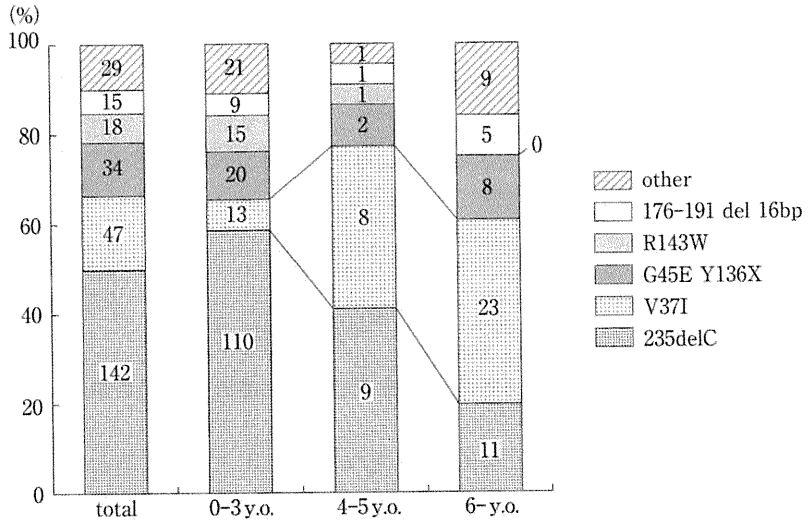

図3　*GJB2*遺伝子変異の種類と発見年齢(文献[7]より引用)

対する人工内耳の有用性は既に報告されており，人工内耳を選択する際の情報として有用である[8,9]．

また*GJB2*遺伝子変異症例では，耳鳴，めまい，内耳奇形の頻度が両側感音難聴患者と比較し有意に低く，*GJB2*遺伝子変異による難聴の臨床的特徴として患者に説明可能である[7]．

b. *SLC26A4*遺伝子変異による難聴：内耳奇形を伴い変動しながら進行する難聴

画像診断も原因遺伝子を絞りこむために重要な役割をもつ(**図5**)．先天性難聴児の数％から20％ほどに何らかの内耳奇形が見いだされると報告されているが，種々の内耳奇形の中でも'前庭水管拡大'は頻度が高い奇形として知られ，我が国でも最近この奇形を伴った難聴症例が数多く報告されるようになり注目を集めている．一連の遺伝子解析を通じて，甲状腺腫を伴うPendred症候群の原因遺伝子(*SLC26A4*)が同時に'前庭水管拡大を伴った難聴'の原因遺伝子になっていることが明らかにされている[10]．したがって従来2つの異なる疾患と考えられていた両疾患は今後①前庭水管拡大，②*SLC26A4*遺伝子変異，③変動する難聴を共通の臨床的特徴としてもつ'*SLC26A4*遺伝子の変異が引き起こす同一の疾患群'として診断，加療されるべきだと考えられる．遺伝子診断は難聴の変動性，進行性，予想される随伴症状(めまい，甲状腺腫等)などを説明する際に有用な情報を提供してくれることが多い．

biallelic(ホモもしくは複合ヘテロ接合体)な*SLC26A4*遺伝子変異をもつ難聴患者39人の臨床像(聴力レベル，聴力の変動，進行，めまいの有無，甲状腺腫の有無)，また遺伝子型と表現型について比較検討した結果，中等度から高度難聴であり個人差が大きかったが年齢とともに進行する傾向が認められた[11]．また，いずれの症例も言語習得前の難聴と考えられ，高率で聴力の変動(92.3％)，進行(88.0％)を認めた[11]．また24人(70.6％)の患者でめまいの合併を認めた．10人(27.8％)の患者で甲状腺腫の合併を認めたが，すべて12歳以降の発症であった[11]．遺伝子型による難聴の程度の差，随伴症状の違いは認められなかった[11]．遺伝子診断により，難聴の進行(**図5**)，めまいなど臨床症状の予後に関して，*SLC26A4*遺伝子変異の認められた患者への適切な情報提供が可能となった．

c. ミトコンドリア遺伝子1555A>G，3243A>G変異：発症予防，合併症の早期治療が可能

ヒトミトコンドリアDNAは16,568塩基対か

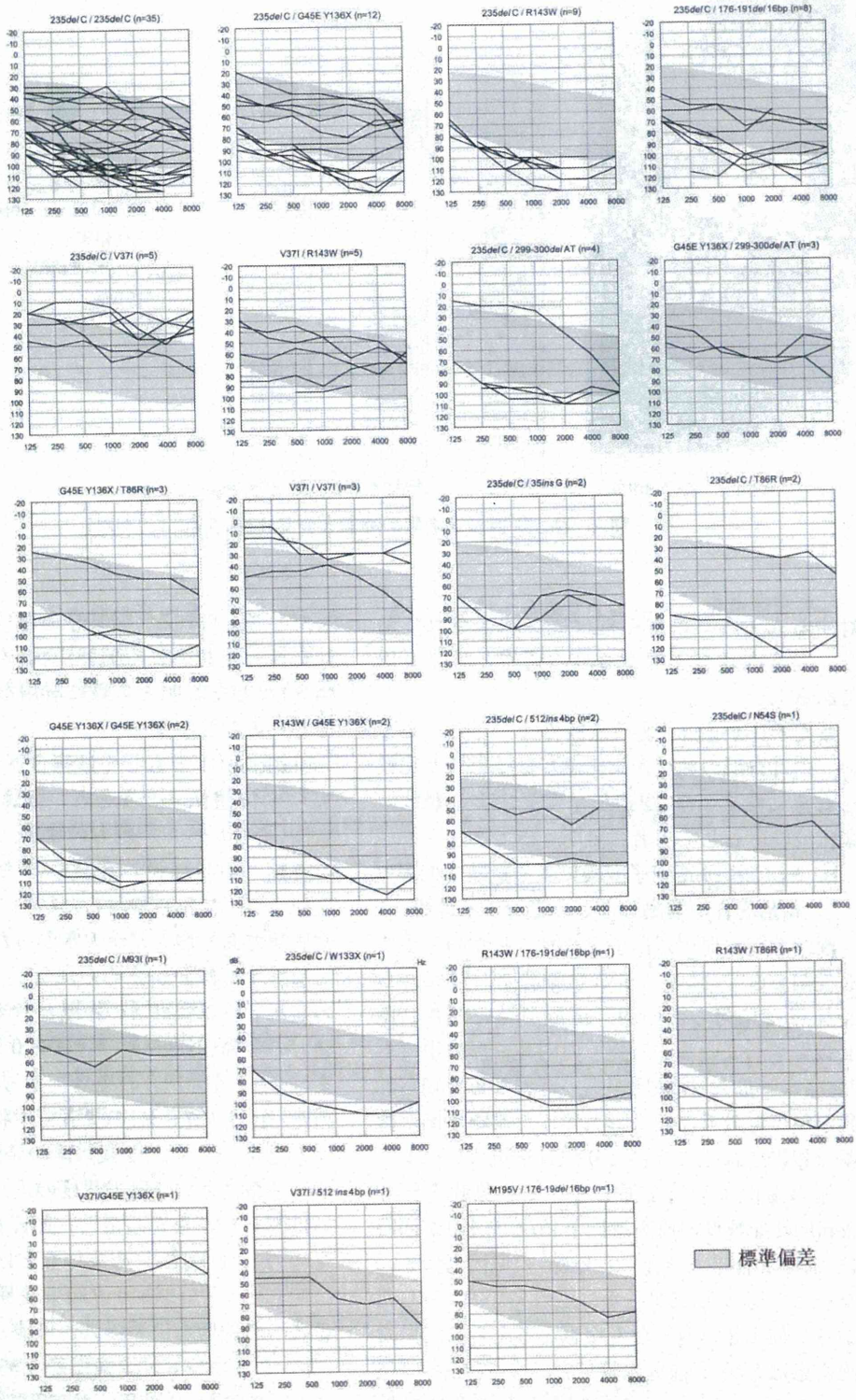

図4　*GJB2* 遺伝子変異による難聴患者の重症度予測
(文献[7]より改変)

