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CASE REPORT

Recurrence of Rosacea Induced by Compound Vitamin Tablets: A Case Report

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Abstract: We present a case of rosacea recurrence in a 37-year-old woman associated with the intake of compound vitamin tablets during the preconception period, with a Naranjo score of 7. These tablets, commonly used for nutritional supplementation to prevent anemia, contain a variety of vitamins, minerals, and trace elements. Despite their widespread use, reports of such supplements causing rosacea recurrence are rare. In this case, the patient experienced a recurrence of facial redness, stinging, and burning after taking the tablets on two separate occasions. Skin dermatoscopy, VISIA imaging, Clinician's Erythema Assessment (CEA), Investigator's Global Assessment (IGA), and Visual Analogue Scale (VAS) all confirmed the recurrence of rosacea. Given her intention to conceive, symptomatic treatment with emollient and reparative dressings was administered. The patient's symptoms gradually resolved after discontinuing the medication, with no recurrence observed during follow-up visits. Women with a history of rosacea should avoid these tablets during preconception, pregnancy, and lactation to prevent recurrence and should choose supplements carefully to minimize the risk of rosacea flare-ups.

Keywords: compound vitamin tablets, rosacea, drug adverse reaction, women of childbearing age, immune inflammatory dermatosis

Introduction

Rosacea is a chronic inflammatory skin condition with four subtypes: Erythematotelangiectatic Rosacea (ETR), Papulopustular Rosacea (PPR), Phymatous Rosacea (PHY) and Ocular Rosacea. It primarily affects the central convex parts of the face, causing facial erythema, papules, pustules and telangiectasia.[1] Global estimates suggest that rosacea may affect approximately 5.5% of the world's population.[2] Rosacea can occur at any age, but it is more common in women over 30.[3] As it is a facial skin disease that imposes certain burdens on patients' appearance and psychology, it could lead to psychological issues, for instance, anxiety and depression.[4–6] Due to the diverse clinical manifestations of the disease, it is difficult to identify rosacea from other diseases, leading to frequent misdiagnosis or oversight.[7]

In recent years, there has been a growing trend the number of people taking compound vitamins containing folic acid during the preconception period and early pregnancy. The main components of compound vitamin tablets include vitamin A, vitamin B1, B2, B6, B12, vitamin C, vitamin D3, vitamin E, biotin, folic acid, niacinamide, calcium pantothenate, and others. These formulations are efficacious in the prophylaxis of fetal anomalies, gestational anemia, hypocalcemia during pregnancy, and a spectrum of complications attributable to deficiencies in micronutrients. As far as we know, reports of adverse reactions to compound vitamin tablets are extremely rare. We reviewed previous studies, among which only two mentioned rosacea flare-ups related to vitamin intake, and both were caused by extremely high doses of vitamin B intake.[8,9] And there is only one reported case of a pregnant woman developing an extensive rash after taking compound vitamin tablets, but the final diagnosis was allergic reaction rather than rosacea.[10]

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In this report, we presented a clinical case of a patient in a stable period of rosacea who underwent a severe relapse after taking compound vitamin tablets. Based on this case, we conducted a literature search to provide a reference for the clinical diagnosis of medication use in patients with rosacea who are planning pregnancy and for the clinical diagnosis of related adverse reactions. The committee of Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine approved the study (2024DZMEC-343-01), and an informed consent has provided.

Case Presentation

A 37-year-old female patient sought consultation at our dermatology outpatient department on the 18th of May, 2024, for the insidious exacerbation of erythematous facial papules, concomitant with sensations of pruritus, thermal discomfort, stinging sensation, and tightness of the facial skin. At the time of presentation, erythema was scattered across the patient's midface region, with a few scattered rashes on the jawline, in the absence of other cutaneous lesions. The patient reported a past medical history of rosacea, yet had maintained a stable skin condition devoid of severe exacerbations over the past two years. This episode of relapse was not preceded by emotional stress, alcohol intake, or solar exposure, and there was no recent alteration in her routine skincare regimen. Microscopic examination for fungi and Demodex mites from multiple skin scrapings were both negative (Figure 1). Dermatoscopic assessment delineated a red backdrop with pervasive polygonal vascular networks, pronounced dilation of pilosebaceous orifices, areas of orange-yellow discoloration, and white squamous debris (Figure 2). The VISIA red zone index was recorded at 21.46%, affecting a surface area of 3.92% (Figure 3). The CEA and IGA scores are 3, the VAS score is 8.[11–13] Synthesizing the clinical features, a diagnosis of "rosacea" was rendered.

