Three-dimensional CT and histopathological findings of airway malacia in Hunter syndrome

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A 19-year-old man with known Hunter syndrome presented with dyspnea, and was admitted to our hospital. Bronchoscopy revealed tracheal narrowing with excessive granulation tissue formation in the trachea. Three-dimensional CT clearly demonstrated severe stenosis in the trachea and both main bronchi. Autopsy showed granulomatous tissue proliferation and deposition of mucopolysaccharide in the tracheal wall. We demonstrated the clinico-radiological-pathological correlation of bronchial lesions in Hunter syndrome, and emphasized that three-dimensional CT is helpful in deciding upon therapeutic strategy to treat stenosis in the large airway.

Key words: Hunter syndrome, bronchial 3DCT, bronchoscopy, airway malacia

INTRODUCTION

Hunter syndrome (Mucopolysaccharidosis II) is an X-linked, recessively inherited, lysosomal storage disorder, and caused by a deficiency of iduronate 2-sulfatase, which results in storage of heparan and dermatan sulfate [1]. Clinically, patients with Hunter syndrome can present with variable symptoms including tracheal or lower airway obstruction [2]. Here, we report a 19-year-old man with known Hunter syndrome, present the bronchoscopical-radiological-pathological findings of bronchial lesions in Hunter syndrome, and discuss the clinical usefulness of three-dimensional CT.

CASE REPORT

A 19-year-old man (height 120 cm, weight 44 kg) with known Hunter syndrome presented with dyspnea. He had a history of mental retardation at 5 years of age, and obstructive sleep apnea, snoring and daytime somnolence at 10 years of age. At 18 years of age, he developed dyspnea, necessitating a tracheostomy. However, excessive secretion, airway narrowing and respiratory infection gradually progressed, and he was eventually admitted to our hospital.

On admission, he exhibited coarse facial features with thick lips and tongue, short neck, systolic murmur, hepatosplenomegaly, and umbilical hernia. Chest X-ray showed atelectasis in the right upper lung field and cardiomegaly. Arterial blood gas analysis at room air was as follows: pH 7.337, PCO_2 41.2 Torr, PO_2 57 Torr, HCO_3^- 21.6 mEq/l. Bronchoscopy revealed tracheal narrowing with excessive granulation tissue formation at the tip of an endotracheal tube (Fig. 1A). This granulation tissue was wedged to the end of tracheal tube on the expiratory phase of respiration (Fig. 1B), and disturbed expiratory flow. Three-dimensional CT demonstrated severe tracheal stenosis from the end of endotracheal tube to 15-mm distal portion around the carina (Fig. 1D and 1E). Conventional CT revealed that internal lumen of the trachea was kept open at the end of tracheal tube (Fig. 2A), and narrowed at the carina level (Fig. 2C), then re-opened at both main bronchi levels (Fig. 2E). Although tracheal stent insertion and/or argon beam laser irradiation were considered, the risk was thought unacceptable. After mechanical ventilatory support for 1 month, the patient was discharged under home oxygen therapy. Care was continued at home, while adjusting the position of the endotracheal tube every month with the aid of bronchoscopy. However, tracheal narrowing gradually progressed from the tracheostomy site distally into the thoracic trachea, and five months later, he suddenly developed respiratory distress. He died within 4 hours after arriving at our hospital due to tracheal collapse and CO_2 narcosis, despite cardiopulmonary resuscitation.

At autopsy, the mucosal surface of the trachea was markedly erosive and irregular (Figure 1C). Microscopical features of the trachea in each level of cranial, medial and caudal levels are shown in Figure

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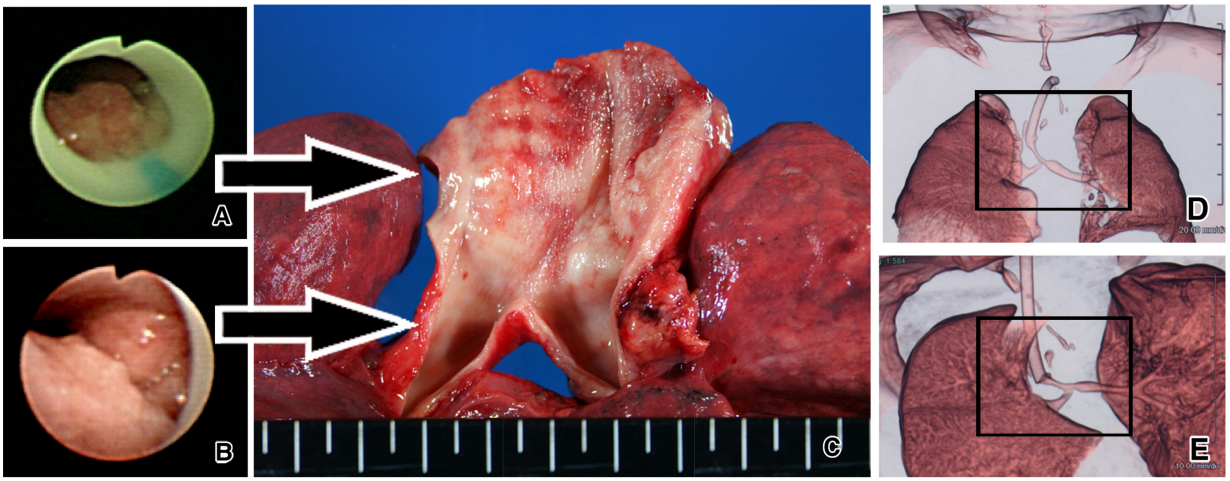