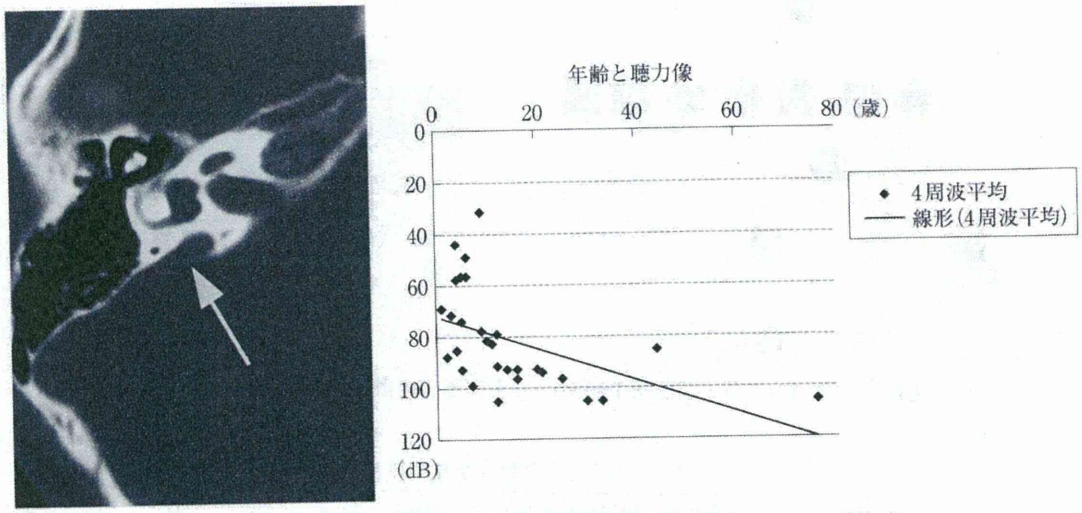

図5　*SLC26A4*遺伝子変異による難聴患者のCT所見と難聴の進行度
(文献[11]より引用)

らなる，二重環構造を示す遺伝子である．13種類の内膜の呼吸複合体遺伝子をコードし，細胞エネルギー産生にかかわっている．ミトコンドリアDNAは受精時で精子からミトコンドリアが脱落するため，ミトコンドリア遺伝子の変異による疾患は母系遺伝を呈する．種々のミトコンドリア変異が難聴と関連していることが知られているが，特に頻度が高い変異として12SrRNA領域の1555A>G変異，*tRNALeu*(*UUR*)遺伝子の3243A>G変異が知られている．インベーダー法による網羅的解析では後天性難聴の母集団に頻度が高く，成人発症の難聴の重要な原因遺伝子変異である．

1) ミトコンドリア遺伝子1555A>G変異

近年，分子遺伝学的にミトコンドリア遺伝子1555A→G変異とアミノ配糖体抗菌薬に対する高感受性との関連性が明らかとなった．この変異は外来を訪れる感音難聴患者の約3％の患者がもっていることが報告されており，この遺伝子変異による難聴患者あるいはハイリスク患者の数は，全国的にかなり多いことが推測されている[12]．またアミノ配糖体抗菌薬による難聴患者に絞ると，約30％に変異が見いだされることが明らかとなり，アミノ配糖体抗菌薬に対する高感受性と関連が深いことが確認されている[12]．また成人の人工内耳の埋め込み患者の約10％に，またアミノ配糖体抗菌薬により高度難聴をきたした人工内耳症例に限ると約60％がこの変異をもっていた[12]．したがってこの変異は日本人の言語習得後失聴の重要な原因の一つであると考えられる．

この遺伝子変異による難聴の特徴は，母系遺伝することである．したがって家族歴の聴取が診断のポイントになる．難聴の程度には個人差が大きいが，難聴は一般的に両側性，対称性，高音障害型で，耳鳴を伴うことが多い[13]．変異をもつ患者の中にはアミノ配糖体抗菌薬の投与歴がなく，いわゆる特発性難聴の形で難聴をきたす症例もあるが，難聴の程度は一般的に軽度のことが多い[13,14]．確定診断は遺伝子診断になる．現在，先進医療'先天性難聴の遺伝子診断'の一項目になっているほか，臨床検査の一つとして外注検査が可能になっている(株式会社ビー・エム・エル：受託検査項目)．

難聴は進行例も認められることから定期的に聴力検査を行い経過観察することが重要である．通常，中等度以上の難聴症例には補聴器が用いられるが，補聴効果の認められない高度難聴に関しては人工内耳の良い適応になることが多い．このミトコンドリア遺伝子1555A>G変異に伴

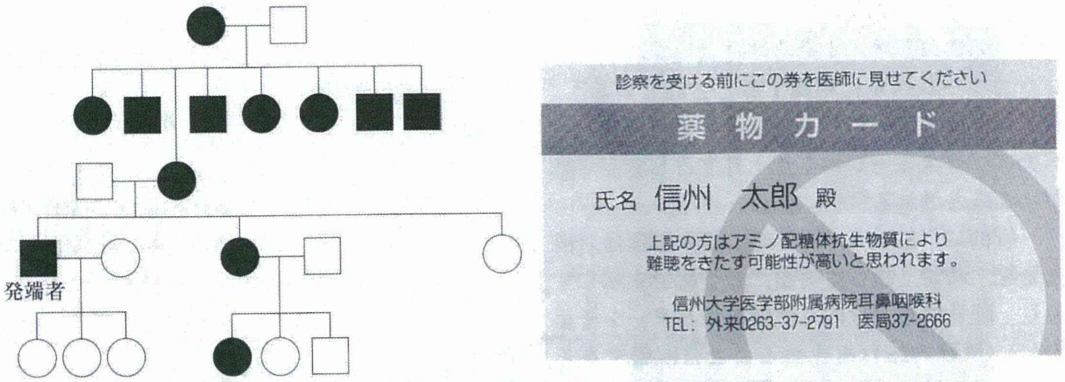

図6　ミトコンドリア遺伝子1555A>G変異患者の家系図と薬物カード(文献[15]より改変)

表2　ハイリスク患者を見つけ出すポイント

(1) 家族歴：母系に難聴者がいないか？
(2) 家族歴：アミノ配糖体抗菌薬による難聴者がいないか？
(3) 両側高音障害型難聴，進行性の難聴に注意
(4) 遺伝子検査

う難聴に関しては，アミノ配糖体抗菌薬の投与を避けることにより高度難聴はある程度予防が可能であることから，現在著者らの施設ではミトコンドリア遺伝子変異のスクリーニングシステムを確立するとともに薬物カード(**図6**)を配布し予防に努めている[15]．

表2にハイリスク患者を見つけ出すポイントについてまとめたが，最近，十分な家族歴の聴取なしにハイリスク患者に漫然と複数回のアミノ配糖体抗菌薬の投与が行われ，難聴が生じた患者・家族が病院側を訴え病院側が非を認めた事例があった．またアミノ配糖体を含んだ点耳液により感音難聴を生じ訴訟になった事例も報告されている．今後，このような事例が増えていくことが予想されるが医師サイドでも患者の遺伝的背景には十分留意することが必要である．

2) ミトコンドリア遺伝子3243A>G変異診断による合併症の早期発見

tRNALeu(*UUR*)遺伝子における3243A>G変異は糖尿病と難聴を伴う症候群の原因遺伝子として知られている遺伝子変異である[16,17]．耳鼻咽喉科外来を受診する感音難聴患者の0.3–3％に認められることが知られている[12,18]．ミトコンドリア遺伝子3243変異を同定することにより，難聴の予後(重症度，進行性の有無)が予測できるとともに合併症の予測や対応が可能になる．

この変異は，脳卒中様症状と高乳酸血症を伴うミトコンドリア筋症，脳症Mitochondrial encephalopathy, lactic acidosis and stroke-like episodes(MELAS)症例においても認められている．なぜ同じ遺伝子変異がMELAS，糖尿病，感音難聴などの多彩な障害を起こすのかは明らかにされていないが，臓器ごとでヘテロプラスミーの割合が異なっているためではないかと考えられている．ミトコンドリア遺伝子変異では，変異型ミトコンドリアと野生型ミトコンドリアがどの程度混在しているか(ヘテロプラスミー)が問題となる．ヘテロプラスミーの割合が一定以上になると(閾値を超えると)臨床症状が発症するといわれている．通常の遺伝子検査では末梢血のヘテロプラスミーの割合をみていることになるが，臓器によりヘテロプラスミーの割合は異なるとされ，一般的には神経系，筋肉，内耳などでヘテロプラスミーの割合が高いことが報告されている．理論的にはヘテロプラスミーの割合と臨床症状は相関すると考えら

れるが，必ずしも相関しない場合も多い．3243変異患者の長期間にわたる聴覚は変異型ヘテロプラスミーレベルに相関するとされている[19]．ヘテロプラスミーの程度と発症年齢は関係し，ヘテロプラスミーレベルが上昇すると発症年齢が早まるとされる[20]．

一般的に，3243A>G変異に伴う難聴は，成人発症，両側，高音障害型，感音難聴を示しており，聴覚検査では内耳性難聴のパターンを示す[18,21]．難聴の進行を止めることは困難であるが，進行した場合には補聴器や人工内耳を検討する[22]．糖尿病に関しては，定期検査を行い早期から食事療法や血糖コントロールを行い，進行や合併症を予防することが望ましい．

8. 難聴の遺伝カウンセリングのポイント

遺伝学的検査は通常の臨床検査と異なり，患者個人の遺伝情報を取り扱うという点で個人のアイデンティティに深くかかわる倫理的な側面を併せ持った検査である．遺伝子診断の結果を返す場合には遺伝カウンセリングとともに返すことが望ましい．先進医療として承認された‘先天性難聴の遺伝子診断’では遺伝学的検査を行うだけではなく，結果を遺伝カウンセリングとともに返すまでを医療として位置づけている．信州大学病院では‘遺伝子診療部’と連携して難聴の遺伝子診療を行っているが，難聴の遺伝子医療では難聴のメカニズム，予後，治療の専門知識をもつ耳鼻咽喉科医と遺伝や遺伝子のことについて正確な情報提供ができる臨床遺伝専門医との連携が重要である[2,3]．主なポイントを以下に示す．