The patient reported initiating regular consumption of compound vitamin tablets on the 29th of March, 2024, and subsequently developed a rash on the face from the 14th of April, 2024, which later spread to the chest and back regions. Following a one-week course of loratadine tablets, the rash receded in all areas excluding the face, where they progressively intensified.

The patient ceased the intake of compound vitamin tablets and was offered symptomatic treatment with a medical-grade skin repair biomembrane. In light of the patient's preconception requirements, it was suggested that the patient transition to the oral administration of folic acid tablets, with continuous monitoring of the rash's evolution and further consultations as indicated for any discomfort.

A follow-up with the patient on the 25th of May, 2024, disclosed that following a one-week cessation of the compound vitamin tablets, the facial stinging sensation had resolved, with residual mild pruritus and thermal sensation, and no marked amelioration of facial erythema. On the 1st of June, 2024, a subsequent follow-up indicated that after a two-week discontinuation of the compound vitamin tablets, the patient experienced no significant subjective discomfort on the face, with a marginal improvement in facial erythema. On the 8th of June, 2024, during a return clinic visit, the patient's main complaint was the discomfort on the facial skin had essentially receded three weeks after discontinuing the compound vitamin tablets, with a noticeable improvement in facial redness, albeit the skin remained somewhat

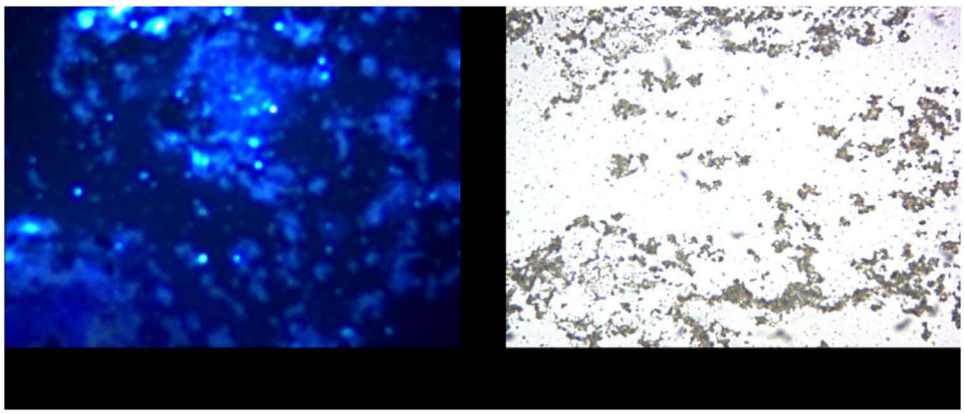

Figure 1 Skin Fungi and Hair Follicle Microscopy.

