

Pharyngeal reconstruction for severe pharyngeal stenosis in Behçet's disease: a retrospective case series

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Abstract

Objective

Pharyngeal scarring stenosis is a rare yet very severe complication in Behçet's disease (BD). Previously, such patients had to undergo tracheostomy for life, which seriously affected the patient's speech and swallowing function. We aim to present the effect of pharyngeal reconstructive surgeries using flaps for severe pharyngeal stenosis in BD.

Methods

The medical history, the surgical procedures of reconstruction and the clinical outcomes of BD cases with pharyngeal stenosis were analysed. British Medical Research Council questionnaire (MRC), Chinese version of the Swallowing Quality-of-Life Questionnaire (SWQOL), the dysphagia score (DS) and the penetration-aspiration scale (PAS) based on videofluoroscopic swallowing study were used.

Results

Six BD cases with pharyngeal stenosis underwent reconstructive operations. Submental island flaps and forearm free flaps were used in reconstructive procedures in three female and three male patients, respectively. All patients successfully removed the tracheotomy cannula and nasal feeding tube after reconstruction. Dyspnoea was significantly relieved as MRC scores decreased from 3 (3-4) to 1 (1-2) ($p=0.020$, $Z=-2.333$). SWQOL scores were remarkably improved from 782.5 (657.0-854.0) to 826.5 (768.0-864.0) ($p=0.027$, $Z=-2.207$). There was non-significant decrease in DS (from 2.5 to 1.5, $p=0.066$, $Z=-1.841$) and increase in PAS (from 1 to 1.5, $p=0.317$, $Z=-1.000$).

Conclusion

Reconstructive surgery using flaps is an effective and safe approach to rebuild pharyngeal cavity in BD patients with severe pharyngeal stenosis, which can improve the quality of life of these patients.

Key words

Behçet's syndrome, complications, deglutition disorders, dyspnoea, reconstructive surgical procedures

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Introduction

As firstly reported by Dr Hulusi Behçet in 1937, Behçet's disease (BD) is a chronic multisystem autoimmune disease characterised by relapsing oral and genital ulcers with ocular involvement, which can also affect joints, blood vessels, nervous system, and even gastrointestinal tract (1, 2). Although reports on BD with pharyngolaryngeal involvement are limited (3-5), it becomes more evident that pharyngeal complications in BD are not uncommon. Pharyngeal scar may occur in some patients with BD, and in severe cases it can lead to pharyngeal stenosis and the resultant dyspnoea, dysphagia, or dysarthria, which greatly reduce quality of life of patients and even be life-threatening (3, 6). As pointed out by Gross and Ben-Chetrit (4), pharyngolaryngeal involvement in BD is a new challenge for treatment.

To the best of our knowledge, studies focused on pharyngeal scar as a complication of BD are mostly single-case reports. While surgical treatments are often necessary as medical therapy shows little effect on formed scar, the literature on operative interventions is even less common (7). In this study, we present and analyse the effect of pharyngeal reconstructive surgeries in six BD patients with severe pharyngeal stenosis.

Material and methods

Patients

This retrospective case series included patients who were diagnosed BD with severe pharyngeal stenosis from January 2015 to September 2021 in our hospital. The diagnostic criteria of BD were the presence of recurrent oral ulcerations with any two of the following: genital ulcerations, typical ocular lesions, typical defined skin lesions, or a positive pathergy test (8). The criteria for reconstructive surgery were as follows: 1) without new onset of oral or pharyngeal ulceration for at least 6 months; 2) with symptoms of dyspnoea or dysphagia; and 3) normal erythrocyte sedimentation rate (ESR).

This study was approved by the Ethics Committee of Peking Union Medical College Hospital (Project no. JS2084). Written informed consent was obtained from all study participants.