(1) クライアントが何を求めているかを適切に判断する必要がある．難聴の遺伝子診断の際には，クライアントが難聴の今後の治療に関する情報を求める場合も多く，耳鼻咽喉科専門医とともに臨床遺伝専門医が共同して行うのが望ましい．

(2) 原因遺伝子が特定された場合，耳鼻咽喉科医が中心となりそれぞれの予後や治療法の選択に対し適切な情報や選択肢を与える．

(3) 耳鼻咽喉科医が中心となり難聴は早期診断し，補聴器や人工内耳を用いて早期療育を行えば言語習得が可能であることを説明する．

(4) 原因遺伝子が特定されない場合，臨床遺伝専門医が中心になり，考えられる遺伝形式，それに基づく一般的な再発危険率に基づき説明する．難聴の場合，遺伝性異質性がある(多種類の遺伝子が難聴という同じ表現型をとる)ことに注意して説明する．つまり常染色体劣性遺伝の場合，両親が難聴者であっても原因遺伝子が異なれば子どもが難聴になるとは限らない．また次子を考えている場合，耳鼻咽喉科医は原因は何であれ新生児聴覚スクリーニングによる早期発見，早期療育がポイントであることを説明する．

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An analysis of clinical risk factors of deep neck infection

Jun Hasegawa [a,*], Hiroshi Hidaka [a,b], Masaru Tateda [b], Takayuki Kudo [b], Shun Sagai [b], Makiko Miyazaki [b], Katsunori Katagiri [b], Ayako Nakanome [b], Eiichi Ishida [a], Daiki Ozawa [b], Toshimitsu Kobayashi [b]

[a] *Department of Otorhinolaryngology, Iwaki Kyoritsu General Hospital, Iwaki, Japan*
[b] *Department of Otorhinolaryngology-Head and Neck Surgery, Tohoku University Graduate School of Medicine, Sendai, Japan*

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Abstract

Objectives: To clarify the clinical risk factors that aggravate deep neck infection.
Patients and methods: Sixty-five patients with deep neck infection (abscess or cellulitis), 42 males and 23 females, who were treated at the ear, nose, and throat department in Iwaki Kyoritsu General Hospital in the past 10 years, were retrospectively reviewed. Cases of inflammation of the upper airway including the oral cavity, laryngopharynx, palate tonsil and salivary gland, and cases of lymphadenitis were investigated. These patients were divided into five localized types and one wide range type according to the abscess locations as follows: oral cavity floor type, upper deep cervical type, submandibular type, submental type, retropharyngeal type, and wide range type.
Results: Seventeen of the 65 patients had diabetes, and significantly more diabetics had the wide range type than the localized type ($P < 0.05$, Fisher's test). Diabetes complication was more often seen in the upper deep cervical type among patients aged 61 years or older, and in the wide range type among males aged 41 years or older and elderly women aged 61 years or older. No patients with odontogenic infection or sialolithiasis had associated diabetes mellitus. Two cases developed mediastinitis, and one was caused by retrotonsillar abscess and needed thoracic drainage. More than half of the wide range type cases and more than a quarter of each of the localized type cases except the upper deep cervical type also had laryngeal edema, and eight of them needed emergency tracheotomy. Thirteen of the 40 cases had bacteria belonging to the *Streptococcus milleri* group (SMG), and all were detected in patients who underwent surgical drainage. Four of the 13 cases where SMG was detected showed drug resistance to some sorts of antibiotics.
Conclusion: Oral disorders can develop deep neck infection independently of the presence of diabetes mellitus, compared with other causes. The presence of diabetes mellitus is associated with deep neck infection, aggravating parotitis and wide spread of inflammation. Retrotonsillar abscess often spreads to the retropharyngeal and parapharyngeal spaces, causing mediastinitis, so caution is necessary. Infection due to SMG tends to form abscess independently of diabetes mellitus. Since more than half of the wide range type and more than a quarter of each of the localized types except the upper deep cervical type were associated with laryngeal edema, airway management should be considered.

Keywords: Deep neck infection; Mediastinitis; Retrotonsillar abscess; Laryngeal edema; *Streptococcus milleri* group

1. Introduction

Deep neck infection can occur at any age, and is a serious disorder that often spreads to other organs and sometimes proves fatal [1–9]. The incidence is decreasing, due to the development of antibiotics and better control of laryngopharyngitis, tonsillitis, and upper respiratory inflammation. However, once the inflammation extends to the cervical potential spaces, which are formed by the cervical fascia, the infection spreads rapidly and extensively through these spaces, causing mediastinitis, sepsis, and laryngeal edema. However, no standard protocol has been established for treating or hospitalizing the patients, because of the great variation in the causes and locations of the disease. Therefore, in order to treat such widespread infections, we must have

* Corresponding author at: Department of Otorhinolaryngology, Kyoritsu Soma General Hospital, 142 Tsubogasaku, Niinuma, Soma 976-0011, Japan. Tel.: +81 244 36 5101; fax: +81 244 35 5819.
E-mail address: junha@orl.med.tohoku.ac.jp (J. Hasegawa).

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extensive knowledge of the structures of the deep neck, lymphatic flow, etiology, microbiology, risks of complication, and other factors that aggravate deep neck infection [9].

The present study retrospectively reviewed 65 patients with deep neck infection treated in our department during the past 10 years, and proposes a new categorization system consisting of six groups according to the abscess location. Factors including the causes, ages, risks for mediastinitis and laryngeal edema, complication with diabetes mellitus, and bacterial analyses were analyzed to clarify the important indicators in treating deep neck infection.

2. Patients and methods

Sixty-five patients with deep neck infection (abscess and cellulitis), 42 males and 23 females with mean ages of 51 and 53 years, respectively, were treated at the ear, nose, and throat department in Iwaki Kyoritsu General Hospital from January, 1998 to August, 2007. The clinical records were reviewed retrospectively. Cases of inflammation of the upper airway including the oral cavity, laryngopharynx, palate tonsil and salivary gland, and cases of lymphadenitis were investigated. Cases of abscess limited to the peritonsillar space, isolated salivary gland infection without objective evidence of deep neck space involvement, associated with tuberculosis, or caused by foreign body, injury, or malignancy were excluded.

The cases were categorized according to the location of the abscess, as verified by computed tomography at the initial presentation, into five localized types and the wide range type as follows:

(1) Oral cavity floor type: inflammation has spread to the oral cavity floor and caused acute cellulitis in the sublingual space or just beneath the mucosa. This type includes Ludwig angina, or phlegmon of the floor of the mouth, with inflammation spreading to the submandibular and submental spaces.
(2) Upper deep cervical type: inflammation has spread to the parotid space, and in some cases, also to the masticator and the parapharyngeal spaces.
(3) Submandibular type: inflammation has spread mainly to the submandibular space, and in some cases, also to the parapharyngeal space.
(4) Submental type: inflammation has spread mainly to the submental space.
(5) Retropharyngeal type: inflammation started in the retropharyngeal space, and then spread to the parapaharyngeal space or the danger spaces.

(We did not consider whether these inflammations had spread to the parapharyngeal space or not, because the parapharyngeal space leads to both the submandibular and retropharyngeal spaces, bordering the parotid space [2,10]. Therefore, the parapharyngeal space is often inflamed, influenced by the inflammation of other potential spaces.)

(6) Wide range type was defined as inflammation extending to the deep neck at areas beyond those in (1) to (5) along the upper neck down to the lower neck including necrotizing fasciitis, or inflammation which has spread to two or more locations as specified by types (1) to (5), or in which an abscess is formed inside or outside of the cervical lymph nodes other than (1) to (5).

Bacterial culture tests were performed in 40 cases treated by surgical drainage or puncture. Inflammatory focal region, age, presence of diabetes mellitus, complication with mediastinitis or laryngeal edema, bacterial analysis, and clinical courses were analyzed.

3. Results

3.1. Clinical subgroups

Classification according to the location of inflammation showed that the wide range type was the most common (27 cases, 42%), with the other five localized types accounting for 6% to 17% (Table 1).

In the wide range type, the main sites of inflammation were located in the submandibular space and the front or inside of the sternocleidomastoid muscle, as well as the parapharyngeal space. Inflammation was seen spreading to the parapharyngeal space in 21 patients with the wide range type and 3 with the localized type, of whom two had diabetes mellitus and one was suspected of being immune-compromised.

Forty-five patients underwent urgent surgical drainage (Table 1) and 20 received only intravenous administration of

Table 1
Clinical characteristics of the 65 cases.