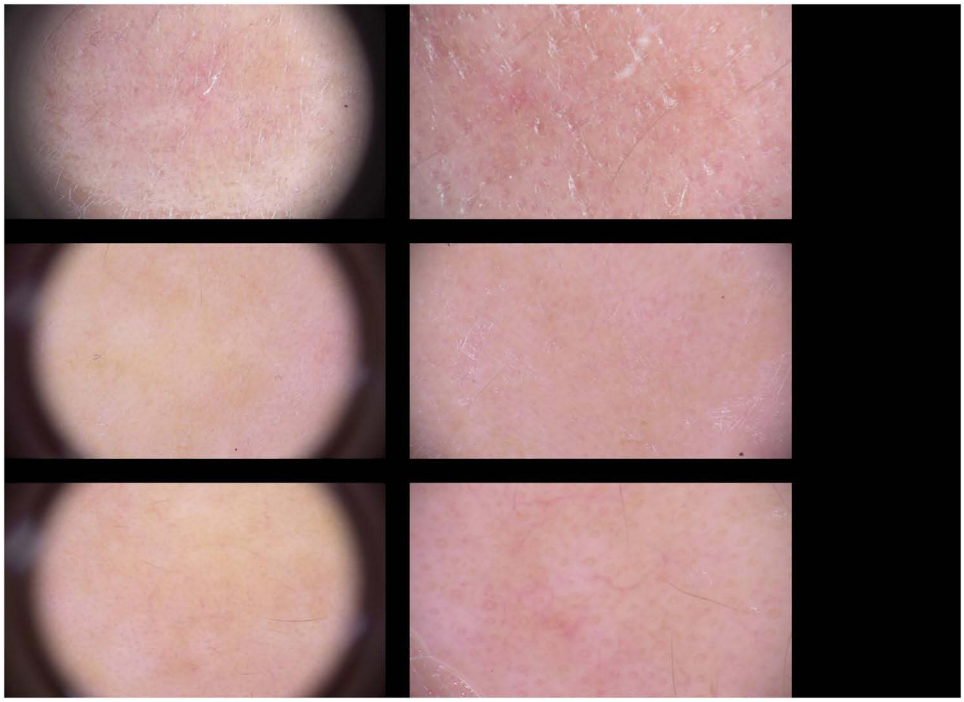

Figure 2 Dermatoscope Image of Facial Target Skin Damage.

desiccated. Dermatoscopic examination revealed a faintly red background with pervasive polygonal vascular networks, pronounced dilatation of numerous pilosebaceous orifices, and minimal areas of orange-yellow discoloration with scant white squamous debris (Figure 2), the VISIA red zone index was 5.08%, affecting a surface area of 1.01% (Figure 4), with CEA, IGA and VAS scores of 1 point each (Table 1). On the 6th of July, 2024, during another clinic revisit, the patient assured an absence of recent facial discomfort, with improved facial redness and no significant alteration in the area of erythema. Dermatoscopic assessment showed a faintly red background with pervasive polygonal vascular networks, pronounced dilatation of numerous pilosebaceous orifices, and orange-yellow regions, devoid of white squamous debris (Figure 2), the VISIA red zone index was 5.56%, affecting a surface area of 1.09% (Figure 5), with CEA score of 1 point, IGA and VAS scores of 1 point each (Table 1). At the same time, we confirmed that the patient was not pregnant throughout the entire medical consultation process.

Discussion

Considering the patient's clinical manifestations and the outcome following the discontinuation of the medication, it is speculated that the recurrence of rosacea in this instance was triggered by the intake of compound vitamin tablets. The patient had previously utilized compound vitamin tablets during a preparatory period in 2021. Similar symptoms of facial erythema, stinging, and thermal discomfort emerged 30 days after initiation of the medication. These symptoms gradually resolved following the cessation of the medication due to the suspension of the pregnancy plan. The patient underwent two cycles of pregnancy preparation and medication intake, with the recurrence of identical symptoms on both occasions, and subsequent improvement was observed after discontinuation of the medication each time. The Naranjo Adverse Drug Reactions Probability Scale yielded a score of 7 points,[14] signifying a "probable" relationship between the patient's rosacea relapse and the ingestion of compound vitamin tablets. Regarding whether the recurrence of the patient's facial rosacea is related to this allergic reaction, given the significant time difference between the appearance of the rashes, with the facial symptoms of redness and burning occurring before the truncal rash, we consider the likelihood of the allergic reaction causing the recurrence of rosacea to be low. The treating physician promptly notified the hospital's clinical pharmacist, who reported this case of adverse reaction to the National adverse drug reaction surveillance system of China.

