Yellow Nail Syndrome With Dramatic Improvement of Nail Manifestations After Endoscopic Sinus Surgery

Yu Hosokawa[1], Akihito Kuboki[1,2], Aya Mori[1], Hiroaki Kanaya[1], Tsuguhisa Nakayama[1,2] and Shinichi Haruna[1]

[1]Department of Otorhinolaryngology-Head and Neck Surgery, Dokkyo Medical University, Tochigi, Japan. [2]Department of Otorhinolaryngology, The Jikei University School of Medicine, Tokyo, Japan.

Clinical Medicine Insights:
Ear, Nose and Throat
Volume 10: 1–4

DOI: 10.1177/1179550617718184
SAGE

ABSTRACT

OBJECTIVES: Yellow nail syndrome (YNS) is a rare disease of unknown cause characterized by the triad of yellow nails, respiratory manifestations, and lymphedema. Although several therapies for YNS have been reported, there is no common consensus in the treatment. In this case report, we present a case of 56-year-old woman with YNS, whose nail manifestation was dramatically improved after endoscopic sinus surgery for the treatment of chronic rhinosinusitis.

METHODS: Endoscopic sinus surgery involving middle meatal antrostomy was performed for the case of YNS with chronic rhinosinusitis and bronchiectasis resistant to antibacterial drugs.

RESULTS: A month after the surgery, the patient's nails eventually showed dramatic improvement.

CONCLUSIONS: Otorhinolaryngologists should recognize that chronic rhinosinusitis can be a symptom of YNS, and that the aggressive treatment including surgical approach for chronic rhinosinusitis may be a useful in the control of nail manifestation in YNS.

KEYWORDS: Yellow nail syndrome, chronic rhinosinusitis, endoscopic sinus surgery

RECEIVED: March 14, 2017. **ACCEPTED:** June 1, 2017.

PEER REVIEW: Seven peer reviewers contributed to the peer review report. Reviewers' reports totaled 415 words, excluding any confidential comments to the academic editor.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

PREVIOUS PRESENTATION: This case report was presented at The 52nd Annual Meeting of the Japanese Rhinologic Society in Fukui, Japan on September 28, 2013.

CORRESPONDING AUTHOR: Akihito Kuboki, Department of Otorhinolaryngology, The Jikei University School of Medicine, 3-25-8 Nishi-Shimbashi, Minato-Ku, Tokyo 105-8461, Japan. Email: kuboxile@jikei.ac.jp

Introduction

Yellow nail syndrome (YNS) is a rare disease of unknown cause characterized by the triad of yellow nails, lymphedema, and respiratory manifestations. It is primarily diagnosed clinically, and when 2 of the 3 cardinal signs are present, it is treated as incomplete YNS in general.[1] Associated respiratory manifestations include pleural effusion and chronic respiratory tract infections such as chronic rhinosinusitis (CRS) and bronchiectasis[2]; however, the mechanism of interplay between respiratory tract infections and nail lesions remains to be clarified. In addition, few reports have been published regarding YNS with CRS compared with reports on other respiratory diseases, indicating a low level of recognition of YNS among otorhinolaryngologists.

As yet, no treatment for the overall syndrome has been established. Although treatments such as oral vitamin E, antifungals, and steroids such as topical triamcinolone acetonide are effective for the nail manifestations of YNS,[3] the effects of these symptomatic therapies on concomitant diseases are inconsistent. Conversely, treatment of concomitant respiratory manifestations such as bronchiectasis reportedly results in improvement of yellow nails.[2] Although the relationships between these manifestations and yellow nails, as well as the detailed mechanism of the pathological condition, are unclear, these findings suggest that the respiratory manifestations may act as focal infections exerting some kind of adverse effect on the nails.

Herein, the case of a patient with YNS and sinobronchial syndrome (SBS), which is a respiratory manifestation involving bronchiectasis and CRS, is reported. Endoscopic sinus surgery (ESS) as a radical treatment for CRS resulted in dramatic postoperative improvement in nail manifestations and satisfactory medium-term progress.

Case Report

A 56-year-old woman had experienced yellowing and thickening of the nails with concomitant bronchitis for several years. Based on her clinical symptoms, she was referred from another clinic to the Department of Dermatology at our institution for further testing and treatment of suspected YNS. Left maxillary sinusitis had been observed on computed tomography (CT) performed at another clinic, and her medical history included CRS that had occurred approximately 10 years previously. The CRS was suspected to be a respiratory manifestation associated with YNS, and she underwent consultation for treatment at our department. Her medical history included nothing else of note. Hematology testing at our