Fig. 1 Clinico-radiological-pathological correlation of bronchial lesions in Hunter syndrome
The tracheal space was narrowed and occupied with granulomatous tissues at the tip of the tracheal tube (A), and the distal portion of the left main bronchus was not clearly seen from the carina (B). Three-dimensional CT clearly demonstrated the collapsed airway in the distal part of the trachea and both main bronchi (D and E), which was confirmed by autopsy finding showing a thin tracheal wall with granulomatous tissues (C).

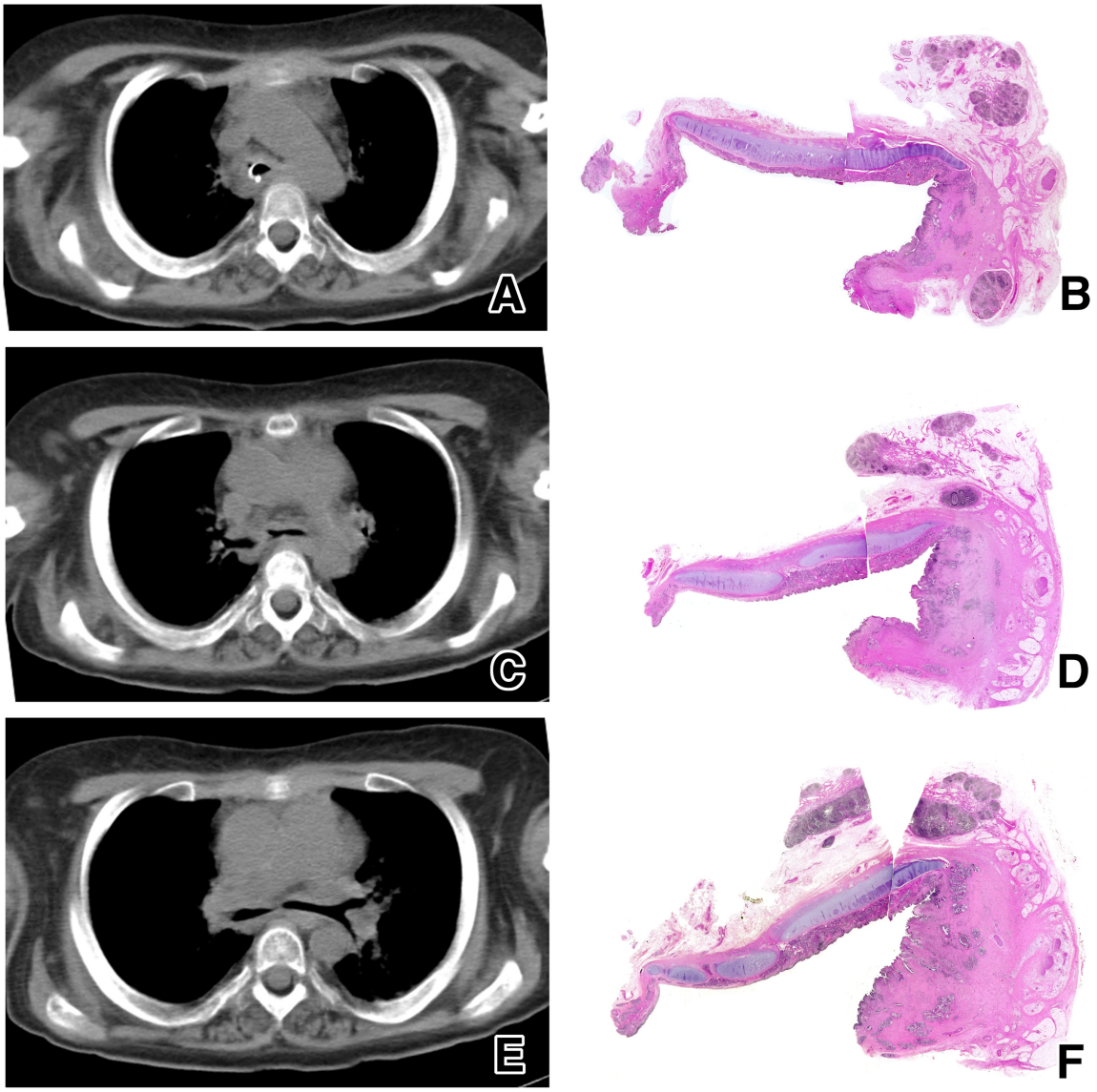

Fig. 2 Axial views of conventional CT and autopsy findings
Conventional CT (A, C, E) serially revealed tracheal narrowing near the carina, which was confirmed by macroscopic pathology indicating a flattened tracheal wall (B, D, F).