Type	Number of cases	Surgical drainage	Mediastinitis	Laryngeal edema	Tracheotomy
1. Oral cavity floor	11	7	0	4	0
2. Upper deep cervical	10	8	0	0	0
3. Submandibular	9	6	0	4	0
4. Submental	4	1	0	1	0
5. Retropharyngeal	4	4	0	1	1
6. Wide range	27	19	2	14	7
Total	65	45	2	24	8

broad-spectrum antibiotic agent. Two patients with wide range type were complicated with mediastinitis, and one of them required thoracic drainage.

Laryngeal edema was present in 52% of the wide range type, in 36% of the oral cavity floor type, 44% of the submandibular type, and 25% each of the submental and retropharyngeal types. Emergency tracheotomy was performed in eight patients, including one with retropharyngeal abscess. Following successful treatment, all patients improved and survived.

Distributions of each type by age, sex, and presence of diabetes mellitus are summarized in Fig. 1. Diabetes mellitus was present in 17 of the 65 patients, and was under poor control in 16 of those 17. Diabetes mellitus was present in 6 of the 38 localized type cases (16%) and 11 of the 27 wide range type cases (41%), showing a statistical difference ($P < 0.05$, Fisher's test). The presence of diabetes mellitus was more common in the upper deep cervical type among patients aged 61 years or older, and in the wide range type among males aged 41 years or older and elderly women aged 61 years or older. Diabetes mellitus was also found in the submental and retropharyngeal types. The retropharyngeal type showed a bimodal distribution consisting of infants and adults with diabetes mellitus [11]. The oral cavity floor and submandibular types tended to occur in males of all ages and particularly elderly females without diabetes mellitus.

Gas gangrene was found in three patients, and all of them were suspected of being immune-compromised.

3.2. Pathogenesis

The pathogenesis of the present cases is shown in Table 2. The oral cavity floor type was caused by odontogenic disease and sialolithiasis. The upper deep cervical and submandibular types were mainly caused by inflammation in the salivary gland. The wide range type was mostly caused by inflammation of the upper respiratory system (i.e., laryngopharyngitis, tonsillitis, retrotonsillar abscess) or lymphadenitis, but the cause was unknown in six cases. Diabetes mellitus was present in patients with laryngopharyngitis, tonsillitis, sialoadenitis, and lymphadenitis, and especially in the wide range type, all six cases had no identifiable causes. No patients with odontogenic infection or sialolithiasis had associated diabetes mellitus (Table 2). Surgical drainage was necessary in slightly more patients with diabetes mellitus than those without. Thirteen (29%) of the 45 patients treated by surgical drainage had diabetes mellitus, compared to 4 (20%) of the 20 patients who did not need drainage.

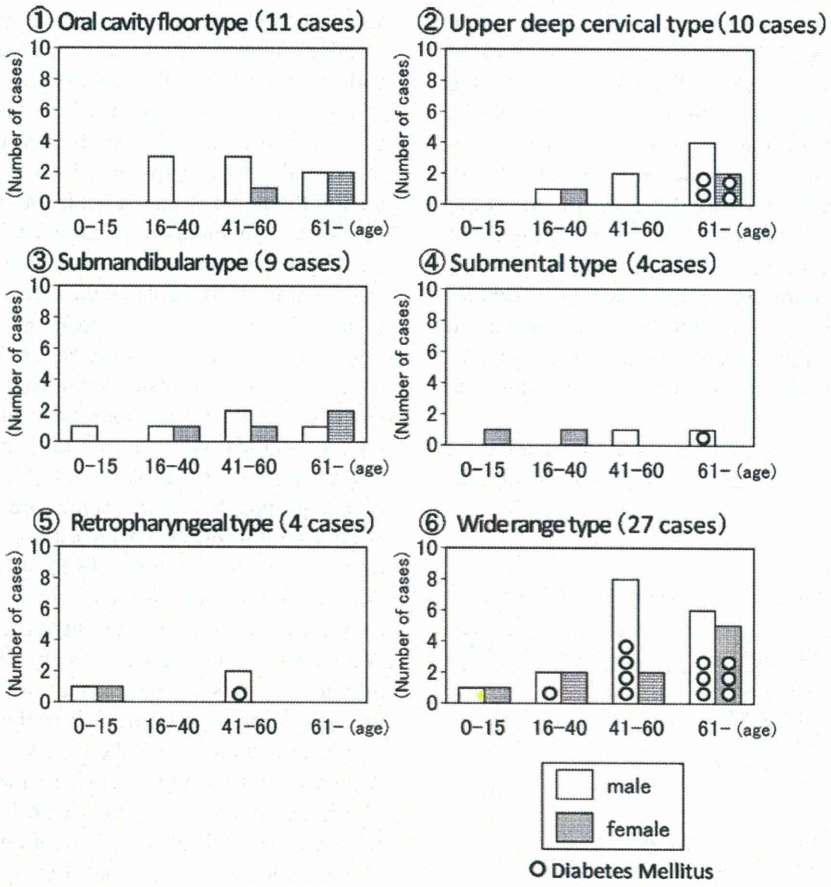

Fig. 1. Distribution of each type by age, sex, and presence of diabetes mellitus.

Table 2
Pathogenesis of the present cases. Numbers in parentheses show the numbers of cases complicated with diabetes mellitus.

Type	Number of cases	Laryngopharyngitis/tonsillitis	Odontogenic	Sialolithiasis	Sialoadenitis	Lymphadenitis	Others/unknown
1. Oral cavity floor	11	0	5	4	0	0	2
2. Upper deep cervical	10	2 (1)	1	0	7 (3)	0	0
3. Submandibular	9	1	2	0	4	0	2
4. Submental	4	1 (1)	0	1	0	0	2
5. Retropharyngeal	4	0	0	0	0	2	2 (1)
6. Wide range	27	17 (4)	0	0	0	4 (1)	6 (6)
Total	65	21 (6)	8 (0)	5 (0)	11 (3)	6 (1)	14 (7)

3.3. Bacterial analysis

Bacterial cultures of samples from the 40 patients who underwent surgical drainage or puncture detected 68 strains, 51 aerobes, 15 anaerobes, and two fungi, such as *Candida*, which could have been contaminants from the skin.

Among aerobes, genus *Streptococcus* was the most common with 30 strains, consisting of 8 *Streptococcus constellatus*, 5 alpha hemolytic *Streptococcus*, 4 *Streptococcus mitis*, 3 *Streptococcus pyogenes* (A), 3 *Streptococcus intermedius*, 3 *Streptococcus salivarius* spp, 2 *Streptococcus anginosus*, 1 *Streptococcus mobilloum*, and 1 *Streptococcus oralis*. Thirteen cases had bacteria belonging to the *Streptococcus milleri* group (SMG), and all of them were detected from the group which underwent surgical drainage. Meanwhile, none of the 5 cases treated with punctures harbored the SMG. The SMG was detected in 6 patients with deep neck infection caused by tonsillitis, including 2 with peritonsillar abscess and 4 with retrotonsillar abscess, 4 with odontogenic infection, and 3 with sialoadenitis (Table 3). Diabetes mellitus was found in only one case of the upper deep cervical type, and the presence of diabetes mellitus was unrelated to the detection of the SMG, which was more common in patients without diabetes mellitus. Four of the 13 cases with SMG infection showed drug resistance to antibiotics such as penicillins, cephems, carbapenems, penems, aminoglycosides, macrolides, and lincosamides.

Anaerobes such as *Prevotella* and *Fusobacterium* were also detected from two of the three cases of gas gangrene.

Table 3
Pathogenesis related to the type and presence of diabetes mellitus in cases with SMG infection.

Type	Pathogenesis	Cases	DM(+)
1. Oral cavity floor	Odontogenic	2	0
2. Upper deep cervical	Sialoadenitis	2	1
3. Submandibular	Odontogenic	2	0
	Sialoadenitis	1	
4. Submental		0	0
5. Retropharyngeal		0	0
6. Wide range	Peritonsillitar abscess	2	0
	Retrotonsillar abscess	4	
Total		13	1

4. Discussion

4.1. Clinical subgroup and pathogenesis

Deep neck infection often starts as cellulitis of the soft tissue in an isolated area adjacent to the source of infection [9]. Since the fascial layers of the neck and the body's natural defense mechanisms help to prevent further spread of infection, there is no typical wide spread progression, but there are various involved areas in this disease [9,12].

Some previous studies have classified deep neck infections into several types [3–5]. For example, deep neck abscess cases were classified according to the abscess locations into the submandibular space, lateral pharyngeal space (parapharyngeal space), retropharyngeal space, and Ludwig's angina groups, by investigating their frequencies and the necessities of tracheotomy [3].

Our proposed classification system is specific in differentiating not only the abscess locations for clarifying the causal relationships but also the complication risk, by adding the upper deep cervical, submental, and wide range types. The inflammation in parapharyngeal space seemed to have been caused by extension of that in localized types. Meanwhile, we thought that the wide range type is a case of a localized type which has spread widely beyond parapharyngeal space or a case of cervical lymphadenitis which has formed an abscess inside or outside the lymph node. By classifying the original sources of infection, we should be able to identify the cause of deep neck infection and the likely subsequent complications. All types occurred across all age groups, but males were more prone to develop deep neck infection (Fig. 1). Deep neck infection is well known to occur more often in males [3,5,9,13], presumably because the infection is more likely to spread to the potential spaces in males, because of the difference in the strength of connective tissue between males and females [13]. In addition, many smokers, alcohol drinkers, and drug addicts are found among deep neck infection patients [9].