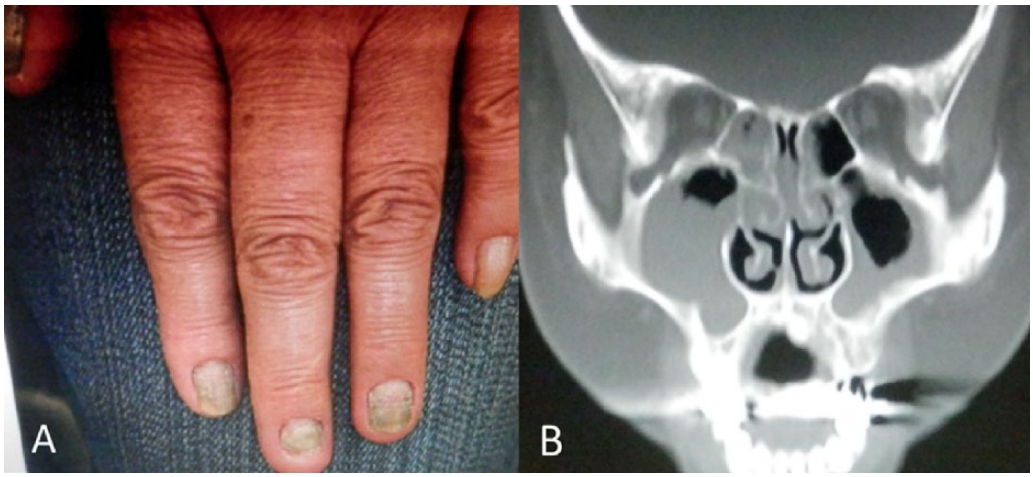

Figure 1. Preoperative fingernails and sinus computed tomographic scans are observed on both hands. (A) Yellowing and thickening of the fingernails are observed on both hands. (B) Homogenous soft tissue densities are seen around the maxillary and ethmoid sinuses on both sides. No clear bone loss or destruction is observed.

institution showed immunoglobulin E levels of 127 IU/mL and an eosinophil count of 7.6% (463/mm^3); otherwise, the test findings were normal. Radioallergosorbent test results were as follows: cedar: 3.59 UA/mL, Japanese cypress: 0.47 UA/mL, orchard grass: 5.01 UA/mL, and dog dander: 6.38 UA/mL. Physical findings comprised yellowing and thickening of the fingernails on both hands (Figure 1A). Crackles were heard bilaterally on auscultation of the chest, and frequent coughing was observed. Lower limb lymphedema was not present. Sinus CT showed soft tissue densities around maxillary and ethmoid sinuses on both sides, confirming CRS (Figure 1B). Bronchitis was suspected on the basis of chest radiograph findings at initial examination; however, subsequent chest CT and sputum examinations in the Department of Pulmonary Medicine confirmed bronchiectasis associated with YNS.

The yellow nails were treated with topical betamethasone valerate and gentamicin sulfate ointment by the Department of Dermatology; however, no clear improvement was observed. Low-dose oral macrolide antibiotics (clarithromycin, 200 mg/d) were administered for the respiratory manifestations, but respiratory symptoms such as cough and spitting were not improved and sinus CT showed little improvement in CRS after 4 months, and treatment was temporarily discontinued. After treatment discontinuation, her cough worsened, and treatment was resumed 1 month later; however, no improvements in CRS were observed, and radical treatment with ESS including middle meatal antrostomy and nasal polyps excision was performed in our department.

Intraoperative intranasal findings revealed nasal polyps in the right middle meatus and left maxillary sinus. These intranasal findings are consistent with typical bacterial CRS. *Pseudomonas aeruginosa* (1+) was detected on bacterial culture of fluid from the left maxillary sinus. Pathological findings comprised mild inflammatory cell infiltration, edema, and localized eosinophil infiltration in the right middle meatus and left maxillary sinus polyps, which were lined with ciliated columnar epithelium. No findings indicating malignancy were observed (Figure 2). Dramatic improvement in nail manifestations was observed from 1 month postoperatively (Figure 3), and the pulmonary symptoms, such as cough and sputum frequency, also decreased. A sinus CT scan taken at 90 days postoperatively is shown in Figure 4. As of 5 years 11 months after surgery, no exacerbation of symptoms or local recurrence has occurred, and her progress has been satisfactory.

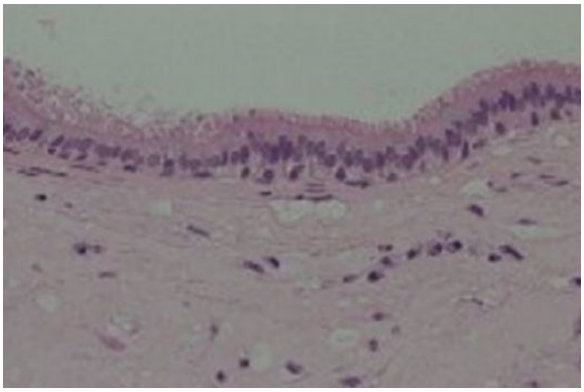

Figure 2. Histopathologic findings in the nasal polyps (hematoxylin-eosin, original magnification ×200). No abnormalities are observed in the mucosal epithelium of the resected sinus mucosa, and there is very mild inflammatory cell infiltration.

