

# Two different tracts and origin of pyriform sinus fistula

Koichi Sakakura<sup>1</sup>, Yoshihito Yasuoka<sup>1</sup>, Masato Shino<sup>1</sup>, Minoru Toyoda<sup>1</sup>, Kisho Obi<sup>1</sup>, and Kazuaki Chikamatsu<sup>1</sup>

<sup>1</sup>Gunma University Graduate School of Medicine

July 20, 2020

## Abstract

**Objective:** Suppurative acute thyroiditis is caused by pyriform sinus fistula (PSF), and PSF frequently elicits deep neck abscess. However, complete fistulectomy is the ideal management of PSF, and studies on surgical findings of PSF are exceedingly rare. This study aimed to reveal the origins of PSF, each route, and clinical presentation. **Methods:** This is a multicenter study. We have conducted 19 complete fistulectomies of PSF in Japan, analyzed routes of the fistulas, estimated the origins, and investigated their histological and clinical findings. **Results:** No recurrence was observed in all cases. Five of 12 cases showed thymic and/or parathyroid tissues around the fistulas, passing inside the inferior horn of thyroid cartilage, were regarded as having 3rd pouch origin, and tended to have low frequency of severe deep neck abscess. The remaining seven cases originated from the 4th pouch running outside of the horn and showed frequent severe infection. **Conclusion:** PSF have two different routes depending on their generation and may present different clinical manifestations.

## Key points

- Nineteen complete fistulectomies of PSF and 12 of 19 histological analyses.
- There were two routes passing inside or outside the inferior horn of thyroid cartilage.
- The cases from 3<sup>rd</sup> pouch origin seemed to route inside the horn.
- The tracts originated from 4<sup>th</sup> pouch appeared to run outside the horn.
- PSF from 4<sup>th</sup> pouch origin tended to cause severe deep neck infection.

**Key words:** pyriform sinus fistula; pharyngeal pouch; fistulectomy; acute suppurative thyroiditis; thyroid

## Introduction

In 1973, the pyriform sinus fistula (PSF) was defined as a fistula that originated from the remnant of the 4th pharyngeal pouch.<sup>1</sup> Then, in 1979, Takai et al. reported that recurrent acute suppurative thyroiditis was caused by PSF.<sup>2</sup> Moreover, 3%–10% of congenital anomalies that originated from the pharyngeal pouch have been known as remnants from the 3rd and 4th pouch, which are considered as origins of PSF. It is different from brachial cyst, so called lateral cervical fistula. The inferior parathyroid glands and thymus that originated from the 3rd pouch moves caudally, whereas the superior parathyroid gland and C cells producing calcitonin that originated from the 4th pouch migrate caudally behind thyroid gland.<sup>3</sup> These two tracts are considered as routes of PSF and sometimes presented as two simultaneous fistulas with two different origins as previously reported.<sup>4</sup> Most PSFs (93.5%) are located on the left side because the left side shows more complex vascular development and that the C cell precursor, ultimobranchial body, and part of the 4th pouch develop from the left side.<sup>5–7</sup>

The diagnosis of PSF is confirmed by fluoroscopy and/or computed tomography with enhancement by barium swallow with Valsalva technique.<sup>5</sup> The decision of radical treatment of PSF depends on the frequency of recurrent acute onset and severity of acute phase with attentive consultation with patients and family members. In 1998, Jordan et al. proposed endoscopic cauterization of PSF<sup>8</sup> although this palliative treatment

frequently causes recurrences (25%) as reported in 15 previous studies.<sup>9</sup> In contrast, 18 cases of surgically complete fistulectomy in India presented no recurrence.<sup>10</sup>

There were case reports on severe acute suppurative thyroiditis and deep neck abscess caused by PSF, but no report has mentioned about the routes and origins of PSF. We analyzed 19 cases of completely resected PSF and found two different pathways of fistulas at surgery. In this study, we distinguished two origins of PSF and compared their routes, histology, and clinical manifestations to understand the pathology and improve treatment of PSF.

