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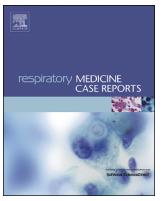

Case Report

Tracheobronchitis and laryngitis associated with Crohn's disease

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ABSTRACT

We report a 68-year-old woman with tracheobronchitis and laryngitis associated with Crohn's disease (CD), which was discovered during the evaluation of suspected lung cancer. She had no symptoms induced by these upper airway diseases (UADs). Bronchoscopy revealed swelling of the epiglottis with edematous change and a mass like epiglottis fold. There were nodular and edematous changes in the trachea and bilateral main bronchus. Histological findings demonstrated infiltration by numerous lymphocytes and plasma cells. Dexamethasone as the premedication for chemotherapy against lung cancer was efficacious for these extraintestinal manifestations of CD. Our case was rare in that bronchial lesion and UADs appeared concomitantly.

1. Introduction

Crohn's disease (CD) is a type of inflammatory bowel disease associated with various systemic manifestations, including pulmonary diseases, but involvement of the upper airways is rare [1–3]. Herein, we report a patient with tracheobronchitis and epiglottitis associated with CD, which was discovered incidentally during scrutiny of lung cancer.

2. Case report

A 68-year-old woman was referred to our hospital because of one month history of back pain on the right side. She denied pharyngeal pain, hoarseness, cough, sputum, wheezing or dyspnea. She had a smoking history of 22 pack-years. Nine years before presentation, she had been diagnosed as having CD based on clinical, endoscopic and histological evidence. Over the past several years, she had suffered from two recurrent episodes. At the second recurrence, colonoscopy showed discontinuous mucosal ulceration at the transverse colon, sigmoid colon and rectum. A “cobblestone” appearance was observed at the sigmoid colon (Fig. 1A). Pathological findings of the colonic specimen revealed a micro-abscess and cryptitis (Fig. 1B), which supported the diagnosis of CD. She had undergone nutritional therapy, mesalazine (4000 mg/day) and adalimumab (80mg every 2 weeks) since then, and gastrointestinal conditions had been well-controlled for the previous 3 years.

Physical examination showed a body temperature of 36.6 °C, and crackles were not audible on auscultation. Cutaneous eruptions were absent and neurological examinations were negative.

Computed tomography (CT) of the chest demonstrated subpleural nodular consolidation (40 mm in diameter) invading the chest wall (Fig. 2A) and another two nodules (6mm and 8mm in diameter, respectively) in the right upper lobe (Fig. 2B). A cavitary nodule

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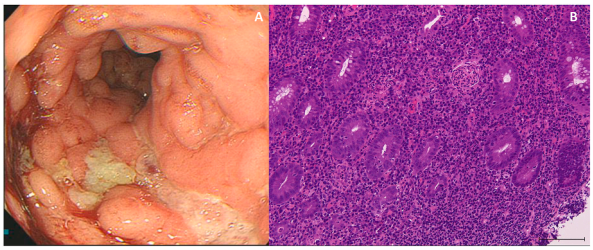

Fig. 1. A: Colonoscopy in the sigmoid colon showing a "cobblestone" appearance. B: Pathological findings of a colonic specimen showing a micro-abscess and cryptitis, thereby supporting a diagnosis of Crohn's disease. Scale = 100 μm.

