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CASE REPORT

Gut microbiota modulation and gold nanoparticle-mediated photothermal therapy for treatment of recalcitrant acne

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Abstract

Recent studies highlight that gut dysbiosis, an imbalanced state of intestinal microbiota, exacerbates skin inflammation. Here, we showed the presence of gut microbiota alterations in two patients with recalcitrant acne and investigated the impact of its therapeutic modulation together with gold nanoshell-mediated photothermal therapy (gold PTT).

KEYWORDS

acne, antibiotics, gold nanoshell, gold PTT, gut dysbiosis, gut microbiota alteration

1 | INTRODUCTION

Recent studies highlight that gut dysbiosis, an imbalanced state of intestinal microbiota, exacerbates skin inflammation.[1,2] Here, we showed the presence of gut microbiota alterations in two patients with recalcitrant acne and investigated the impact of its therapeutic modulation together with gold nanoshell-mediated photothermal therapy (gold PTT).

2 | CASE PRESENTATION

2.1 | Case 1

A 30-year-old Korean male patient was suffered from adult acne that had worsened over the years. Oral isotretinoin was not tolerable due to his dry skin. Therefore, minocycline and doxycycline were used alternately for the acne treatment. Despite additional therapies involving fractional and needle-radiofrequency lasers, inflammatory papules recurred too often and caused pain. Gut microbiota alteration was evaluated by microbial organic acid test (MOAT) identifying yeast and fungal, Clostridia bacterial, and other bacteria markers: Urine samples were sent to the Great Plains Laboratory, Inc. (Lenexa, KS, United States) for analysis.[3] The result of his MAOT indicated an abnormal overgrowth of candida and harmful bacteria of the intestinal tract with an elevation of arabinose and hippuric acid of urine. We discontinued oral antibiotics and performed gold PTT as an alternative. Each treatment of gold PTT included facial washing and then applying an ample of gold nanoparticle suspension (inno.N Co. Ltd,) into the facial skin by sonophoresis after obtaining informed consent.[4] A 40 khz low-frequency ultrasound (BellaSonic, Umbrella Inc.,) was used to transdermally deliver gold nanoparticles into sebaceous glands and follicles. The residual nanoparticle suspension of superficial skin was wiped off to prevent unexpected thermal injury to the epidermis. After that, laser purses from long-pulsed 1064 nm Nd:YAG laser (Cosjet SR, Won Technology,) was applied to the patient's facial skin for photobiomodulation (pulse duration 0.3 ms; fluence 10 J/cm^2; 1500 laser shots) and photothermolysis (pulse duration 10/20/30 ms;

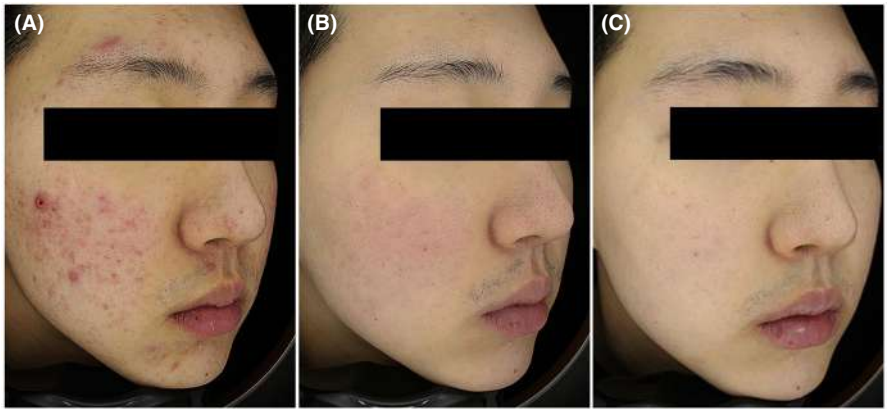

FIGURE 1 Clinical improvement of acne lesions in patient #1 after gold nanoshell-mediated photothermal therapy (gold PTT) with gut microbiota modulation: (A) before treatment, (B) after nine sessions of gold PTT, and (C) 12 months after the last procedure