## Materials and methods

### Patient characteristics

Nineteen cases of PSF in [removed for blind peer review] Prefecture in [removed for blind peer review] had been completely resected from 1997 to 2011 in the following six hospitals by a single chief surgeon (YY): [removed for blind peer review] University Hospital with 10 cases, [removed for blind peer review] Hospital with three cases, [removed for blind peer review] Hospital with two cases, [removed for blind peer review] Hospital with two cases, [removed for blind peer review] Hospital with one case, and [removed for blind peer review] Hospital with one case. The Institutional Review Board in [removed for blind peer review] University approved this study (No. 2017-196). Patient characteristics are summarized in Table 1. All fistulas were preoperatively detected by fluoroscopy and CT. Although some patient data were missing because this is a multicenter study, all cases, except one, were located on the left side. All cases were euthyroid and did not show high thyroglobulin level. One of the patients was in remission phase of acute megakaryoblastic leukemia.

### Surgical procedure

Generally, we do not recommend palliative endoscopic cauterization since this noninvasive technique also shows high recurrence rate. Most surgeries were performed after at least a couple of months until the final episodes of acute infection.

Prior to fistulectomy, a crystal blue dye was injected using a feeding tube for neonates by direct laryngoscopy under general anesthesia to find the fistula easily at fistulectomy. In fistulectomy, the inferior constrictor muscle of the pharynx at the affected side was widely exposed initially from the superior pole of the thyroid gland to the front and side of larynx. The inferior horn of the thyroid cartilage was detected; then, a filamentary object dyed by crystal blue was detected around it. In most cases, the fistula could not be found by the naked eyes in the scar tissue after severe recurrent infection so that the microscope was essential to trace the fistula. Next, the fistula was cut before the hypopharynx with double ligatures, and the superior one-third of the unilateral robe of the thyroid gland was also dissected with the fistula.

### Histological analysis

Two independent investigators (KS and KO) observed pathological hematoxylin-eosin staining samples under the microscope in 12 of 19 cases. Immunohistochemical staining of calcitonin was conducted in 2 of 12 cases, while no positive case was found. The pattern of the epithelium, structure of the wall, and contents in the lumen of the fistula were evaluated. Moreover, the characteristics of inflammation cells and thyroid, thymic, and parathyroid tissues around the fistula were also analyzed.

## Results

### Surgical findings

All patients, except one with congenital large goiter, underwent crystal violet staining from the fistula opening in the PSF before resection. The fistula cannot be detected during surgery in one of these stained cases, while the fistula was resected completely under microscopic surgery. No fistula cannot be distinguished as 3<sup>rd</sup> or 4<sup>th</sup> pouch origin by preoperative analyses. All patients showed no recurrent nerve paralysis or recurrence. One patient had wound infection, and another developed a keloid on the surgical scar postoperatively.

Table 2 shows the surgical and histological features of all 12 cases. Other 7 cases in this study cannot be used for analyses by various reasons. We could track the pathological specimens. Four fistulas (Cases 1, 7, 11, and 12) started inside the thyroid cartilage, and most cases were located behind the thyroid gland. Meanwhile, seven cases that originated outside the thyroid cartilage penetrated the thyroid gland at the superior pole. Therefore, we believe that there were two different routes in PSF as shown in Figure 1: one passes inside the inferior horn of the thyroid cartilage (Fig. 1a); another runs outside the horn (Fig. 1b).

## Histological findings

Then, we corresponded the anatomical/surgical classification to histological findings (Table 2). In terms of embryonic development, thymic and parathyroid tissues must strongly imply its generation from the 3rd pouch (Fig. 2 for Cases 1, 2, and 8). Immunohistochemical staining by calcitonin for detection of C cell is essential in defining the origin from the 4th pouch; however, staining was not conducted in our PSF cases except two negative cases. While negative C cells were supposed to develop from the 3rd pouch, we did not regard these two cases as 3rd pouch origin since immunohistochemical staining of calcitonin was technically difficult and the positivity seemed to depend on the slice. Therefore, based on the thymic tissues around the PSF, we classified PSF into two origins: 3rd pouch with thymic tissues around the fistulas (five cases with shadow in Table 2) and 4th pouch without thymic tissues (seven cases).