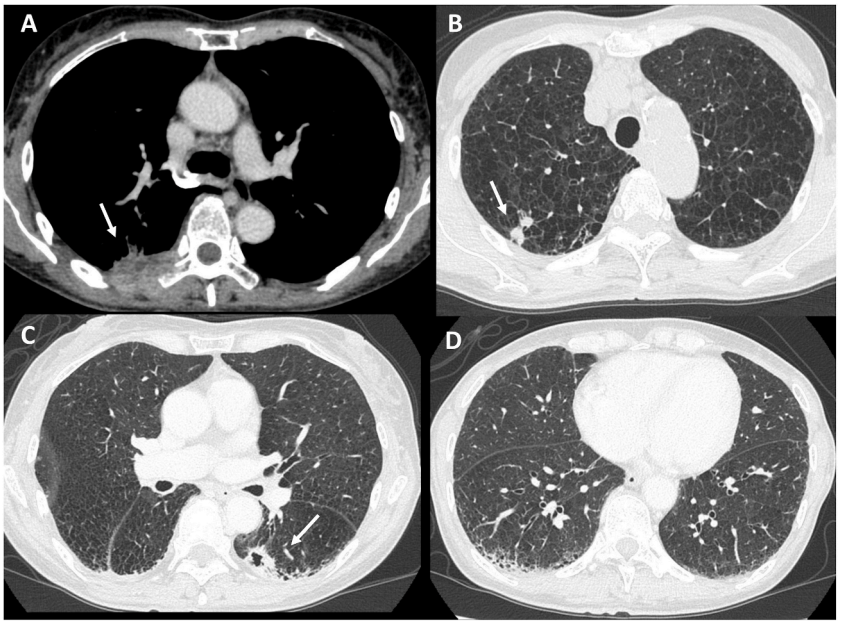

Fig. 2. A: Contrast-enhanced computed tomography of the chest (soft-tissue windows), showing partially enhanced subpleural nodular consolidation (40 mm in diameter) invading the chest wall. B: Computed tomography of the chest (lung windows) showing two nodules (6 mm and 8 mm in diameter, respectively) in the right upper lobe. C: Computed tomography of the chest (lung windows) showing a cavitary nodule (21mm in diameter) in the left lower lobe. D: Computed tomography of the chest (lung windows) showing reticulonodular shadows in the periphery of bilateral lower lobes, suggesting the interstitial pneumonia.

(21mm in diameter) was noted in the left lower lobe (Fig. 2C). Reticulonodular shadows in the periphery of the bilateral lower lobes were present (Fig. 2D), which suggested the interstitial pneumonia. In addition, the oropharyngeal wall, epiglottis and aryepiglottic fold were swollen, with mild enhancement of contrast medium (Fig. 3).

Laboratory examination showed a white blood cell count of 8800/μL, C-reactive protein of 0.18mg/dl, carcinoembryonic antigen of 7.6 ng/ml, and cytoketatine-19 of 6.3 ng/ml. Levels of rheumatoid factor and myeloperoxidase-antineutrophilic cytoplasmic antibodies were 25 IU/ml and 7.9 U/ml, respectively, but the level of proteinase 3-antineutrophil cytoplasmic antibodies was within normal range.

Bronchoscopy revealed swelling of the epiglottis with edematous change (Fig. 4A) and mass-like epiglottis fold (Fig. 4B). The pyriform recess was not clear. There were nodular and edematous change in the trachea and bilateral main bronchus had an almost cobblestone appearance (Fig. 4C and D). Endobronchial biopsy demonstrated infiltration by numerous inflammatory cells (lymphocytes and plasma cells) without any atypical or malignant cells (Fig. 5). An evaluation for infectious causes of tracheitis and epiglottitis was unrevealing, including bacterial, fungi and acid-fast bacilli of expectorated sputum as well as serologic evaluation for *Aspergillus* species, *Cryptococcosis* species and latent tuberculosis. Histology of the epiglottic fold also showed infiltration by inflammatory cells. Hence, we diagnosed the lesion in the upper airways and tracheal as oropharyngitis, epiglottitis and tracheitis associated with CD. Transbronchial biopsy of the cavitary nodule at the left lower lobe was negative, but the cytological finding of bronchial brushing was suspicious of squamous cell carcinoma.

Positron emission tomography using ^{18}F-fluorodeoxyglucose (FDG) showed high uptake of FDG in the nodular consolidation in the right upper lobe (maximum standard unit value (SUVmax) = 22.3). FDG uptake was also increased in the left cavitary nodule and nodules in the right upper lobe, with SUVmax of 8.0 and 6.6, respectively. She was diagnosed with double primary pulmonary carcinoma of clinical stage IIB in the right upper lobe and stage IA3 in the left lower lobe. Whether the two nodules in the right upper lobe were metastasis or inflammatory changes was not known.