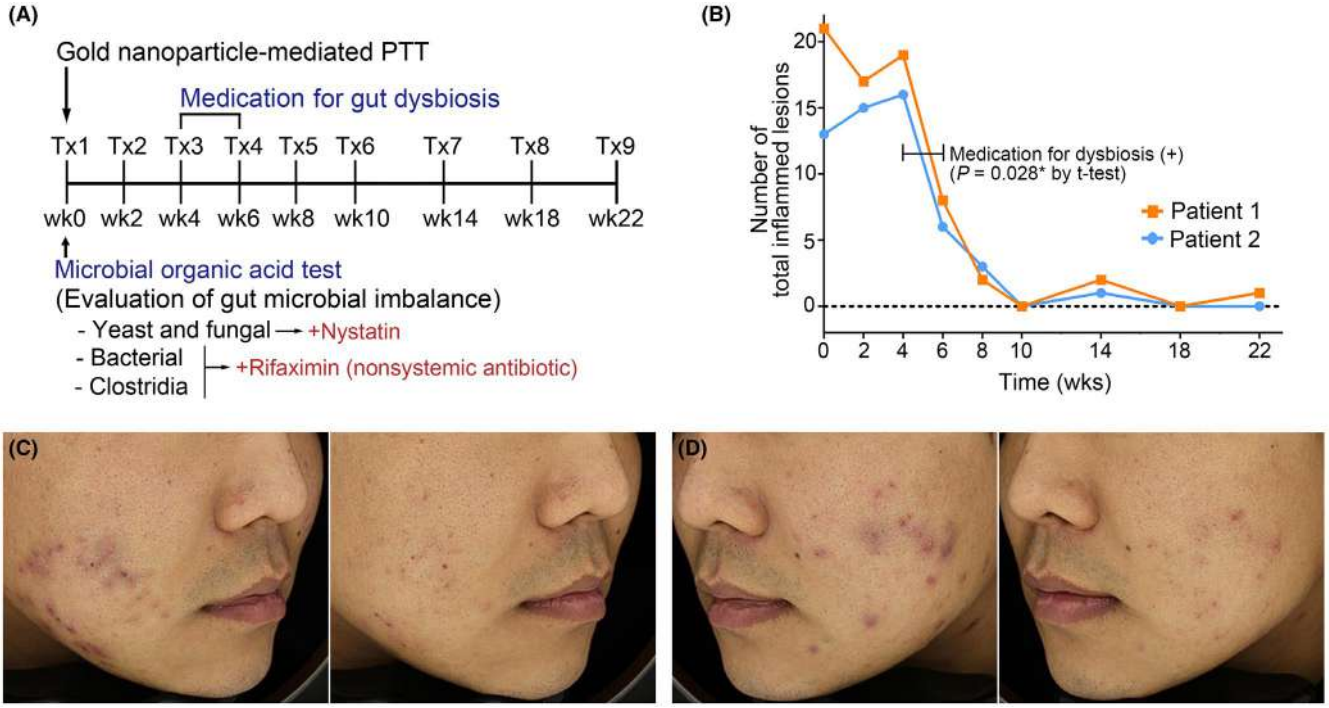

FIGURE 2 (A) Schematic diagram showing the timing of gold nanoshell-mediated photothermal therapy (gold PTT) and gut microbiota modulation. (B) Graph showing changes of the number of facial inflamed lesions in the two patients with recalcitrant acne. (C, D) Clinical photographs of patient # 2 before (left) and after six sessions of gold PTT (right)

fluence 12 J/cm^2; 500 shots, respectively, for each pulse duration) with an interval of 2–4 weeks. In addition, the patient received nystatin (1.5 million units/day) and rifaximin (1200 mg/day) for 2 weeks to restore yeast and bacterial dysbiosis.[5] The MAOT result returned to normal and clinical improvement was well maintained at 1-year follow-up after the last procedure (Figure 1).

2.2 | Case 2

A 38-year-old Korean male patient presented with recurrent acne of the cheek that lasted for 15 years. He had been taking doxycycline repeatedly for a period whenever his acne got worse. The MAOT result revealed Clostridia bacterial and other bacterial overgrowth of gut with increased urinary levels of hippuric acid and HPHPA. Rifaximin (1200 mg/day) was prescribed for 2 weeks to reverse microbial dysbiosis, and the patient underwent gold PTT as described above without oral acne medications. The acne lesions were dramatically reduced after six treatment sessions of PTT (Figure 2). Moreover, no major recurrences were observed during a follow-up period of 14 months after the ninth session of PTT.