Surgical procedures

All patients underwent general anaesthesia followed by endotracheal intubation except for patients with the tracheostomy tube. Before reconstruction, the pharyngeal scar tissue was removed as much as possible and the normal laryngeal structure was preserved. There were two types of soft-tissues used in pharyngeal reconstruction, namely submental island flaps and forearm free flaps. Submental island flaps were designed with facial artery and submental artery as pedicles. After removal of pharyngeal scar, the centre of flap was aligned with midline to reconstruct the lateral and posterior pharyngeal wall. For forearm free flaps, the donor sites were all in left forearms, and the artery and vein of flap were anastomosed to the facial artery and the external jugular vein, respectively. Reconstructive method of forearm free flap was same as that of submental island flap. All patients received tracheotomy and placement of nasogastric tube to assist breathing and feeding.

Evaluation of respiratory and swallowing functions

Medical Research Council questionnaire (MRC) has been used for many years for assessing the effect of dyspnoea on daily activities, and it allows patients to indicate the extent to which their dyspnoea limits their mobility (9). MRC was used in our study to evaluate the respiratory ability in patients. Chinese version of the Swallowing Quality-of-Life Questionnaire (SWQOL) was applied to subjectively evaluate patients' swallowing function (10). For an objective evaluation of swallowing ability, videofluoroscopic swallowing study (VFSS) was performed. Briefly, VFSS was conducted as using a fluoroscope machine to record how the oral and pharyngolaryngeal muscles work after patients swallowed 5 ml of a semiliquid mixture [76% meglucamine diatrizoate solution plus 6.4 g of a thickening agent (Resource®, Nestle Deutschland AG, Germany)] (11). Based on VFSS results, the dysphagia score (DS) was determined according to the scoring system firstly proposed by Frowen, which was initially used in the dysphagia evaluation for patients with head and neck

Compliance with Ethical Standards.

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Competing interests: none declared.

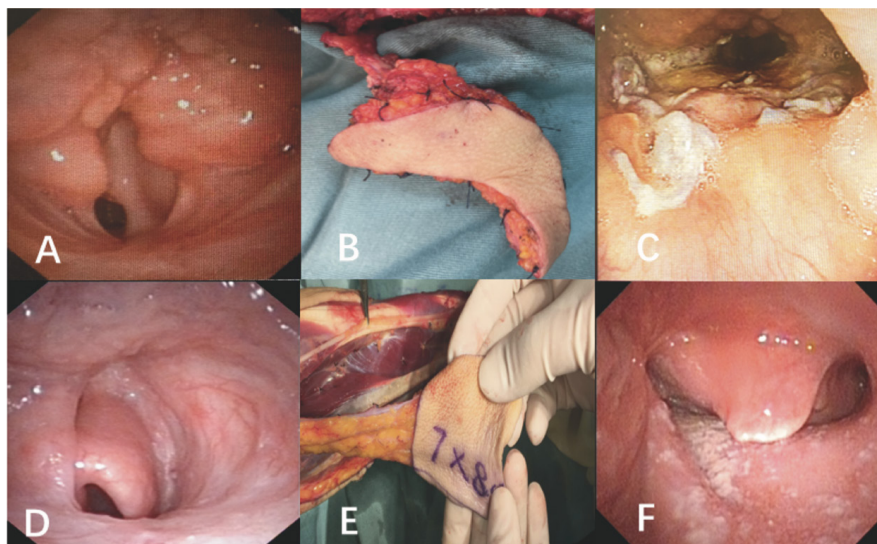


Fig. 1. Representative pictures of severe pharyngeal stenosis, flaps used in reconstruction, and the reconstructed pharyngeal cavities.

(A) Pharyngeal stenosis of Case 3 caused by supraglottic laryngopharyngeal scar. (B) Submental island flap used in the reconstructive procedure of Case 3. (C) Laryngoscopy after six months showed a significant expansion in pharyngeal cavity of Case 3. (D) Pharyngeal stenosis of Case 2 caused by oropharyngeal scar at epiglottic level, which compressed the epiglottic and narrowed the airway. (E) Forearm free flap used in the reconstructive procedure of Case 2. (F) Oropharyngeal cavity of Case 2 after 2 years.

cancers (12). The penetration-aspiration scale (PAS), an 8-point scale used to assess the depth and response to airway invasion, was also determined based on VFSS results according to the methods proposed by Rosenbek (13).