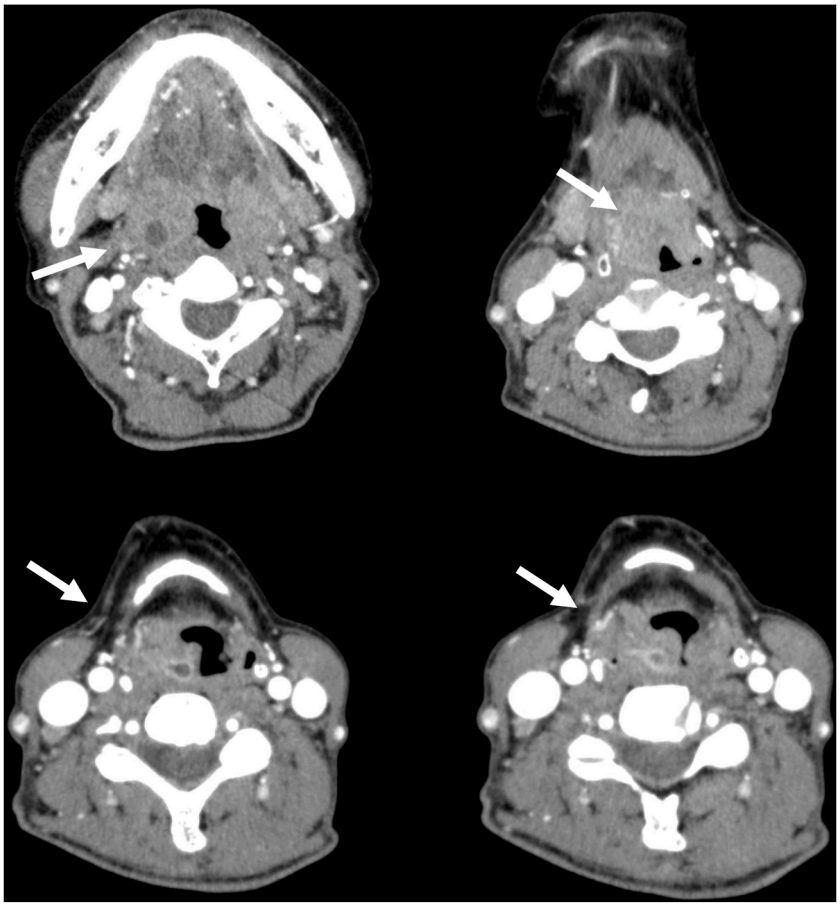

Fig. 3. Contrast enhanced computed tomography of the neck (soft-tissue windows) showing swelling of the oropharyngeal wall, epiglottis and aryepiglottic fold with mild enhancement of contrast (white arrows).

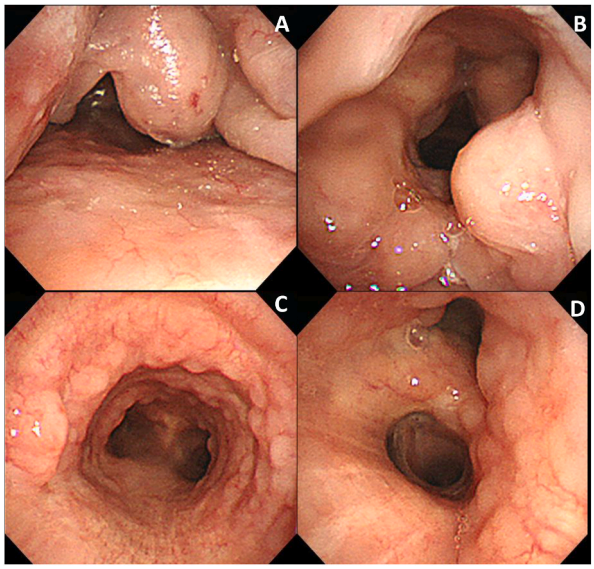

Fig. 4. Bronchoscopic findings showing swelling of the epiglottis with edematous change (A) and a mass-like epiglottis fold with edematous change (B). The pyriform recess was not clear (B). There were nodular and edematous change in the trachea and bilateral main bronchus having an almost cobblestone appearance (C: trachea, D: right main bronchus).

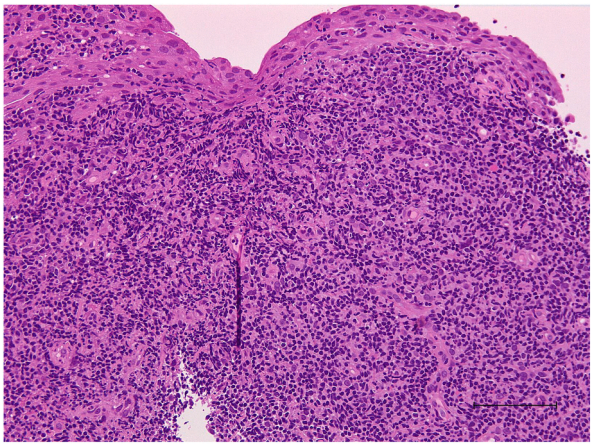

Fig. 5. Histological findings of endobronchial biopsy showing infiltration of numerous inflammatory cells (lymphocytes and plasma cells) without non-caseating granulomas or malignant cells. Hematoxylin and eosin staining. Scale = 100 μm.