3 | DISCUSSION

The treatment of acne in adult patients may take several years; the chronic use of oral antibiotics can turn the gut

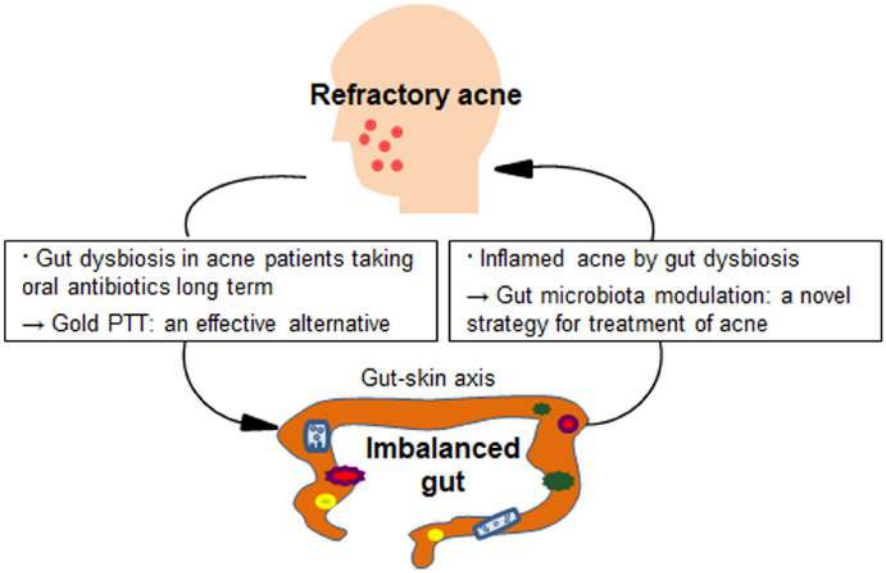

FIGURE 3 Summary of the function of gold nanoshell-mediated photothermal therapy (gold PTT) and gut microbiota modulation in acne treatment

microbiota into a dysbiotic state. It has been noted that doxycycline, but not isotretinoin, causes immediate and long-term changes of murine gut microbiot*a in vivo*.[1] In order to discontinue oral acne antibiotics, we used gold PTT as an alternative. Gold PTT is recently highlighted as a safe and effective treatment for recurrent acne.[4] About 150 nm-sized gold nanoparticles are designed to be applied topically and transported into sebaceous glands and follicles by the trans-appendageal route. When the gold nanoparticles are exposed to pulses of light, they exhibit plasmon resonance, strongly absorb light from 700 to 1200 nm, and cause thermal injury to surrounding tissues. Therefore, in gold PTT for acne treatment, light-absorbing gold nanoparticles can selectively destruct sebaceous follicles in accordance with the principles of selective photothermolysis.[6] Gold PTT is practically painless with minimal systemic and local side effects; however, our clinical experience has found that acne improvement is maintained for about 3 months after gold PTT monotherapy in Korean patients. No acne recurrences over a year in these two patients thus suggest that therapeutic intervention for gut dysbiosis may allow a longer period of remission after this PTT (Figure 3). Although further studies are necessary to elucidate the mechanism by which gut microbiota imbalance affect acne exacerbation, recent studies highlight gut microbiota alterations in acne patients.[1,2,7] Though not yet fully understood, the impaired integrity and increased permeability of intestinal epithelium caused by gut dysbiosis may result in systemic inflammatory effect, such as increased plasma interferon-gamma and interleukin-1β, leading to skin inflammation.[8] In addition, in a disturbed intestinal barrier, gut microbiota and their metabolites enter the bloodstream, accumulate in the skin, and influence skin homeostasis. Metabolites from the gut microbiota also promote acne by overactivating the mTOR signaling pathway.[1] Therefore, therapeutic strategies for managing gut microbiota alterations can be beneficial in the treatment of refractory acne.

ACKNOWLEDGMENT
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CONFLICTS OF INTEREST
The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTION
J.S. designed the study and wrote the manuscript. H.J.R. and J.Y.J. conceived and designed the study.

ETHICAL APPROVAL
This study conforms to the journal's recognized standards.

CONSENT
Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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