Statistical analysis

Statistical analyses were performed using SPSS v. 17.0 statistical software (SPSS, Chicago, IL). Quantitative data without a normal distribution were expressed as median and interquartile

range and were compared using the Wilcoxon rank sum test. *p*-values less than 0.05 were considered statistically significant.

Results

A total of six patients were diagnosed BD with severe pharyngeal stenosis and accepted pharyngeal reconstructive surgeries. The median age of patients, the median onset time of BD, and the median time of pharyngeal stenosis were 26.5 (25–60), 15 (8–30), and 7.5 (5–14) years, respectively. All cases suffered from oral and pharyngeal lesions. Pharyngeal scars were mainly distributed from oropharynx to hypopharynx, especially severe at the level of epiglottis. Severe scarring compressed the epiglottis, causing it to curl and thus narrowed the airway (representative laryngoscope picture showed in Figure 1D). Additionally, gastrointestinal, joint, mucocutaneous, ocular, and genital involvement were also found in one, one, four, four, and four patients, respectively. All patients received medicine treatment including glucocorticoid and immunosuppressive agent in Department of Rheumatology. Before admission to our hospital, six patients accepted a to-

Table I. Demographic, clinical characteristics and treatment status of Behçet's disease patients with pharyngeal stenosis.

Case	Gender	Age (year)	BD duration (year)	Pharyngeal stenosis duration (year)	Organ involvement	Previous medication ¹	Perioperative medication ²	Number of previous surgeries	Preoperative tracheotomy	Preoperative ESR (mm/h)	Preoperative CRP (mg/L)
1	Male	26	17	12	Oral and pharyngeal cavity; Genital; Skin; Eyes	Glucocorticoid; Colchicine; Immunosuppressive agent; Biologic agent	Biologic agent	3	No	6	4.21
2	Male	42	15	9	Oral and pharyngeal cavity; Genital; Eyes	Glucocorticoid; Immunosuppressive agent; Thalidomide	Thalidomide	2	Yes	6	1.25
3	Female	25	13	5	Oral and pharyngeal cavity; Eyes; Skin	Glucocorticoid; Immunosuppressive agent; Thalidomide	Colchicine	2	No	3	0.21
4	Female	27	15	6	Oral and pharyngeal cavity; Genital; Eyes	Glucocorticoid; Immunosuppressive agent; Thalidomide	None	4	Yes	4	0.58
5	Male	60	30	14	Oral and pharyngeal cavity; Inferior digestive tract; Skin	Glucocorticoid; Immunosuppressive agent; Colchicine	Thalidomide	3	No	7	8.88
6	Female	25	8	3	Oral and pharyngeal cavity; Genital; Skin; Joints	Glucocorticoid; Immunosuppressive agent; NSAIDs	None	2	No	7	0.82

1. Medications used at least 6 months before surgery; 2. Medications used within 6 months before surgery.

BD: Behçet's disease; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; NSAIDs: non-steroidal anti-inflammatory drugs.

Table II. Perioperative details of pharyngeal reconstruction in Behçet's disease patients with pharyngeal stenosis.

Case	Type of flap	Hospital stay (days)	Postoperative decannulation time (days)	Postoperative nasogastric tube removal time (days)	Follow-up time (months)
1	Forearm free flap	17	35	35	60
2	Forearm free flap	15	28	18	48
3	Submental island flap	21	32	20	24
4	Submental island flap	14	28	28	28
5	Forearm free flap	15	40	25	36
6	Submental island flap	16	29	28	24

tal of sixteen transoral scar excision or stenosis dilatation operations elsewhere with the median frequency as 2.5 (2–4) times. During these previous surgical interventions, intraoperative massive haemorrhage (more than 1000 ml blood loss) occurred in Case 1 and Case 4. Two patients used tracheotomy cannula to breathe, but no tube feeding was required before reconstruction (Table I).