Discussion

Yellow nail syndrome was first described in 1964 by Samann and White as a disease that involves delayed nail growth resulting in nail thickening, sclerosis,[4] and discoloration. Subsequently, the 2 other associated symptoms of lymphedema and chronic respiratory tract infection became known, and currently, patients presenting with 2 of these 3 cardinal signs are diagnosed with clinically incomplete YNS.[1] Yellow nail syndrome tends to occur more commonly in middle age with no sex predisposition.[5] According to a previous report, CRS is

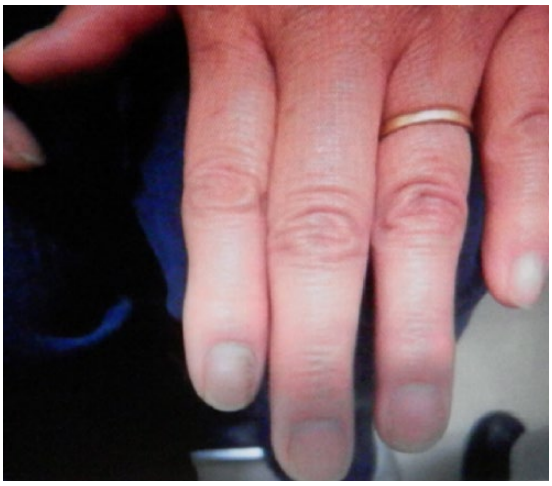

Figure 3. Nail findings observed 8 months after endoscopic sinus surgery. Nail yellowing and thickening are dramatically improved compared with the findings before surgery.

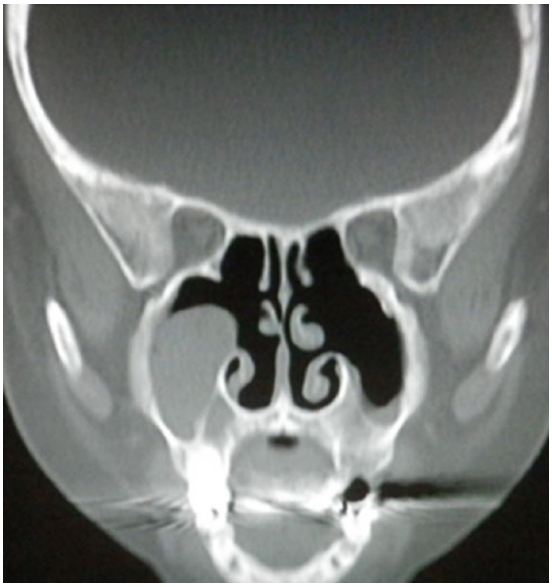

Figure 4. Sinus computed tomographic scan 90 days after surgery. A mucosal retention cyst is observed in the right maxillary sinus; however, no clear residual or exacerbated chronic rhinosinusitis is present.

found in approximately 40% of YNS cases.[6] Although the timing of onset of each symptom varies among patients, with new symptoms appearing every few years in some cases,[1] lung disease usually appears before the manifestation of yellow nails.[5] In terms of respiratory manifestations, the present patient presented with bronchiectasis with CRS, also known as SBS. Endoscopic sinus surgery as radical treatment for CRS resulted in not only improvement of respiratory symptoms such as CRS and sputum but also dramatic improvement in nail manifestations, which had been present since several years. The present findings suggest that CRS, which has long been known in the field of otorhinolaryngology as a focal infection, is in some manner pathologically related to the nail changes in YNS.

Many aspects of the components of each sign and the disease state in YNS remain to be clarified. Previous studies have explained the various manifestations including lymphedema, pleural effusion, and nail deformation as resulting from lymphatic obstruction due to the presence of some kind of functional and structural abnormality of the lymphatic vessels.[7] However, the study by Maldonado et al[6] reported the reversibility of the nail manifestation as an interesting feature of YNS, and they indicated that the improvement of the yellow nails seems to be associated with better control of recurrent sinopulmonary infections including bronchiectasis and chronic sinusitis. These results imply that not only the lymphatic abnormality is likely due to functional, not structural, disability, but also the chronic airway inflammations may exaggerate the lymphatic abnormality inducing the nail manifestation. Although there are a little research showing the effect of ESS on bronchiectasis in patients with CRS and bronchiectasis, namely, SBS, previous report has shown that functional ESS as a treatment of CRS was significantly effective in the control of the bronchiectasis condition in the patients with SBS compared with medication therapy. Based on this knowledge, we speculate that ESS for treatment of CRS may have fully resolved the chronic inflammation associated with bronchiectasis as well as CRS as a respiratory manifestation and improved lymphatic circulation, which contribute to the normalization of the nail manifestation. However, lymphedema and abnormality of the lymphatic vessels in the sinus mucosa were not observed in the present patient. Thus, the exact mechanism by which chronic airway inflammation causes lymphatic obstruction and how this specifically affects the distally located nails remain unclear.