Complication with diabetes is well known to exacerbate deep neck infection [3,5,6,14], but the clinical characteristic of aggravation remains unclear. In this study, complication with diabetes mellitus was more often seen in the upper deep cervical and wide range types (Fig. 1). Surgical drainage was performed in 45 cases, and 13 (29%) were complicated with

diabetes mellitus. Many cases complicated with diabetes mellitus had unclear primary regions but extensive inflammation outside the capsule which tended to spread outwards with increasing seriousness.

The present study identified three cases of upper deep neck type caused by sialoadenitis, which does not contradict the previous report that parotid abscess is strongly related to diabetes mellitus [15]. Therefore, we believe that since diabetes mellitus tends to aggravate deep neck infection, especially in the upper deep cervical and wide range types, it is also involved with aggravation of parotitis and wide expansion of inflammation.

Declining neutrophil function resulting in impaired phagocytosis and decreased bactericidal action occurs in the elderly patients requiring hemodialysis, and patients with diabetes [5,6]. Systemic hyperglycemia results in derangement of the immune system including the neutrophil function, cellular immunity, and complement function. Therefore, glycemic control is crucial in the management of diabetic infections [6]. Moreover, diabetic infections might be populated with various bacterial flora, so it is important to obtain culture and sensitivity data for their management [6].

Although the present study found little difference in the incidence rate of diabetes mellitus between patients requiring surgical drainage and those not, this result does not deny the necessity of surgical drainage. Even a patient with diabetes mellitus could probably be cured by intravenous administration of antibiotic alone, before the condition became so bad that surgical drainage was needed. However, once an abscess is formed, inflammation spreads rapidly unless surgical drainage is performed. Therefore, diagnostic imaging or immediate surgical drainage should be considered, especially in patients with diabetes mellitus or poor immune reaction associated with a high-degree of inflammation.

The causes of deep neck infections vary according to the standards or the patients surveyed [3,6], and the prevalence of cases with unknown cause has been reported from 17% to 67% [3,4,7]. The present study suggests that inflammation in some structures carries a high risk of deep neck infection as shown in Table 2. Laryngopharyngitis or tonsillitis was responsible for 21 (32%) of all cases of deep neck abscess (63% of the wide range type), and 2 cases of the upper deep cervical type were also due to the spread of inflammation around the palate tonsil to the masticator and the parotid spaces. These conditions are considered to cause deep neck infection, and if complicated with diabetes mellitus, may become even more aggravated.

Spread of inflammation in the odontogenic region caused five (45%) of 11 cases of the oral cavity floor type, and two (22%) of 9 cases of the submandibular type (Table 2). Inflammation of the second and third mandibular molars is known to drain to the submandibular lymph nodes, but odontogenic infection can also affect the submental lymph nodes [9,12,16,17]. One of our cases of the upper deep cervical type required surgical drainage, because the odontogenic infection had spread and formed an abscess around the mandibular bone, directly extending to the parotid space. Since odontogenic infection may spread to the surrounding structures, causing the danger of mediastinitis [7,18], all odontogenic infections should be treated thoroughly.

In the present study, there was no case that was obviously caused by odontogenic infection or sialolithiasis. This may indicate that oral disorders can develop deep neck infection with or without diabetes mellitus, compared with causes of other causes (Table 2). We think that unsanitary oral cavity conditions and poor immune condition are involved in deep neck infection as previously suggested [9].

Among the deep cervical structures, an understanding of the anatomy of the cervical fascia, which is the fibrous connective tissue that envelopes and divides the structures of the neck and creates potential spaces, is critical for assessing the location of a deep neck infection and predicting the extent of infection, because infections in these spaces can result from direct extensions from other spaces of the head and neck, or from the primary sites [2,8]. The parapharyngeal space is divided into the prestyloid and poststyloid compartments. The prestyloid compartment, the bottom of which is partitioned by the hyoid bone, is connected to the submandibular and sublingual spaces, and also to the retropharyngeal space [7,8,10,19]. The poststyloid compartment is the carotid space and leads to the mediastinum [10,20]. On the other hand, the danger space, which is located behind the retropharyngeal space, extends into the posterior mediastinum, and mediastinitis occurs if inflammation spreads to that area and then downward [2,11,19,21]. Infection is reported to pass through the retropharyngeal space in 70% of cases, the carotid space in 21%, and the pretracheal space in 8% [1]. Thus, there are several routes that infection can take to spread from the neck to the mediastinum. If the infection is likely to spread to these danger regions, complete and total treatment including urgent drainage will be essential.

In one of our two cases with mediastinitis, the cause was unclear and infection had spread into the mediastinum through the pretracheal space. It had a complication of diabetes mellitus. Meanwhile, the other had no complications and was caused by retrotonsillar abscess, and infection had spread through the pretracheal and retropharyngeal spaces, and thoracic drainage was needed. In fact, retrotonsillar abscess occurs close to parapharyngeal and retropharyngeal spaces (Fig. 2A), so it often spreads to these spaces, leading to life-threatening complications [22–24]. In our present study, the cause for deep neck infection was peritonsillar abscess in 7 cases, and retrotonsillar abscess in 8 cases. In addition, while 5 of the 7 peritonsillar abscess cases had complication of trismus, it was only one that had it among the 8 retrotonsillar abscess cases. This may mean that unlike peritonsillar abscess (Fig. 2B), retrotonsillar abscess does not usually cause trismus, presumably because it is anatomically far from the masticator space. However, this condition must not be overlooked as deep

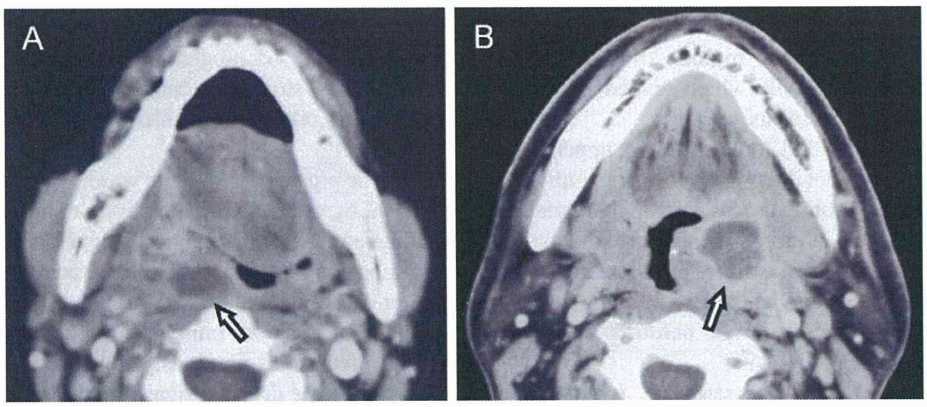

Fig. 2. (A) Representative case of retrotonsillar abscess (arrow) in a 39-year-old female. (B) Representative case of peritonsillar abscess (arrow) in a 34-year-old male.

neck infection may result. Therefore, we consider that both peritonsillar abscess and retrotonsillar abscess carry high risk of developing deep neck infection and sometimes also cause mediastinitis, so we should make an immediate diagnosis and surgical drainage.

The airway must also be examined and treated at the initial visit, because inflammation in the neck can spread to the larynx. In our series, more than a quarter of each localized type, excluding the upper deep cervical type, and more than half of the wide range type were associated with laryngeal edema (Table 1). These types are considered to carry the risk of edema of the larynx, and the complication ratio of laryngeal edema is high in patients with serious deep neck infection. Oral intubation may be difficult in patients with serious deep neck infection, because of trismus, neck swelling, mass effect, or edema of the tongue, pharynx, or larynx, but urgent airway control may become necessary. Therefore, we should not hesitate to perform emergency tracheotomy in order to immediately secure airway management. In addition, patients with neck infection who underwent tracheotomy had shorter stays in the hospital and intensive care unit compared with those who were intubated [25]. This suggests that tracheotomy provided better use of critical care resources with reduced cost.

4.2. Bacterial analysis

Various aerobic and anaerobic bacterial species causing deep neck infection have been detected [3,5,9]. The members of the SMG are normal inhabitants of the mucosal surface of the mouth capsule, and include *S. constellatus*, *S. intermedius*, and *S. anginosus*. In recent years, the SMG has been suspected to be involved in not only oral infection but also in such systematic purulent diseases as empyema, hepatic abscess, and cerebral abscess [26–29]. The SMG was responsible for 33% of the deep neck abscess cases in a previous series [28], emphasizing the importance of these bacteria. SMG infection of the mucosal surface results in production of tissue-destroying enzymes and immunosuppressive substances. As a result, the phagocytic and bacteria-killing abilities of neutrophil cells are suppressed, and the infection spreads rapidly. SMG infection also induces growth of resident anaerobes in the oral cavity, resulting in synergic infection [26–29]. In addition, it is reported that SMG caused cervical necrotizing fasciitis [29]. If the SMG is detected as the causative microorganism of oral infection, measures to prevent worsening of infection and strict control of the whole body as well as the local area are necessary [29].