The pharyngeal cavity was reconstructed with forearm free flap in three male patients and with submental island flap in three female patients. The median time of hospital stay, decannulation, and removal of nasal feeding tube were 15.5 (14–21), 30.5 (28–40), and 26.5 (18–35) days, respectively. The median of last follow-up time after reconstructive surgery was 32 (24–60) months. All patients continued to follow up regularly in Department of Rheumatology and received assessment and treatment of the primary disease, namely BD (Table II, Fig. 1).

Tracheotomy cannula and nasogastric tube were successfully removed in all patients post-operatively. Dyspnoea was significantly relieved as MRC score decreased from 3 (3–4) to 1 (1–

2) after reconstruction ($p=0.020$, $Z=-2.333$). SWQOL scores were remarkably improved from 782.5 (657.0–854.0) to 826.5 (768.0–864.0) ($p=0.027$, $Z=-2.207$). However, there was non-significant decrease in DS (from 2.5 to 1.5, $p=0.066$, $Z=-1.841$) and increase in PAS (from 1 to 1.5, $p=0.317$, $Z=-1.000$) (Table III, Fig. 2).

Discussion

As a systematic inflammatory disease with undetermined origin, BD is characterised by a wide spectrum of clinical features including multi-site ulcerations, non-granulomatous uveitis, lower extremity vein thrombosis, aortic aneurysms, and neurological impairment (14). However, research focused on the pharyngeal involvement in BD is limited. In 1951, Kennet reported one BD case with pharyngeal involvement, who showed no response to cortisone and received multiple tracheotomies as a result (15). Since then, Brookes *et al.* (16), Hamza *et al.* (17, 18), Nonomura *et al.* (19), Gross *et al.* (4), Li *et al.* (5), Ghazal *et al.* (20) and others have presented case reports on pharyngeal scarred stenosis in BD.

Based on these sporadic cases, it seems that pharyngeal involvement is a rare complication in BD. Nevertheless, the research in Nordic population in 2015 showed that, pharyngeal complications occurred in third of BD patients (5/15) when evaluated by an otolaryngologist using flexible laryngoscope (3). Another study in China demonstrated that 8.5% of BD patients suffered from pharyngeal ulcerations (6). This discordance between common pharyngeal involvement and rare reports may be attributed to the lack of otolaryngologic assessment in the early phase of BD. Regardless of the lack of a precise definition of this syndrome, the aims of treatment for BD are to suppress inflammatory exacerbations and to prevent irreversible damage which would impact on patients' quality of life. While systemic administration of corticosteroid, immunosuppressive drugs, and immunomodulatory drugs is the mainstay of medication treatment of BD, management focused on major organ involvement should be individualised. Surgical interventions to BD-related severe pharyngeal scar are necessary but sporadically reported. Tracheotomy was the main approach to relieve dyspnoea in early reports (15). Nonomura *et al.* reported a BD case of extended pharyngeal scar tissue excision after the failure of local excision (19). Li *et al.* previously shared a case of successful treatment using forearm flap treatment (5). In this study, all enrolled patients had received multiple times of local scar tissue excision, but their dyspnoea could not be significantly relieved. Notably, in Case 1 and Case 4, intra- and post-operative

Table III. Evaluation of respiratory and swallowing function in Behçet's disease patients before and after surgical reconstruction.

Case	MRC		SWQOL		DS		PAS	
	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
1	3	1	764	833	2	2	1	1
2	4	1	832	842	5	2	2	2
3	3	1	758	819	3	1	1	1
4	4	2	657	768	3	1	2	2
5	3	1	801	820	2	2	1	1
6	3	1	854	864	2	1	1	2

MRC: British Medical Research Council questionnaire; SWQOL: Chinese version of the Swallowing Quality-of-Life Questionnaire; DS: dysphagia score; PAS: penetration-aspiration scale.