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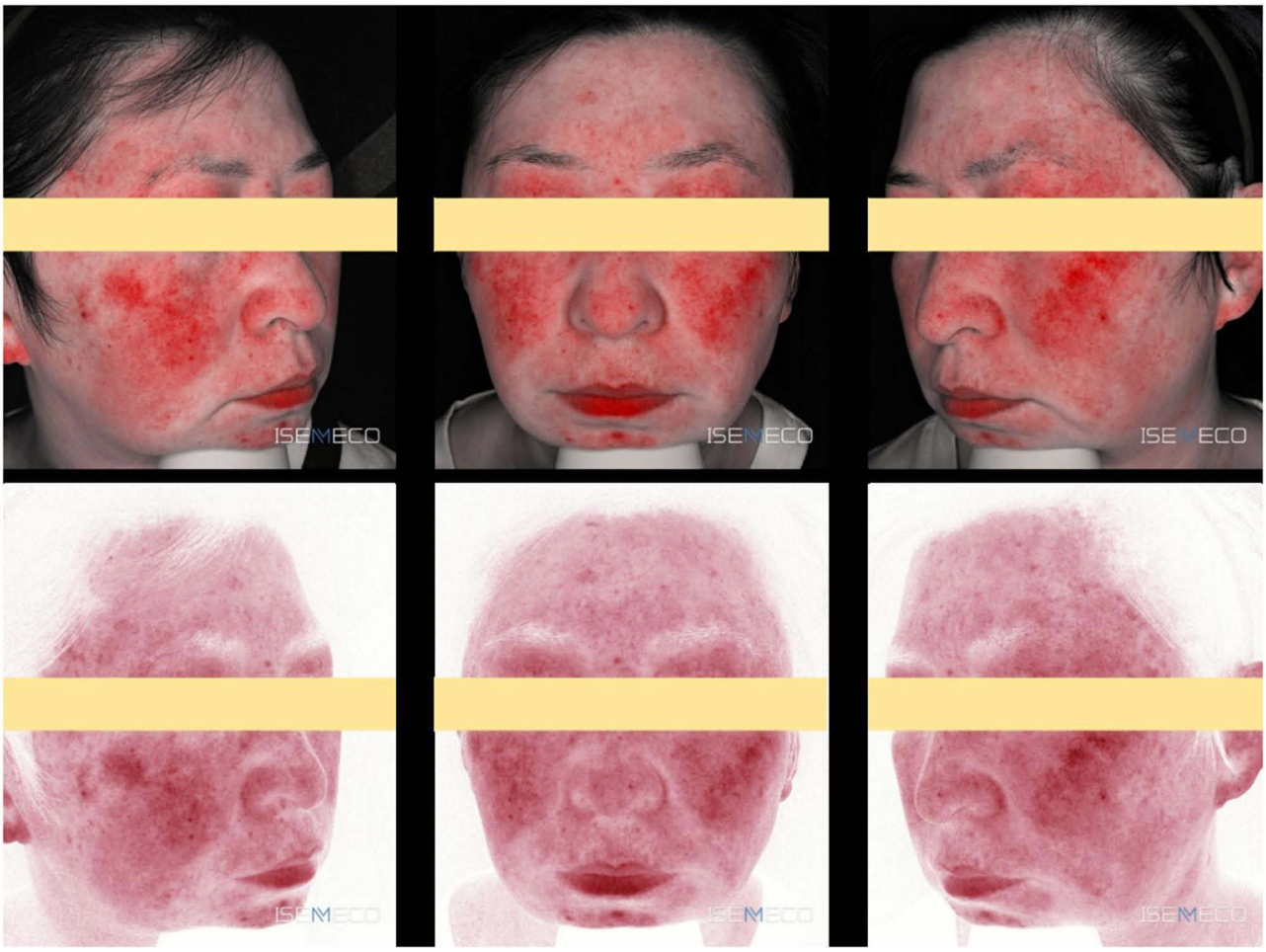

Figure 3 VISIA Image (collected on May 18, 2024).