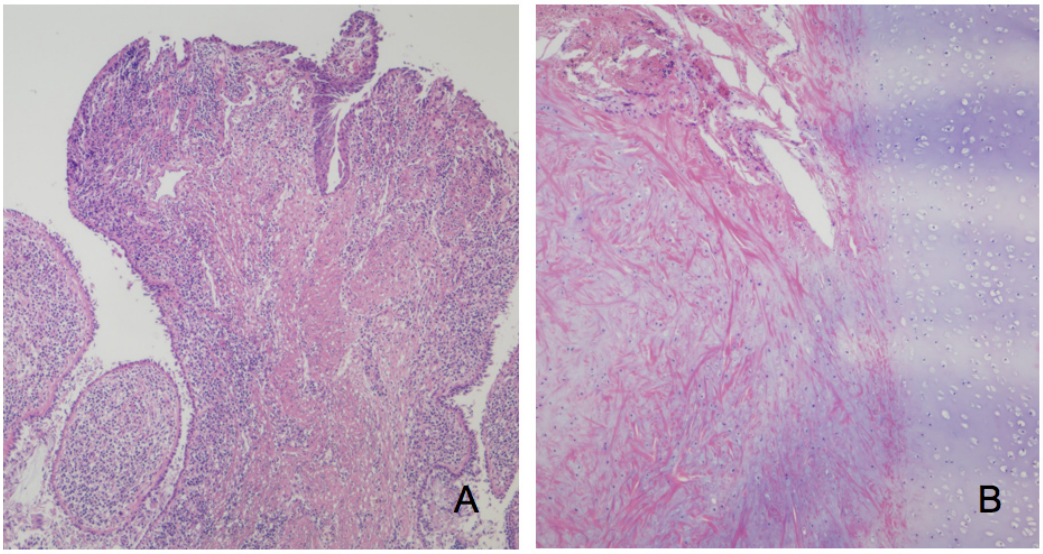

Fig. 3 Microscopic findings of the tracheal wall
Granulomatous tissue proliferation (A) and the deposition of mucopolysaccharide, indicated by a blue color (B), were seen in the tracheal wall.

2B, 2D and 2F, respectively. The tracheal wall was markedly thickened due to fibrosis, inflammation and granulation tissues. Microscopic examination (hematoxylin and eosin staining) showed erosive changes in mucosal surface and reactive infiltration of lymphocyte in the fibrous stroma (Fig. 3A), and the deposition of mucopolysaccharide within connective tissue around the cartilaginous tissue (Fig. 3B).

DISCUSSION

Clinically, patients with Hunter syndrome can present with variable symptoms including skeletal deformities, organomegaly, short stature, stiff joints, coarse facial features and airway obstruction [1]. Tracheal or lower airway obstruction often occurs due to floppy tracheal cartilage, redundant respiratory epithelium, or pedunculated nodule [2]. In this patient, granulomatous changes with reactive infiltration of lymphocyte in the tracheal lumen, as shown in bronchoscopy and pathological examination, may occur mainly due to mechanical stimulation by the endotracheal tube, and partly due to the deposition of mucopolysaccharide. Finally, progressive obstruction with minor upper respiratory infections or pneumonia may result in severe hypoxemia and acute respiratory insufficiency [3]. The clinical course in our patient was typical.

In this report, we have demonstrated the bronchoscopical-radiological-pathological findings correlation of bronchial lesions in Hunter syndrome. As shown in Figure 2, conventional CT serially revealed tracheal narrowing near the carina, which was confirmed by macroscopic pathology indicating a flattened tracheal wall. Furthermore, three-dimensional CT (Figure 1D and 1E) clearly demonstrated the collapsed airway from the various angles. These changes seen in three-dimensional CT were also confirmed by autopsy, which revealed a thin tracheal wall with softening of the supporting cartilage and granulomaous tissues. Although bronchoscopic visualization is useful up to the occluded site of the trachea, three-dimensional CT can reveal the status of the whole airway passage, which is helpful for deciding on therapeutic strategy to treat stenosis, and for the prediction of the patient's prognosis. Thus, we would like to emphasize the clinical usefulness of three-dimensional CT.

Treatment for airway obstruction in Hunter syndrome is still controversial. The usefulness of tracheal stent insertion [4] and argon beam laser treatment following stenting [5] has been reported. However, these treatments involve a risk of tracheal rupture, mucous impaction, the formation of postoperative granulation tissue, airway spasm, and pulmonary hemorrhage [4]. We discussed this issue with surgeons and otolaryngologists in our hospital, requested a second opinion from an otolaryngologist at a pediatric hospital, and discussed treatment policy with the patient's family, and the decision was made not to try these interventions. Methods for safe and easy airway management for patients with Hunter syndrome remain to be developed.

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