast carcinoma (7,8). Time lag between completion of radiotherapy and start of symptoms ranged from 2 to 6 months, as compared to 1.5 and 3.5 months in the present cases. It is worth noting that the process in all cases appeared to first affect the lung, of which only a small subpleural slice had been irradiated, before subsequently ‘migrating’ to the contralateral non-irradiated side. Bronchiolitis obliterans organizing pneumonia in the first patient was diagnosed by open biopsy from the lung that had been partially irradiated, whereas in the second patient, BOOP was demonstrated in the contralateral lung, excluding direct radiation injury. The classical view of radiation injury is of a pneumonitis confined to the irradiated lung field which may ultimately result in fibrosis. Bronchiolitis obliterans organizing pneumonia is not a typical finding in radiation injury to the lung, although its occurrence has been reported in a patient who had been irradiated for small cell carcinoma of the lung (9). Unilateral radiotherapy may induce bilateral lesions on chest radiograms and gallium scans, and material obtained by BAL has shown T-cell lymphocytosis in such cases reminiscent of hypersensitivity pneumonitis (10). The relevance of these findings in relation to the present cases is uncertain, however, as they encompassed both symptomatic and asymptomatic cases, and have not included histological analysis.

It is concluded that clinicians caring for patients with breast carcinoma should be aware of the possibility that migratory BOOP may ensue after radiotherapy. Recognition of its distinctive features and subsequent prompt institution of treatment with corticosteroids will alleviate or clear signs and symptoms.

References