In recent years, the prevalence of rosacea among young women is gradually increasing. This may be attributed to the misuse of cosmetic products or the impact of beauty interventions. It might also associated with increased pressures from life, work, and childbearing among young women. Although the pathophysiological mechanisms of rosacea are not fully explicit yet, it is currently believed to be related to genetic factors, abnormalities in neurovascular regulation, immune-inflammatory responses, disruption of the skin barrier, and immune reactions to infections by certain microorganisms, such as Demodex mites.[15] Among these, immune-inflammatory responses play a significant role in the clinical onset and progression of rosacea. The upregulation of Toll-like receptor-2 (TLR-2) could trigger a series of inflammatory and vasoactive peptides to be processed into LL-37.[16] Once LL-37 is released from the epidermis, it activates macrophage inflammation and recruits neutrophils, forming a feedback loop that generates more LL-37.[17] LL-37 can exacerbate inflammatory responses and induce angiogenesis, which is an important mechanism leading to the development of inflammatory reactions in rosacea.[18] Further studies have demonstrated that polymorphisms in genes such as glutathione S-transferase, vitamin D receptor, vascular endothelial growth factor (VEGF), and human leukocyte antigen are associated with the pathogenesis of rosacea.[19–22] These genetic polymorphic sites include rs3333631, rs763035, and rs111314066, which can exacerbate the inflammatory response in patients with rosacea by upregulating the expression of factors related to inflammatory pathways, such as Toll-like receptors and the JAK3 pathway.[23] Psychological stress can activate the hypothalamic-pituitary-adrenal axis, promoting the release of inflammatory factors such as interleukin-1β and tumor necrosis factor, thereby intensifying the facial erythema symptoms in patients.[4] Moreover, it can indirectly regulate the expression of related inflammatory factors such as Toll receptor 2 and matrix metalloproteinase 9 by affecting sleep quality, thus worsening the patient's condition.[24] Obesity is considered to worsen the inflammatory