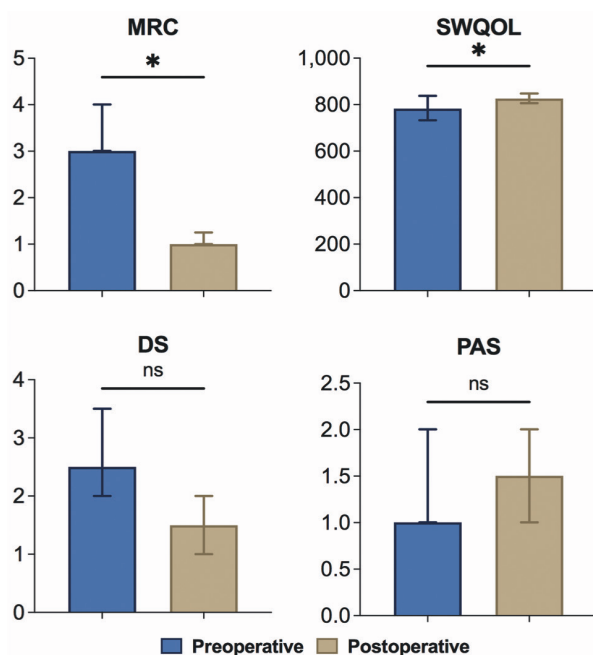


Fig. 2. Pre- and post-operative evaluation of respiratory and swallowing functions.

Data are presented as median with interquartile range.

**p*-value was less than 0.05.

ns: not significant; MRC: British Medical Research Council questionnaire; SWQOL: Chinese version of the Swallowing Quality-of-Life Questionnaire; DS: dysphagia score; PAS: the penetration-aspiration scale.

treatment focuses on decreasing scar forming to prevent life-threatening conditions. The participation of otolaryngologists in the management of BD is also recommended.

Conclusion

Severe pharyngeal stenosis, as a rare complication of BD, needs more attention. For BD patients with severe pharyngeal stenosis who showed little response to medications, reconstructive surgery using flaps following pharyngeal scarring tissue excision is an effective approach to rebuild pharyngeal cavity, and it can improve the quality of life of these patients.

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fatal pharyngeal haemorrhage occurred due to the unclear anatomic marks in transoral approach. Therefore, in our study we chose traditional open approach to perform extended pharyngeal scar tissue excision followed by reconstructive procedures. Reconstructive options for the circumferential pharyngeal defect include submental island flap, pectoralis major myocutaneous pedicled flap, radial forearm free flap, and anterolateral thigh fasciocutaneous free flap (21). Submental island flaps have been known for their suitability for narrow cavity, the high survival rate of them, the single surgical field, and the relatively less trauma (22). Similar to the literature report, in our experience, submental island flaps do have the above advantages and are more suitable than other types of flaps in reconstruction of pharyngeal cavity. However, considering that, compared to women, most men have beards, it is likely that hair will continue to grow in the reconstructed pharyngeal cavity after the use of submental island flap, interfering with feeding and ventilation. For male patients, from the perspective of reducing trauma and shortening operation time, the use of free forearm flap with appropriate thickness can be a good solution to this problem. Therefore, in this study, submental island flaps were only applied in female

patients and forearm free flaps with appropriate thickness were used in male cases. Except for the preference of flaps used in reconstruction, patient's gender would not affect the surgical procedures.

Our results showed that the outcomes of excision of pharyngeal scar tissue and simultaneous reconstruction of pharynx to restore normal cavity were satisfied in severe pharyngeal stenosis cases. Dyspnoea was the major problem in BD patients with pharyngeal stenosis, and pharyngeal reconstructive surgery showed satisfactory results in relieving dyspnoea. Although objective evaluation of dysphagia (DS and PAS) showed non-significant improvement, the swallowing quality of life (SWQOL) was remarkably improved partially because of the amelioration in respiratory. Nevertheless, it should also be stressed that these surgical procedures are relatively traumatic and not the first choice for treatment. Furthermore, rheumatologist played key roles perioperatively and remained irreplaceable in aspects of determining the timing of operation, the medicine treatment after surgery, and so on. Considering that pharyngeal involvement of BD could result in severe pharyngeal stenosis and symptoms like dyspnoea, which showed little response to medicine (4), it is preferred that medicine

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