In recent years, YNS has been shown to be associated with a diverse range of diseases other than chronic respiratory tract infection and lymphedema, including malignant tumors such as lung cancer, laryngeal cancer, and non-Hodgkin lymphoma, as well as autoimmune diseases such as chronic rheumatoid arthritis and Hashimoto disease; the state of these diseases may affect the prognosis of yellow nails.[3,8,9] Iqbal et al[8] reported recovery of yellow nails following healing of lung cancer associated with YNS, whereas dramatic improvement in yellow nails was also observed after laryngectomy for laryngeal cancer.[9] These findings suggest not only that multiple conditions acting as focal infections may be involved in YNS but also that yellow nails could also indicate the state of concomitant diseases.[10] However, most of these studies are case reports, and no research to date has demonstrated a direct causal relationship with the disease state; thus, further research is required to clarify the disease state.

Although various treatment methods have been reported, no established treatment approach exists. Previous studies have reported the effectiveness of treatment with oral vitamin E and itraconazole (antifungal medication) and with topical triamcinolone acetonide[3,5,11]; however, treatment results are not necessarily satisfactory. Dramatic improvement in nail symptoms in the present patient was achieved with radical treatment for

CRS without administering the drug therapy mentioned above. The present findings indicate that controlling the disease state and providing aggressive treatment, including surgery for respiratory manifestations and other associated diseases, may be important in the treatment of YNS, and that previously reported drug therapies are not necessarily essential. Further investigation is required regarding optimal treatment policies in cases where yellow nails do not improve despite good control of concomitant diseases or when treatment of concomitant diseases is challenging.

Conclusions

Although YNS is an extremely rare disease, otorhinolaryngologists should be aware of its existence. For treatment of YNS with bronchiectasis and CRS, the aggressive treatment of CRS with ESS may be effective approach.

Author Contributions

AK conceived and designed the experiments and made critical revisions and approved final version. AK and YH analyzed the data, wrote the first draft of the manuscript, and contributed to the writing of the manuscript. AK, YH, AM, HK, TN, and SH agree with the manuscript results and conclusions. HK jointly developed the structure and arguments for the paper. All authors reviewed and approved the final manuscript.

Disclosures and Ethics

As a requirement of publication, author(s) have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following: authorship and contributorship, conflicts of interest, privacy and confidentiality, and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. Any disclosures are made in this section. The external blind peer reviewers report no conflicts of interest.

REFERENCES

1. Hiller E, Rosenow EC 3rd, Olsen AM. Pulmonary manifestations of the yellow nail syndrome. *Chest*. 1972;61:452–458.
2. Woodfield G, Nisbet M, Jacob J, et al. Bronchiectasis in yellow nail syndrome. *Respirology*. 2017;22:101–107.
3. Imadojemu S, Rubin A. Dramatic improvement of yellow nail syndrome with a combination of intralesional triamcinolone, fluconazole, and sinusitis management. *Int J Dermatol*. 2015;54:497–499.
4. Samman PD, White WF. The yellow nail syndrome. *Br J Dermatol*. 1964;76:153–157.
5. Piraccini BM, Urciuoli B, Starace M, Tosti A, Balestri R. Yellow nail syndrome: clinical experience in a series of 21 patients. *J Dtsch Dermatol Ges*. 2014;12:131–137.
6. Maldonado F, Tazelaar HD, Wang CW, Ryu JH. Yellow nail syndrome: analysis of 41 consecutive patients. *Chest*. 2008;134:375–381.
7. DeCoste SD, Imber MJ, Baden HP. Yellow nail syndrome. *J Am Acad Dermatol*. 1990;22:608–611.
8. Iqbal M, Rossoff LJ, Marzouk KA, Steinberg HN. Yellow nail syndrome: resolution of yellow nails after successful treatment of breast cancer. *Chest*. 2000;117(5):1516–1518.
9. Guin JD, Elleman JH. Yellow nail syndrome. Possible association with malignancy. *Arch Dermatol*. 1979;115:734–735.
10. Hayashi I, Abe R, Yanagi T, Abe Y, Shimizu H. Yellow nail syndrome: nail change reflects disease severity. *J Dermatol*. 2012;39:415–416.
11. Tosti A, Piraccini BM, Iorizzo M. Systemic itraconazole in the yellow nail syndrome. *Br J Dermatol*. 2002;146:1064–1067.