In the present study, the SMG was identified in 13 (33%) of the 40 cases in which bacteria were detected. Their causes were tonsillitis (peritonsillar and retrotonsillar abscess), odontogenic infection, and sialoadenitis (Table 3), and surgical drainage was needed in all the cases with the SMG. We thought that the presence of the SMG might promote abscess formation, and consequently increase the need for surgical drainage in patients without diabetes mellitus.

Few case reports have described drug resistance to the SMG [30], but we detected some types of bacteria with resistance to beta-lactams, aminoglycosides, and lincosamides. If the SMG has similar drug resistance, we should perform surgical drainage as soon as possible and then carefully observe the subsequent course, since satisfactory improvement cannot be expected with the administration of intravenous antibiotics alone. To prevent the spread and development of inflammation and promote early improvement, identification of the causative bacteria and selection of antibiotics are as important as surgical drainage.

5. Conclusion

The present retrospective study investigated those factors that aggravate deep neck infection. Males were more prone to develop deep neck infection. Oral disorders like odontogenic infection or sialolithiasis can develop to deep neck infection independently of the presence of diabetes mellitus, presumably because of unsanitary oral cavity conditions and immunodeficiency. The presence of diabetes mellitus was

considered to aggravate deep neck infection by exacerbating parotitis and promoting wider spread of inflammation. Infection due to the SMG can form abscess independently of diabetes mellitus. Retrotonsillar abscess easily spreads to the retropharyngeal and parapharyngeal spaces and can cause mediastinitis. Additionally, those deep neck infections that have developed to anatomically dangerous areas required careful treatments including immediate diagnostic imaging and surgical drainage during the clinical course. Since more than half of the wide range type and more than a quarter of each of the localized types except the upper deep cervical type were associated with laryngeal edema, we should take airway management into consideration.

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ARTICLE

Precipitating factors in the pathogenesis of peritonsillar abscess and bacteriological significance of the *Streptococcus milleri* group

H. Hidaka · S. Kuriyama · H. Yano · I. Tsuji · T. Kobayashi

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Abstract Peritonsillar abscess (PTA) is conventionally considered to be a complication of acute tonsillitis, but no pathogenical association has been demonstrated. To investigate the precipitating factors in the pathogenesis of PTA, the clinical status of 117 patients with PTA and 78 patients with peritonsillar cellulitis (PC) were reviewed, comparing them with 188 cases of acute tonsillitis as a control group. The period between the onset of symptoms and the date of starting hospitalized medication was 4 to 5 days in all the three groups, with no significant differences. Higher prevalence of smoking habit was noted in the PTA group (odds ratio, 1.92; 95% confidence interval, 1.17–3.16). Bacteriological culture revealed that 55 of 67 aerobic isolates were *Streptococcus* subspecies, with the *Streptococcus milleri* group (SMG) as the most common (20 isolates). Twenty-three anaerobic species were isolated. Only 51% of the patients with neither the SMG nor anaerobic bacteria were smokers, whereas 90% of the patients with both the SMG and anaerobic bacteria were smokers. We hypothesize that delay or failure to receive medical care do not contribute to the pathogenesis of PTA or PC, and that smoking is positively correlated with the occurrence of PTA, as well as the bacteriological character.

H. Hidaka
Department of Otolaryngology, Iwaki Kyoritsu General Hospital, Iwaki, Fukushima, Japan

H. Hidaka (✉) · T. Kobayashi
Department of Otolaryngology—Head and Neck Surgery, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai 980-8575 Miyagi, Japan
e-mail: ZAY00015@nifty.com

S. Kuriyama · I. Tsuji
Department of Epidemiology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan

H. Yano
Department of Clinical Microbiology with Epidemiological Research & Management and Analysis of Infectious Diseases, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan

Introduction

Peritonsillar abscess (PTA) is the most common type of deep neck infection and is associated with significant morbidity and occasional mortality. Progression of PTA leads to further compromise of the pharynx as well as the larynx, resulting in dysphagia, and interference in the airway. PTA is conventionally considered to be a complication of acute tonsillitis or peritonsillar cellulitis (PC) [1]. However, no studies have demonstrated the association between PTA and tonsillitis empirically [2, 3]. Thus, the purpose of this study was to investigate the precipitating factors in the pathogenesis of PTA, focusing on (1) a delay in the treatment, (2) a history of smoking, and (3) the coexistence of the *Streptococcus milleri* group (SMG) with anaerobes. Specifically, we retrospectively reviewed the clinical features of 117 patients with PTA and 78 patients with PC treated in the last 5 years at our department, and 188 patients with acute tonsillitis, who received inpatient care during the same period, as a control group.

A few reports have examined cigarette smoking in patients with PTA [4–6]. However, these studies were comparisons with the prevalence of smoking in the general population. The present study analyzed the prevalence of smoking in our three patient groups.

Streptococcus intermedius, *Streptococcus constellatus*, and *Streptococcus anginosus* are collectively referred to as the SMG [7]. These common inhabitants of the mouth and

gastrointestinal tract can become aggressive and cause abscess formation in the body [8]. Although the SMG was not well recognized as important previously, the co-existence of the SMG with anaerobes may accelerate inflammation [9, 10]. We reviewed cultures obtained from the patients with PTA, and analyzed the relationships between prevalence of smoking and co-existence of SMG with anaerobes.

Materials and methods

Study population

Our 117 patients with PTA and 78 patients with PC were admitted to Iwaki-Kyoritsu General Hospital between August 2002 and July 2007. Iwaki City has a population of 350,000 people, and is located on the northern Pacific Ocean side of Japan. Our hospital is one of only two hospitals in Iwaki City which provide full-time otolaryngological medical care. The other hospitals have only part time otolaryngeal examination programs or private clinics. Thus, almost all patients who should receive ENT hospitalization care are referred to our department from the local district. Patients were routinely interviewed regarding onset of symptoms, smoking habits, and previous medical care before admission to our department. Patients who admitted to smoking more than one cigarette per day on average over the previous year were included in the smoking group.

Differentiation of PTA from PC is sometimes difficult and a common diagnostic problem [2], so the diagnosis of PTA was based not only on the typical clinical signs (swelling of the involved peritonsillar tissues, with bulging of the tonsillar pillars or soft palate), but was verified by the presence of pus at aspiration or incision. In acute tonsillitis, both tonsils become swollen, bright red, and/or coated in acute tonsillitis. These physical findings are clearly different from those of PC. All patients with PTA or PC admitted to our department received inpatient hospital care including systemic administration of antibiotics and hydration. The control group of 188 patients with acute tonsillitis received inpatient care during the study period. Normally, patients with acute tonsillitis receive outpatient medical care in our department. These control patients had severe inflammatory findings on both sides of the tonsils, and could not take nutrition via the mouth.

This study was approved by the ethics committee of Iwaki Kyoritsu General Hospital, and informed consent was obtained from the subjects.

Bacteriological analysis

Cultures were obtained by needle aspiration of the purulent contents or by incisional drainage. The material collected with a syringe or swabs was immediately sealed and generally transported to the laboratory within 15 hours. For aerobic bacteria, sheep blood, chocolate agar plates were incubated at 37°C in 5% CO_2 for 48 hours. For anaerobic bacteria, the specimen material was placed onto prereduced vitamin K10 enriched brucella blood agar, and incubated in GasPac jars for 48 hours. Plates that showed growth were incubated for at least 7 days. Aerobic bacteria were identified with standard methods, and anaerobic bacteria were identified using the API 20 A (Sysmex bioMérieux Co., Ltd., Tokyo, Japan) including Gram staining.

Statistical analysis

The differences in frequencies between groups were statistically examined by the chi-square test or Fisher's exact test. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated with Statview (SAS Inc., Cary, NC, USA) using unconditional logistic regression models to assess the strength of associations between PTA or PC and potential risk factors.

Results

Age and sex distribution

Figure 1 shows the distribution of each patient group by sex and age. The most common age of the patients with PTA was in the 20s, ranging from 6 to 75 years of age. The mean ages were 36.0±14.4 years for the 87 male patients, and 34.9±14.4 years for the 30 female patients. The most common ages of the patients with PC were in the 20s and 40s. The mean age was 38.5±15.0 years for the 57 male patients, and 40.2±20.5 years for the 21 female patients. The most common age of the control patients was in the 20s, which were similar to the PTA group. However, there were fewer patients older than 40 years compared with the PTA group. The mean age was 29.9±8.9 years for the 128 male patients, and 28.7±10.7 years for the 60 female patients, showing that the control group was younger than the PTA and PC groups. The ratios of male to female (2.9 and 2.7, respectively) were slightly higher in the PTA and PC groups compared to the control group (2.1). However, sex was not positively associated with the risk as shown in Table 1.