Case 10 was previously reported as a double-tract PSF. One fistula that was regarded as having 3rd pouch origin had epithelium, while another (considered as having 4th pouch origin) was filled with granulation tissue and did not have epithelium.

## Clinical presentation

Four of five PSF cases with 3rd pouch origin passed outside the inferior horn of the thyroid cartilage (Fig. 1b), and two cases did not cause deep neck abscess, which was localized within acute suppurative thyroiditis. Meanwhile, half of PSF cases originated from the 4th pouch run inside the horn (Fig. 1a), and almost all cases had deep neck abscess. Three of five PSF cases from the 3rd pouch showed extrathyroidal thyroid tissue around the fistula (Fig. 3 for Case 8) although only one of seven cases from the 4th pouch had thyroid tissue.

## Discussion

In this study, we demonstrated that there were two different pathways of PSF and each pathway seemed to represent their origin. We first reported two different routes of PSF, and these two arms presented each unique characteristic. The inferior parathyroid gland and thymus that originated from the 3rd pouch should migrate a long distance, passing outside the thyroid cartilage, and the remnant of the pathway is the PSF from the 3rd pouch, whereas the superior parathyroid gland and C cells need not move a long distance behind the thyroid gland. These two kinds of tract represent not only their pathways of development but also clinical manifestations. The differences in histological and clinical presentations of PSF between the 3rd and 4th pouch are presented in Table 3. Given that the 3rd pouch generates the thymus and inferior parathyroid gland, extrathyroid tissues around the PSFs the originated from 3rd pouch is interesting. Since most cases penetrate the thyroid gland, the fistulas may carry some thyroid tissues during migration.

However, we have a limited number of cases, and there are tendencies of distinction between the 3rd and 4<sup>th</sup> pouch in the clinical presentation. PSF from the 3rd pouch is frequently observed in men, while that from the 4th pouch is commonly observed in women. Since the 3rd pouch tends to run outside the inferior horn of the thyroid cartilage covered by inferior constrictor muscle of the pharynx, infections are limited locally. On the contrary, infections caused by PSF from the 4th pouch with a tendency of routing inside are considered to expand easily via loose connective tissue inside the superior pole and isthmus of the thyroid gland. Regarding two routes of remnant by the 3rd and 4th pouch, our PSF with double tracts (3rd and 4th pouch, Case 10) previously reported was sufficiently probable.<sup>4</sup>The fistula with 4th pouch origin in this case and Case 9 did not have epithelium in the lumen. Since both cases had severe deep neck abscess, the epithelium may be exfoliated by severe inflammation and granulation.

To date, there is no analysis on PSF cases with complete fistulectomy with one report by Madana et al. in 2011.<sup>10</sup> They reported 18 cases of fistulectomy, with no recurrence, and insisted that 15 cases had 3rd pouch origin and three cases had 4th pouch origin. This proportion is quite different from our cases (5:7 vs. 15:3); however, this previous report did not show any criteria or evidence for distinction of 3rd and 4th pouch origin. They also did not show any histological findings of accompanied tissues around the fistulas. Additionally, a previous study<sup>10</sup> and this study showed no recurrence although palliative endoscopic cauterization showed recurrence at 25%.<sup>9</sup> Now, we have recommended fistulectomy for not only understanding of its route and origin but also prevention of recurrence.

This study has some limitations. We conducted 19 complete fistulectomies, while we obtained only 12 pathological slides and two calcitonin immunohistochemical stains, which were judged as having no positive cells. Due to lack of calcitonin staining, we could not clearly and exactly classify PSF generated from the 4th pouch. Only PSFs accompanied by thymic and parathyroid tissues were defined as having 3<sup>rd</sup> pouch origin, and others should be regarded as having 4th pouch origin. As a result, our classifications in histology and clinical manifestation did not present a clear cutoff.

## Conclusion

We reported two possible routes of PSF, and proposed corresponding two origins of pharyngeal pouch (3rd and 4th). The difference in these two pathways of PSF is supposed to reflect clinical manifestation and severity of acute suppurative thyroiditis caused by PSF.