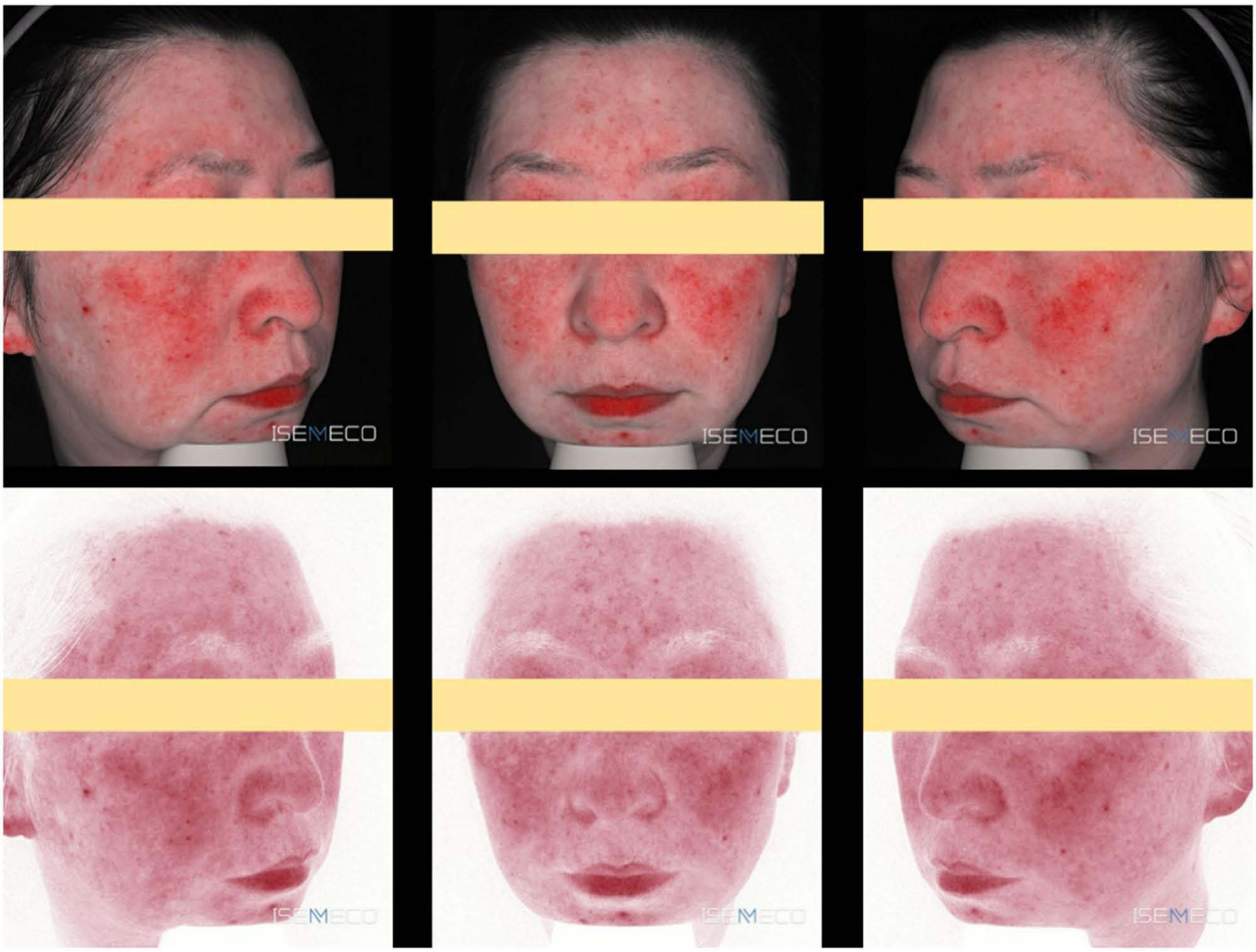

Figure 4 VISIA image (collected on June 8, 2024).

response in patients with rosacea by promoting the expression of inflammatory factors such as IL-6 and TNF-α.[25] Extrinsic factors like ultraviolet (UV) radiation can promote inflammation and angiogenesis in patients by upregulating the expression of LL37 in keratinocytes.[26] UVB can induce the expression of endothelin-1, causing mast cell degranulation, and thereby triggering neurogenic inflammatory responses in patients.[27]

Rosacea exhibits a variety of clinical manifestations and is prone to misidentification with other facial inflammatory skin diseases.[28] Consequently, auxiliary diagnostic techniques are commonly used in conjunction with differential diagnosis.[29–33] In this case, dermatoscopy and VISIA both indicated that the facial erythema was primarily due to telangiectasia, which sufficiently supports and corroborates the clinical diagnosis of "rosacea". Concurrently, upon re-examination seven weeks after discontinuation of the medication, well beyond the drug's metabolic cycle, the patient exhibited an improvement in facial redness. However, the extent of erythema was not markedly different from that observed four weeks after discontinuation, indicating pre-existing telangiectatic conditions characteristic of "rosacea". This observation is consistent with the clinical features of the disease and substantiates the diagnostic findings, allowing

Table 1 Indicators Before and After Withdrawal 3 weeks

Date	VISIA Red Zone Value	VISIA Red Zone Area	CEA	IGA	VAS
2024.05.18	21.46%	3.92%	3	3	8
2024.06.08	5.08%	1.01%	1	1	1
2024.07.06	5.56%	1.09%	1	0	0