Period between onset and medical care

The periods between the onset of pharyngeal pain and starting hospitalized medical care were compared. Almost all patients in the PTA group underwent drainage procedures within 2 days of hospitalization. The only exceptions were three patients who underwent drainage 3 or 4 days

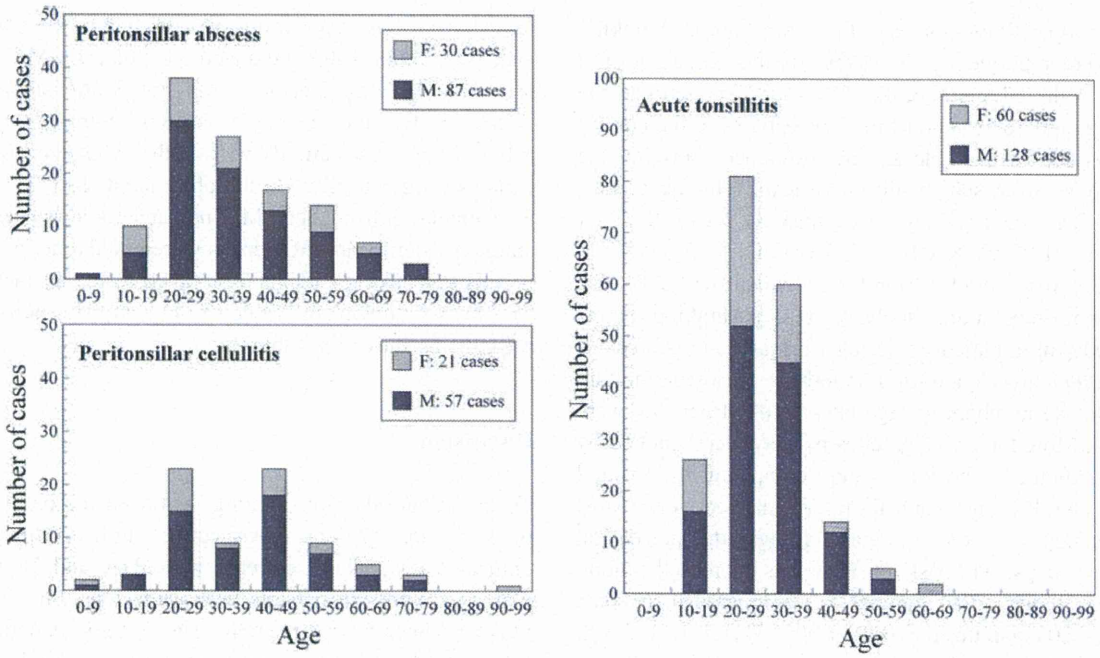

Fig. 1 Age and sex distributions of patients treated for peritonsillar abscess, peritonsillar cellulitis, and acute tonsillitis

after hospitalization. Therefore, the period between onset of pain and hospitalization reflected the period in medical care after the onset of symptoms. The mean period for the PTA, PC, and control groups was 5.4 days, 4.4 days, and 4.5 days, respectively, with no statistical differences (one-way analysis of variance, F=2.09).

To further address the hypothesis that failure to receive medical care might result in PTA, analyses were conducted addressing whether patients had received medical care before being admitted to the department (Table 1). In the PTA group, 71 (61%) of 117 patients had received medical care at another clinic, compared to 126 (67%) of 188 patients in the control group. Surprisingly, more patients had received no medical care in the PC group (51%) than in the PTA and control groups.

Comparison of smoking habits

Clinical records about smoking habits were not available in four males and three females of the PTA group, one male of

Table 1 Odds ratios (ORs) and 95% confidence intervals (CIs) from logistic regression models for the association between types of disease and sex, previous medication and smoking

Risk factor	Parameter	Peritonsillar abscess	Peritonsillar cellulitis	Acute tonsillitis	P for trend
Sex	Female	30 (26%)	21 (27%)	60 (32%)	
	Male	87 (74%)	57 (73%)	128 (68%)	
Male vs. female (reference)	Crude OR (95% CI)	1.36 (0.81–2.28)	1.27(0.71–2.23)	1.00 (referent)	0.22
	Age-adjusted OR (95% CI)	1.33 (0.78–2.25)	1.23 (0.67–2.26)	1.00 (referent)	0.28
Previous medication	Received	71 (61%)	38 (49%)	126 (67%)	
	None	46 (39%)	40 (51%)	62 (33%)	
None vs. received (reference)	Crude OR (95% CI)	1.32 (0.82–2.13)	2.14 (1.25–3.66)	1.00 (referent)	0.17
	Age–sex-adjusted OR (95% CI)	1.25 (0.77–2.05)	2.01 (1.15–3.53)	1.00 (referent)	0.31
Smoking	None	34 (31%)	35 (45%)	86 (46%)	
	Smoker	76 (69%)	42 (55%)	100 (54%)	
Smoker vs. none (reference)	Crude OR (95% CI)	1.92 (1.17–3.16)	1.03 (0.61–1.76)	1.00 (referent)	0.01
	Age–sex-adjusted OR (95% CI)	1.75 (1.02–2.99)	0.90 (0.50–1.61)	1.00 (referent)	0.05

the PC group, and two males of the control group. Smoking habits were reported by 76 (69%) of the remaining 110 patients in the PTA group, 42 (55%) of 77 patients in the PC group, and 100 (54%) of the 186 patients in the control group, as shown in Table 1. The differences between the three groups were statistically significant (chi-square test, $p<0.05$). The crude and age–sex-adjusted ORs for the PTA group were 1.92 (95% CI, 1.17–3.16) and 1.75 (95% CI, 1.02–2.99), respectively. Therefore, a patient with PTA was about two times more likely to report smoking habits compared with a patient suffering from acute tonsillitis.

To further investigate the relationship between smoking and PTA, the numbers of cigarettes smoked per day were analyzed. More than 19 cigarettes per day were smoked by 49% of patients in the PTA group, compared to 31% and 35% in the PC and control groups, respectively. Most female patients smoked less than ten cigarettes per day in all three groups. The risk of PTA was increased among patients smoking ≥20 cigarettes/day compared to patients smoking <20 cigarettes/day (OR, 1.80; 95% CI, 1.11–2.90). With regard to the PC group, the risk of PC was not increased among patients smoking ≥20 cigarettes/day compared to patients smoking <20 cigarettes/day (OR, 0.84; 95% CI, 0.48–1.49). A similar incidence risk was noted for the period of smoking. The incidence risk of PTA was increased among patients smoking for ≥10 years compared to patients smoking for <10 years (OR, 1.86; 95% CI, 1.15–3.01). With regard to the PC group, the incidence risk was not increased among patients smoking for ≥10 years compared to patients smoking for <10 years (OR, 1.01; 95% CI, 0.58–1.75).

Bacteriological analysis

Bacteriological culture tests were performed in 65 of 117 PTA cases. Only aerobic or facultative bacteria were recovered in 38 specimens, only anaerobic bacteria in three, and mixed aerobic and anaerobic bacteria in 17. Cultures showed no growth in seven cases. A total of 90 bacterial isolates and two *Candida* subspecies (spp.) isolates were recovered (1.4 isolates per specimen), as shown in Table 2.

A total of 23 anaerobic species were identified, including *Prevotella* spp. (9 isolates) and *Peptostreptococcus* spp. (8 isolates). A total of 67 aerobic and facultative species were detected, including *Streptococcus* spp. in 55 isolates. SMG were the most common type of *Streptococcus* spp. (20 isolates), consisting of 13 isolates of *S. constellatus* and 7 isolates of *S. intermedius*. None of the 20 cases with positive SMG infection had two or more isolates of the SMG.

Half of the 20 cases with SMG infection also had anaerobic bacteria infection. We thus divided the 65 cases into four groups according to the isolates of the SMG and anaerobes: both SMG and anaerobic isolates, SMG but not anaerobic isolates, anaerobic but not SMG isolates, and neither SMG nor anaerobic isolates. Surprisingly, nine (90%) of the ten patients with both SMG and anaerobic isolates were smokers. On the other hand, 18 (51%) of the 35 patients with neither SMG nor anaerobic isolates were smokers. Significant differences were noted among the four groups in smoking patients (two-tailed Fisher's exact test, $p<0.05$), as shown in Table 3, but not in non-smoker patients, as shown in Table 3.

Discussion

To investigate the precipitating factors in the pathogenesis of PTA, the present retrospective study compared the clinical status of 117 patients with PTA and 78 patients with PC, with 188 patients with acute tonsillitis receiving inpatient hospital medication. The control patients were limited to those suffering from severe tonsillitis. If patients with acute tonsillitis who received outpatient care had been included in the control group, greater differences from the PTA and PC groups might be expected. The only factor that might be overestimated is the delay or failure of previous medicine, whereas our preliminary analysis did not find any significant differences in this period. Therefore, our control group probably did not lead to overestimation of differences in the clinical status of the PTA or PC group from the acute tonsillitis control group.

