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CASE REPORT

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# Granulation after stenting for tuberculous bronchial stenosis treated with tranilast: A case report

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**Abstract**

A 63-year-old woman was diagnosed with tuberculous bronchial stenosis of the left main bronchus following recurrent pneumonia. She underwent airway dilatation and stenting for long and severe stenosis. Initially, a Dumon Y-stent was implanted, but repeated granulation occurred at the distal end of the stent. The granulation reappeared repeatedly despite cauterization and stent replacement. An attempt at stent removal led to worsening of scar stenosis; therefore, it was reinstalled. Finally, two self-expandable metallic stents were implanted sequentially, and she remained asymptomatic for 14 months. After this, she presented with fever and a computed tomography showed obstructive pneumonia due to associated granulation at the distal end of the stent. She was then started on tranilast to treat the granulation with the stent in situ. Granulation almost completely disappeared after 4 months and no recurrence was noted at 12 months since the start of tranilast.

**KEYWORDS**
bronchial stenosis, granulation, tranilast

## INTRODUCTION

The treatment of benign airway stenosis, including tuberculous bronchial stenosis, is stenting if surgical resection is not possible.[1] Stenting maybe complicated by granulation or restenosis. In this study, we report a case of granulation at the distal end of a stent, placed for tuberculous bronchial stenosis, treated successfully with tranilast.

## CASE REPORT

A 63-year-old woman with recurrent pneumonia was diagnosed with stenosis of the left main bronchus. She was diagnosed with tuberculous bronchial stenosis due to previous bronchial tuberculosis (Figure 1B). The stenosis extended over 3 cm of the 4-cm left main bronchus (Figure 1A), and as surgical resection was not possible, airway dilatation was performed. Because of the high degree of stenosis, a Dumon Y-stent (Novatech SA, La Ciotat, France) was placed. However, she continued to develop new granulation tissue at the distal end of the stent. For repeated granulation, we applied mitomycin C to the granulation using a flexible bronchoscope, but mitomycin C was not effective. Therefore, a self-expandable metallic stent (SEMS) was implanted at the distal end of the Dumon Y-stent. Nevertheless, the distal end of the SEMS developed granulation, and the SEMS was removed. We decided to cauterize the peripheral granulation of the Dumon Y-stent, but the cough reflex was so strong that repeated treatment with local anaesthesia was difficult. Because the stent was irritating and granulation continued, the Dumon Y-stent was temporarily removed, but restenosis was observed. Finally, a series of SEMS (Ultraflex Tracheobronchial Stent, 12 mm × 40 mm) was implanted at the distance of the SEMS

Takuya Ohashi and Miwako Miyasaka are joint first authors.

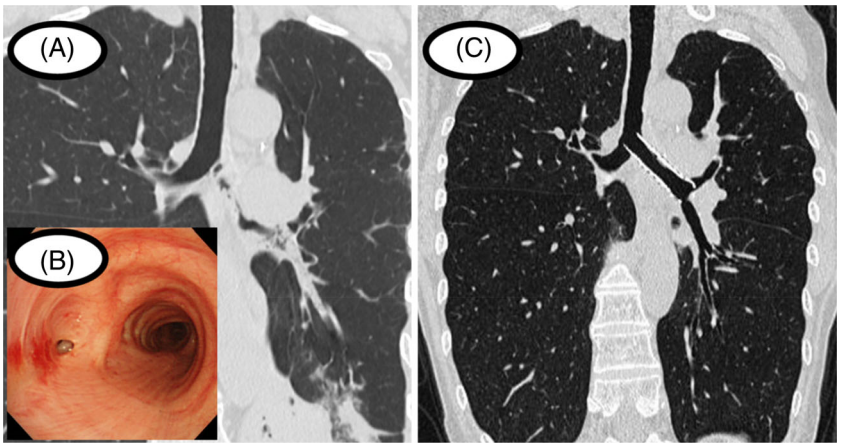


**FIGURE 1** Imaging findings before the onset of obstructive pneumonia. (A) Chest computed tomography (CT) shows extensive stenosis of the left main bronchus before stenting. (B) Bronchoscopic findings showed severe stenosis of the left main bronchus. (C) Chest CT shows patency of the left main bronchus after stenting