We initiated radiotherapy (30Gy in 10 fractions) for the mass in the right upper lobe invading the chest wall. We undertook four course cytotoxic chemotherapy with carboplatin and paclitaxel, which included dexamethasone (19.6 mg) on day 1 with H1 and H2 blockers for antiemetic therapy and prophylactic treatment for anaphylaxis. These treatments resulted in a partial response from the tumor. The size of two nodules in the right upper lobe also decreased. Follow-up bronchoscopy after these treatments showed improvement of epiglottitis, oropharingitis and tracheobronchitis.

3. Discussion

UAD in CD is a rare, and may involve the pharynx, larynx, trachea and mainstem bronchi [1–3]. The most common finding in the larynx and hypopharynx is edema, which can be subtle or marked, localized or generalized [4–7]. In our patient, epiglottis, supraglottic larynx and hypopharynx were edematous in a mild-to-moderate manner. Localized significant edema was seen in the arytenoid region. Other reported manifestation of laryngeal CD includes ulcerations, granulation tissue, and limited mobility of the vocal cord folds [4–7]: our patient did not have any of these findings.

Pulmonary involvement could happen in both ulcerative colitis (UC) and CD. Tracheobronchial diseases dose not correlate with inflammatory bowel disease activity and can occur after cololectomy [8]. Usually, the bronchoscopic findings of tracheobronchial involvement in CD involve mucosal inflammation with exuberant pseudo-tumoral lesion, deformities, whitish lesions and luminal narrowing [9–13]. Tracheal ulcerations and stenosis have also been reported [14,15]. In our case, the gross appearance of the trachea upon bronchoscopy showed nodular, erythematous and edematous change, which were similar to a cobblestone appearance upon colonoscopy. The histological findings of endobronchial biopsy showed mucosal and submucosal infiltrations by inflammatory cells (lymphocytes, plasma cells and macrophages). These findings were non-specific, but have been reported in patients with CD-related tracheabronchitis [9,11,13]. Hence, with the exclusion of other diseases process, we suspected that the tarcheobronchial lesions in our case were associated with CD.

UAD in CD usually presents with hoarseness, stridor and severe respiratory distress, in addition to cough, phlegm and dyspnea [1–3]: our patient did not have any of these symptoms. She had back pain in the right side, which was induced by tumor invasion into the chest wall. If CD-related UADs are left untreated, some patients will be put at risk of developing irreversible destruction of the airways [1–3]. Hence, a certain degree of clinical suspicion is required. Also, meticulous history-taking, findings by CT of the chest and direct visualization by bronchoscopy should be considered for the early diagnosis and appropriate treatment of these conditions.

Studies have suggested the efficacy of corticosteroids administered systematically (prednisone, 1mg/kg/day orally or methylprednisolone 60–80mg intravenously per day) for the initial treatment of CD-related UADs [1–3]. Some patients show marked and long-standing responses to administered of inhaled corticosteroids [9,10]. These suggestions have been drawn from case reports [4–7,11–15]. It has been estimated that fewer than 25% of patients with oropharyngeal CD have spontaneous resolution of disease [16]. Hence, the treatment of CD-related UADs is dependent upon the pattern and degree of involvement and disease severity. Our patient was administered dexamethasone (19.6 mg) every 3 week on four occasions as premedication for chemotherapy, which is efficacious against CD-related UADs. Further investigations are needed to ascertain the appropriate treatment for CD-related UADs.

Authors' contributions

SN, TH, MM, YM, KN, SM, MH, TU, JS, and SI contributed to the decision-making of treatment, collecting clinical data, data analysis, and writing the manuscript. SN, MM, TH, YM, KN, SM, MH, TU, JS, SI and TS contributed to discussion about the patient. All authors approved the final version of the manuscript.

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The authors received no financial or other material support for this study.

Declaration of competing interest

I declare on behalf of my co-authors and myself that we do not have any conflict of interest to declare.

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