The symptomatology of sore throat has been reported to begin only 3 to 5 days from the onset of PTA [1, 6]. If PTA develops secondary to acute tonsillitis, delay or failure to receive medical care will lead to the development of PTA. However, the PTA, PC, and acute tonsillitis control groups showed no significant differences in the period between the onset of pharyngeal pain and the date of starting hospitalized medical care. Also, the prevalence of previous medication in the PTA group was almost the same as in the control group. These findings suggest that delay in starting to receive medical care or failure to receive medication do not contribute to the development of PTA. Interestingly, the PC group showed higher prevalence of no previous medication, presumably because the attending physicians, who were mostly expecting ENT problems, recognized the risks of PC and immediately referred the patients to our department without starting treatment.

Cigarette smoking is related to a wide variety of still poorly known toxic mechanisms leading to oxidative injury. A clinicopathological study of the palatine tonsil found that smoking induces problems with adequate immune response, increasing incidence of pharyngotonsillar infections [11]. Since the link between smoking and

Table 2 Culture results of peritonsillar abscess (PTA) patients

Anaerobic isolates	Number of isolates	Aerobic and facultative isolates	Number of isolates
Prevottela spp.	9	*Sterptococcus milleri* group	20
Peptostreptococcus spp.	8	*Streptococcus pyogenes*	9
Fusobactrrium spp.	3	*Streptococcus mitis*	9
Bacteroideus spp.	1	Other *Streptococcus* spp.	17
Other species	2	Other species	12
Total	23		67

quinsy was first suggested [4], only a few of studies have investigated the relationship of smoking with PTA. These studies found that the prevalence of smoking was higher than that of the general population [5, 6]. Our study was stronger than previous studies examining the association between smoking and risk of PTA because the prevalence of smoking habit was compared not only with the general population, but also with patients with acute tonsillitis; and the number of cigarettes per day and period of smoking were also analyzed.

The smoking rates in the Japanese general male and female populations are 39.9% and 10%, respectively, derived from the survey by the Ministry of Health, Labour and Welfare of Japan [12]. The prevalence of smoking in the male patients in the PTA, PC, and control groups were 83% (69/83), 66% (37/56), and 61% (77/126), respectively. In all three groups, ratios of smokers among male patients were higher than in the general male population. The prevalence of smoking in the female patients in the PTA, PC, and control groups were 26% (7/27), 24% (5/21), and 38% (23/60), respectively. In all three groups, ratios of smokers among female patients were also higher than in the general female population [12].

We found significant prevalence of smoking habits in patients with PTA (69%) compared with those with acute tonsillitis (54%) (Table 1), higher than previously reported [5]. This previous study defined patients in the PTA group as those who received abscess tonsillectomy, which might include patients with PC, whereas we defined the PTA group by the presence of pus detected by aspiration or incision. Combining the PTA and PC groups gave a prevalence of smoking of 63%, similar to the previous report [5]. The PTA group also had a significantly higher prevalence of smoking ≥20 cigarettes/day, and significantly longer smoking history, which are consistent with previous findings that a longer history along with greater daily number of cigarettes smoked are clearly correlated with both recurrent infections and histological changes [11, 13].

Table 3 Association between the existence of anaerobic and *Streptococcus milleri* group (SMG)

Category	Anaerobic (+)	Anaerobic (-)
Smokers[a]		
SMG (+)	9	7
SMG (-)	5	18
Non-smokers[b]		
SMG (+)	1	3
SMG (-)	5	17

[a] Fisher's exact test: $P<0.05$

[b] Fisher's exact test: $P>0.999$

Our bacteriological survey of 65 PTA cases isolated 23 anaerobic microorganisms. Only four isolates contained only anaerobic bacteria, and the others yielded mixed aerobic and anaerobic species. These results are consistent with previous reports showing the polymicrobial nature and importance of anaerobic bacteria in PTA [14, 15]. Meticulous anaerobic culture technique showed that anaerobes were present in all PTA cases, with only anaerobes in 19%, and aspiration methods rather than swabs were recommended [14]. In our study, aspiration failed to collect pus in some patients, so specimens were collected by swabs followed by incisional drainage. These factors might be responsible for the relatively low rates of isolation of anaerobes (31%) and positive cultures (1.4 isolates per specimen). Despite these issues, our bacteriological analyses revealed some interesting findings. The SMG was the most frequent isolate (31% of cases), which is recently recognized as an important cause of pyogenic infection and head and neck abscess [8, 16, 17]. Fifteen of the 20 patients with positive SMG were males, consistent with previous reports showing a higher incidence of infections among males [8, 18].

The detailed pathogenesis of the SMG remains unclear, but mucous infection by normal flora is thought to occur due to an imbalance between the organisms and host immunodefense in the deep neck abscess, including our previous report [9, 17]. Our bacteriological analyses showed that patients with mixed infection of anaerobes and the SMG had significantly higher smoking prevalence (90%) than the other patients. Moreover, patients with positive SMG and negative anaerobic isolation revealed higher smoking prevalence (70%) than those with negative SMG and positive anaerobic isolation (55.6%). These findings indicate that cigarette smoking is correlated with infection of pathogens which accelerate abscess formation.

Other than smoking, a few variables are associated with PTA. One aspect of pathogenesis may involve Weber's gland in the supratonsillar space, which acts to clean debris on the tonsillar crypts, and could easily develop infections leading to cellulitis or abscess into the supratonsillar space [1]. Another aspect of pathogenesis is based on the similar bacteriological and epidemiological association between periodontitis and PTA [19, 20].Approximately 20% of 84 patients with PTA were reported to have significant dental caries and allergies [19]. Since our study did not examine the role of periodontitis as an independent variable, further studies are necessary to explore whether treatment of periodontal disease could also have a prophylactic effect against PTA. Moreover, self report of smoking may be unreliable, and objective test for smoking may have resulted in a different smoking rate. More study including the measurement of blood cotinine levels would be helpful to overcome these limitations in accurately assessing smoking habit.

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Conflicts of interest We declare that we have no conflict of interest.

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OTOLOGY

Effects of neck muscle vibration on subjective visual vertical: comparative analysis with effects on nystagmus

Tetsuaki Kawase · Atsuko Maki · Yusuke Takata · Hiromitsu Miyazaki · Toshimitsu Kobayashi

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Abstract In patients with unilateral vestibular dysfunction, vibratory stimulation to the neck muscles not only induces shift of the subjective visual vertical (SVV), but also enhances the generation of nystagmus. In the present study, the effects of neck vibration on the SVV were compared with those on nystagmus in patients with unilateral vestibular schwannoma (14 patients; 6 males and 8 females, mean age 54.2 years). The results indicated that the presence of nystagmus and magnitude of the SVV were generally correlated, neck vibration significantly increased the abnormal shift of the SVV and the presence of nystagmus, and the effects of vibration to the ipsilateral dorsal neck were significantly larger than those to the contralateral dorsal neck on the SVV, whereas no significant difference was observed in slow phase velocity of nystagmus. The present study suggests that both SVV and nystagmus induced by vibration have many similar clinical features and may be important in assessing the unilateral vestibular dysfunction.

T. Kawase (✉)
Laboratory of Rehabilitative Auditory Science,
Tohoku University Graduate School of Biomedical Engineering,
1-1 Seiryo-machi, Aoba-ku, Sendai 980-8574, Japan
e-mail: kawase@orl.tohoku.ac.jp

T. Kawase
Department of Audiology, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku,
Sendai 980-8574, Japan

T. Kawase · A. Maki · Y. Takata · H. Miyazaki · T. Kobayashi
Department of Otolaryngology, Head and Neck Surgery,
Tohoku University Graduate School of Medicine,
1-1 Seiryo-machi, Aoba-ku, Sendai 980-8574, Japan

Keywords Subjective visual vertical · Neck muscles vibration · Nystagmus

Introduction

Human subjects can align the subjective visual vertical (SVV) to within 2–3° of the gravitational vertical [1–4]. This subjective directional sensation is believed to be significantly related to the vestibular otolith function, and is shifted to the ipsilateral side to the lesion in patients with unilateral vestibular dysfunction [1–7]. This pathological shift of the SVV is largest during the acute phase of vestibular dysfunction and is reduced by the vestibular compensation process [6, 7]. Detection of such pathological shift of SVV may be based on vibration of the neck or mastoid area, which is known to increase the pathological SVV shift, and is useful to detect unilateral vestibular deficit [4]. On the other hand, neck vibration also induces nystagmus in patients with unilateral vestibular dysfunction, of which the slow phase is directed to the lesion side [8–11]. However, the relationship between the vibration-induced SVV shift and vibration-induced nystagmus is not fully clarified.

The present study compared the effects of neck vibration on the SVV with those on nystagmus in patients with unilateral vestibular schwannoma, examined on the same day.

Materials and methods

This study included 14 patients with vestibular schwannoma, 6 males and 8 females aged 31–73 years (mean 54.2 years), who underwent assessment of the effects of