## References

- 1) Tucker HM, Skolnick ML. Fourth branchial cleft (pharyngeal pouch) remnant. *Trans Am Acad Ophthalmol Otolaryngol.* 1973;77(5):1368-71.
- 2) Takai SI, Miyauchi A, Matsuzuka F, Kuma K, Kosaki G. Internal fistula as a route of infection in acute suppurative thyroiditis. *Lancet* 1979;1(8119):751-2.
- 3) Ford GR, Balakrishnan A, Evans JN, Bailey CM. Branchial cleft and pouch anomalies. *J Laryngol Otol.* 1992;106(2):137-43.
- 4) Shino M, Yasuoka Y, Nakajima K, Chikamatsu K. A case of pyriform sinus fistula infection with double tracts. *Case Rep Otolaryngol.* 2014;2014:126840.
- 5) Nicoucar K, Giger R, Pope HG, Jaeklin T, Dulguerov P. Management of congenital fourth branchial arch anomalies: a review and analysis of published cases. *J Pediatr Surg.* 2009;44(7):1432-9.
- 6) Miyauchi A, Matsuzuka F, Kuma K, Katayama S. Piriform sinus fistula and the ultimobranchial body. *Histopathology.* 1992;20(3):221-7.
- 7) Nicollas R, Guelfucci B, Roman S, Triglia JM. Congenital cysts and fistulas of the neck. *Int J Pediatr Otorhinolaryngol.* 2000;55(2):117-24.
- 8) Jordan J, Graves J, Manning S, McClay JE, Biavati MJ. Endoscopic cauterization for treatment of fourth branchial cleft sinuses. *Arch Otolaryngol Head Neck Surg.* 1998;124(9):1021-4.
- 9) Josephson GD, Black K. A review over the past 15 years of the management of the internal piriform apex sinus tract of a branchial pouch anomaly and case description. *Ann Otol Rhinol Laryngol.* 2015;124(11):947-52.
- 10) Madana J, Deeke Yolmo R, Kalaiarasi S, Gopalakrishnan S, Saxena SK, Krishnapriya S. Recurrent neck infection with brachial arch fistula in children. *Int J Pediatr Otorhinolaryngol.* 2011;75(9):1181-5.