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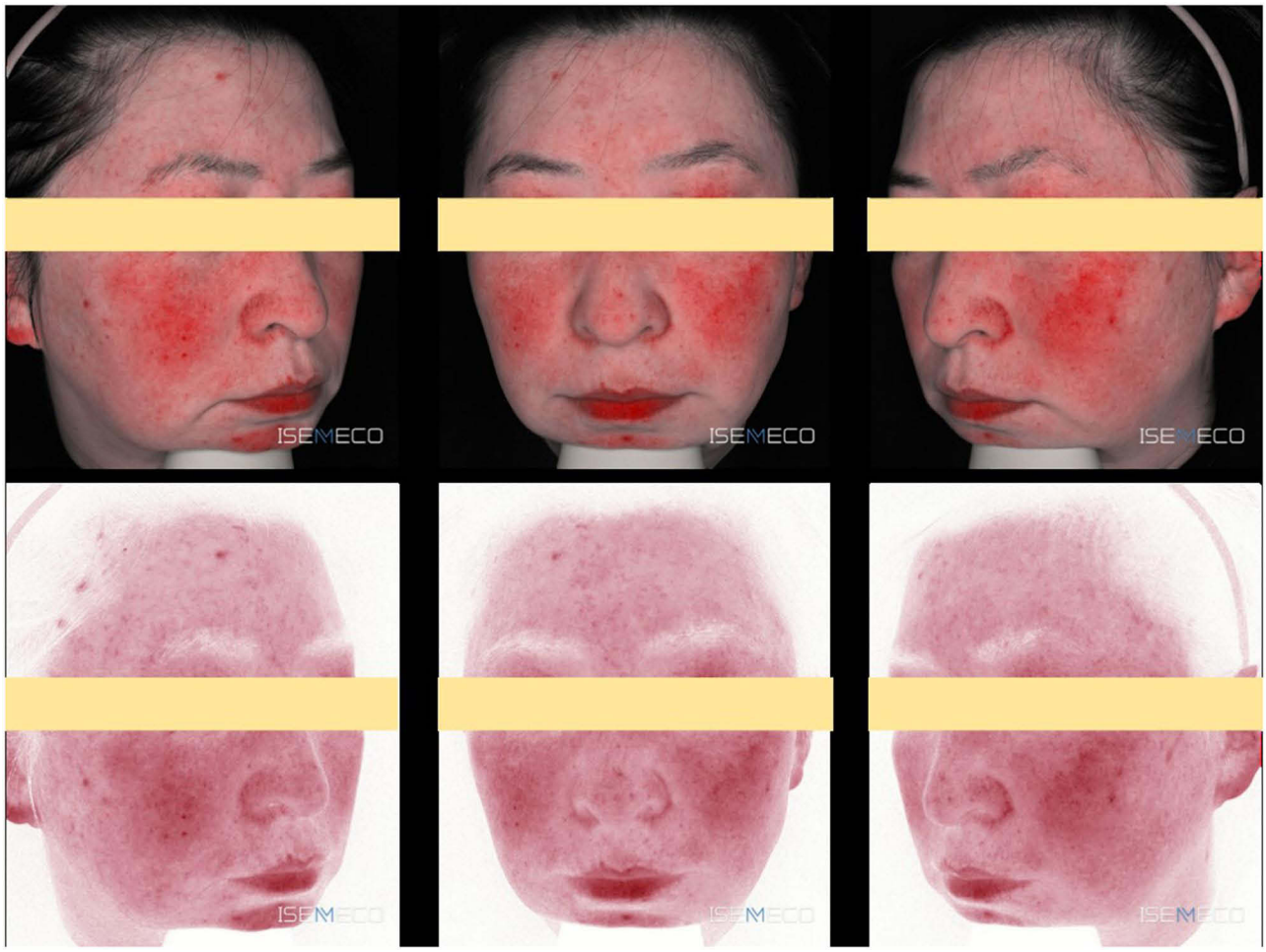

Figure 5 VISIA image (collected on July 6, 2024).

for a clear distinction from facial allergic dermatitis. In summary, this case can be distinguished from general drug allergic reactions and can also be differentiated from previously reported adverse drug reactions as a distinct type of drug-induced adverse event. Currently, there have been no reports of compound vitamin tablets causing rosacea.

We conducted a literature search for similar case reports related to our case report. We identified two case reports of rosacea associated with vitamin supplementation,[8,9] as well as a case report of an allergic reaction to the same formulation of compound vitamin tablets during pregnancy,[10] which are summarized in Table 2.