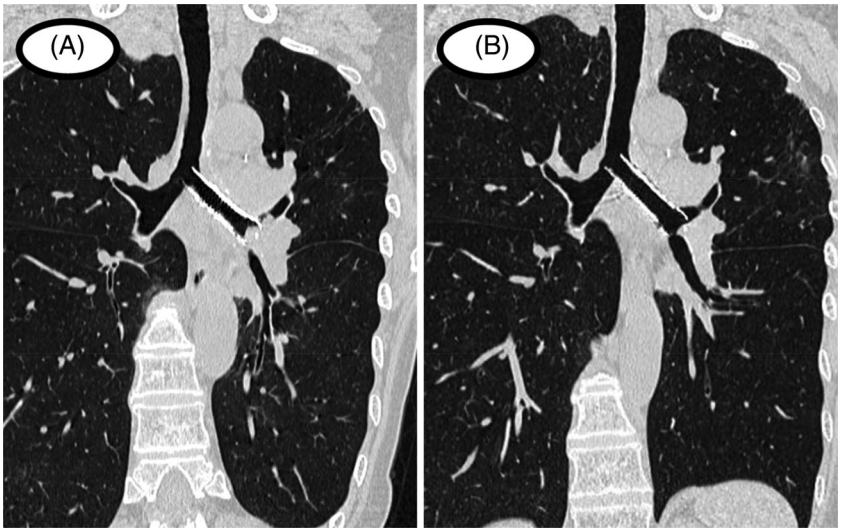


**FIGURE 2** Imaging findings before the onset of obstructive pneumonia. (A) Before tranilast administration, stenosis due to granulation at the distal end of the stent. (B) After tranilast administration, granulation at the distal end of the stent has regressed

(AERO Fully Covered Tracheobronchial Stent, 12 mm × 30 mm) (Figure 1C). She then progressed without additional treatment for 14 months.

The patient then presented with pneumonia, and chest computed tomography (CT) showed new granulation at the distant end of the stent (Figure 2A); obstructive pneumonia caused by granulation was diagnosed. She was treated with levofloxacin hydrate at 500 mg/day as an outpatient for 2 weeks, but the pneumonia did not improve. Therefore, she was admitted to the hospital and removal of granulation was attempted. On admission, bronchoscopy revealed circumferential granulation of the distal bronchi at the end of the stent. We attempted to cauterize the granulation with argon laser; however, the cough reflex was strong making it difficult to continue the treatment. Based on the imaging and bronchoscopic findings, irritation due to the stent was thought to cause the granulation. We considered removal of the stent or placement of an additional stent more distally. However, since the patient's condition had been well controlled for a long time with the current stent and the granulation has been recurrent, we started her on tranilast to try to eliminate the granulation with the stent in situ. Tranilast was administered daily at 300 mg/day. One week later, obstructive pneumonia improved. Chest CT scan 4 months after the start of treatment showed almost complete disappearance of the granulation (Figure 2B). No recurrence was noted at 12 months of follow-up.

## DISCUSSION

Tranilast (*N*-[3,4-dimethoxycinnamoyl]-anthranilic acid), an analogue of a tryptophan metabolite, inhibits the release of chemical mediators from mast cells and is used as an

anti-allergic drug for the treatment of bronchial asthma, atypical dermatitis and allergic conjunctivitis. It is also used in the treatment of inflammatory diseases, such as keloids and hypertrophic scars, because it inhibits collagen synthesis in fibroblasts by suppressing the release of transforming growth factor (TGF)-β1.[2]

The causes of tracheobronchial granulation include scar stenosis after tracheostomy, benign airway lesions and stent placement. Tracheobronchial granulation is a refractory lesion that can be treated by airway dilatation or granular cautery alone, however, with repeated restenosis.[3]

The treatment for bronchial granulation is surgical resection whenever possible. It has been reported to be effective in 93.7% of patients. However, the longer the trachea to be resected, the more the tension placed on the anastomosis, leading to serious complications.[4] Therefore, stenting may be considered in cases in which surgical resection is difficult.[1]

The use of SEMS for benign airway stenosis is controversial, but it has been reported to be effective in a limited number of cases, such as those in whom silicone stents cannot be implanted or in patients with recurrent stenosis.[5,6]

While stents can open up stenoses caused by granulation, they can also trigger granulation. Therefore, frequent removal of granulation is necessary when it occurs at the distal end of the stent.[1] The mechanism of granulation in the trachea and bronchi is the excessive accumulation of collagen via the TGF-β family and Wingless/Int-1, which results in granulation formation.[7]

As mentioned above, tranilast inhibits the release of TGF-β and may be useful in the treatment of tracheobronchial granulation; Sato et al. also reported a case in which granulation after bifurcation was eliminated by multidisciplinary treatment including tranilast.[8]

Tranilast is effective for allergic diseases of the trachea such as bronchial asthma, but only a few reports of its administration for granulation of the trachea have been reported; even fewer reports of tranilast administration for tracheobronchial granulation after stenting.

In our case, the patient had extensive granulation in the left main bronchus, extending into the second carina, making it impossible to place an additional stent distal to the existing one. In addition, irritation by the stent was thought to be the cause of granulation, but its removal led to restenosis. Therefore, the stent was left in place and tranilast was administered. Four months later, the granulation had disappeared.

This case is useful because tranilast can be a new treatment option for granulation after stent implantation. Although this is only one case, the usefulness of tranilast in the treatment of tracheal and bronchial granulation needs to be investigated in future studies.

## CONFLICT OF INTEREST

None declared.

## AUTHOR CONTRIBUTION

Takuya Ohashi and Miwako Miyasaka were involved in study design and data interpretation. Mitsumasa Kawago, Yoshimitsu Hirai, Megumi Kiyoi, Yumi Yata, Mari Kawaji, Aya Fusamoto, Hideto Iguchi, Hitomi Nakanishi and Yoshiharu Nishimura were involved in the data analysis. All authors critically revised the report, commented on drafts of the manuscript and approved the final report.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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