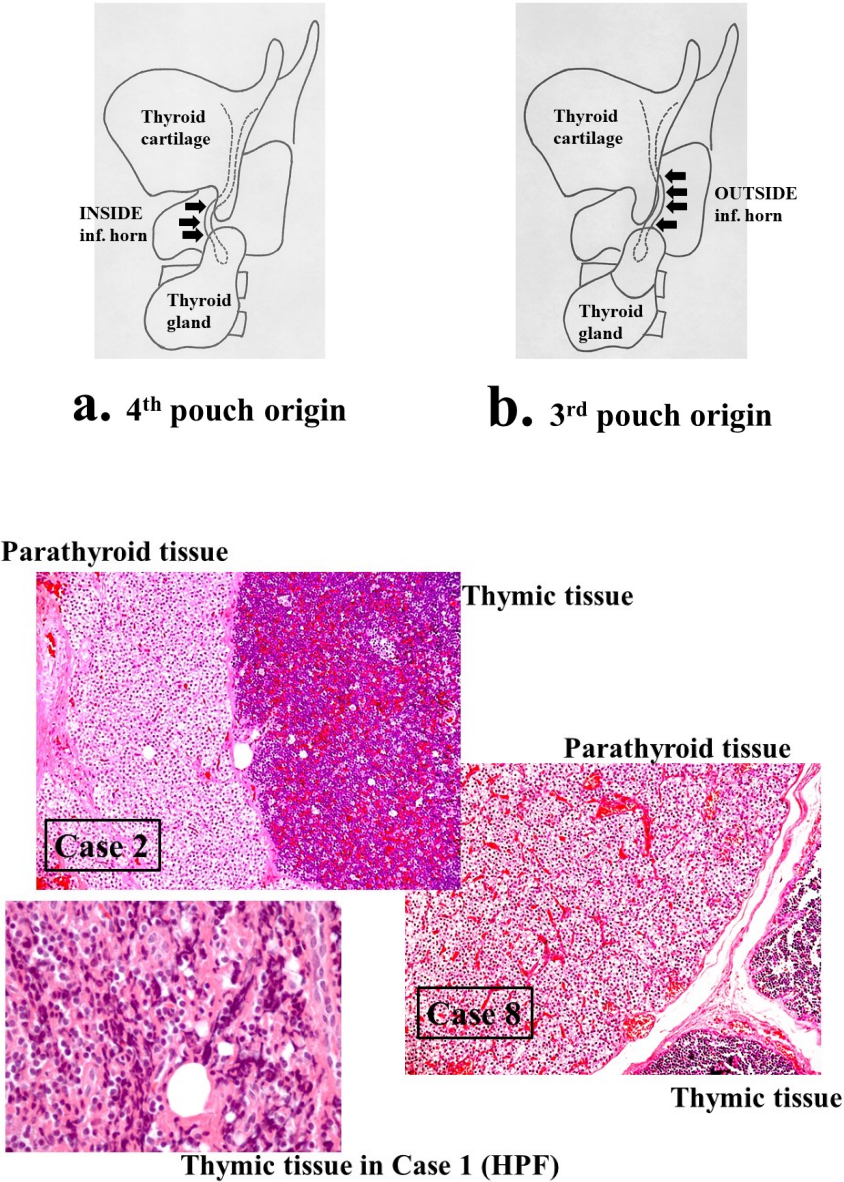
## Figure Legends

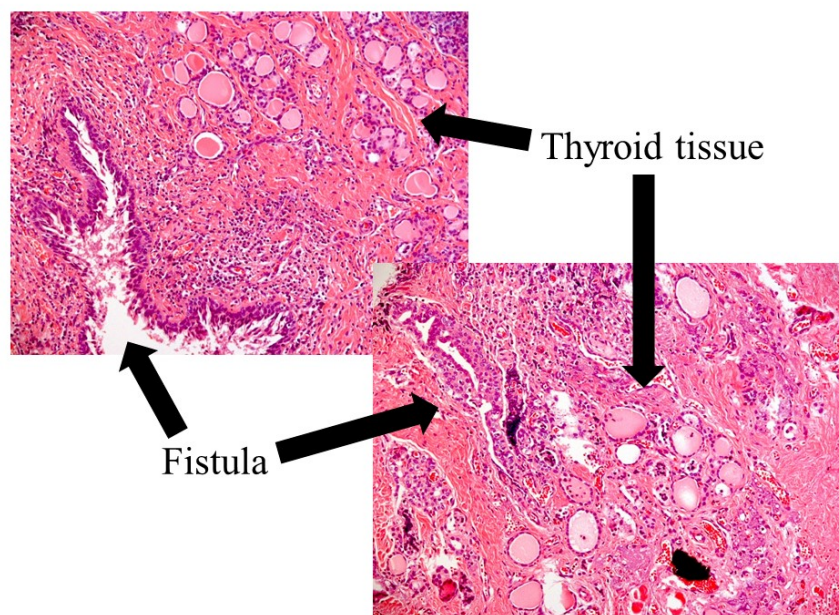
**Fig. 1.** Two different routes of pyriform sinus fistula (PSF). Route **a.** passing inside the inferior horn of the thyroid cartilage implies 4th pouch origin, while route **b.** running outside the horn indicates 3rd pouch

origin. This difference in pathways affected the severity of clinical presentation.

**Fig. 2.** Accompanying tissues around the PSF in Cases 1, 2, and 8. These PSFs had parathyroid and thymic tissues so these were regarded as having 3rd pouch origin.

**Fig. 3.** Extrathyroid tissue beside the fistula in Case 8, indicated as having 3rd pouch origin.





#### Hosted file

Table 1-02.docx available at <https://authorea.com/users/344175/articles/470847-two-different-tracts-and-origin-of-pyriform-sinus-fistula>

#### Hosted file

Table 2-02.docx available at <https://authorea.com/users/344175/articles/470847-two-different-tracts-and-origin-of-pyriform-sinus-fistula>

#### Hosted file

Table 3-02.docx available at <https://authorea.com/users/344175/articles/470847-two-different-tracts-and-origin-of-pyriform-sinus-fistula>