Unlike our case, both patients in case reports of rosacea only consumed supplements of vitamin B at doses far exceeding the recommended daily intake.[8,9] Additionally, neither patient had a history of rosacea. The symptoms described in these cases, combined with the recent diagnostic criteria for rosacea, seem more consistent with a widespread flare-up of acne vulgaris rather than rosacea. In terms of treatment, although the rashes in the aforementioned cases improved after discontinuing the supplements, systemic treatment with oral corticosteroids and other medications was still required to significantly alleviate the symptoms. The treatment plans primarily focused on anti-allergic and anti-inflammatory therapies. While various systemic treatments can be used to manage rosacea, doxycycline remains the only oral medication approved by the US Food and Drug Administration for rosacea treatment to date.[34,35] The cases mentioned above did not involve the use of doxycycline or report poor efficacy. Overall, we believe these cases differ significantly from our case report. However, we cannot rule out the possibility that the recurrence of rosacea in our case may be related to the intake of vitamin B. Therefore, our case suggests that, unlike previous reports, even low doses of certain vitamins in a multivitamin tablet may trigger a relapse in patients with a history of rosacea.

Table 2 Comparison of Vitamin-Induced Rosacea Literature With the Current Study

Article	Baseline Information of Patient	Daily Intake of Medication	History of Rosacea	Symptoms of Current Episode
This Article	Female, 37 years old	Compound Vitamin Tablets (Vitamin A-1.2mg, Vitamin B1-1.6mg, Vitamin B2-1.8mg, Vitamin B6-2.6mg, Vitamin B12-4.0μg, Vitamin C-0.1g, Vitamin D3-12.5μg, Vitamin E-15mg, Biotin-0.2mg, Folic Acid-0.8mg, Niacinamide-19mg, Calcium Pantothenate-10mg, Calcium-0.125g, Magnesium-0.1g, Phosphorus-0.125g, Copper-1mg, Iron-60mg, Manganese-1mg, Zinc-7.5mg)	Yes	Gradually worsening erythematous papules on the face, accompanied by itching, burning, stinging, and skin tightness
[8]	Female, 38 years old	Composite Vitamin B (Vitamin B12-1g, B6-500mg, B1-500mg)	No	Erythematous papules and plaques on both cheeks, with isolated pustules
[9]	Female, 17 years old	Vitamin B6-80mg, Vitamin B12-20μg	No, but with a history of acne vulgaris	Numerous confluent nodules and papulopustules on the cheeks and chin, with some papulopustules on the neck. Seborrhea is present in the affected areas. No comedones or telangiectasia were observed.
[10]	Female,23 years old, pregnant	Compound Vitamin Tablets (Vitamin A-1.2mg, Vitamin B1-1.6mg, Vitamin B2-1.8mg, Vitamin B6-2.6mg, Vitamin B12-4.0μg, Vitamin C-0.1g, Vitamin D3-12.5μg, Vitamin E-15mg, Biotin-0.2mg, Folic Acid-0.8mg, Niacinamide-19mg, Calcium Pantothenate-10mg, Calcium-0.125g, Magnesium-0.1g, Phosphorus-0.125g, Copper-1mg, Iron-60mg, Manganese-1mg, Zinc-7.5mg)	No	Symmetrical erythema on the trunk accompanied by severe itching, gradually spreading to the lower limbs.

In the case involving the same compound vitamin tablets, the diagnosis was allergic reaction rather than rosacea. Additionally, this case occurred during pregnancy, and the reaction may be related to hormonal changes associated with pregnancy.[10]

The limitations of this case report include the lack of a controlled study design, which precludes establishing a definitive causal relationship between compound vitamin tablets and rosacea recurrence. Additionally, the findings are based on a single case and may not be generalizable to other individuals, highlighting the need for further research in a larger cohort.

Conclusion

Reports of rosacea being triggered by usual doses of compound vitamin tablets are very rare. This case highlights the potential risk of rosacea relapse associated with the ingestion of compound vitamin tablets. Women of reproductive age with a history of rosacea should exercise caution when taking such supplements during preconception, pregnancy, and lactation. Further research is warranted to elucidate the underlying mechanisms and to develop more tailored preventive strategies.

Abbreviations

ETR, Erythematotelangiectatic Rosacea; PPR, Papulopustular Rosacea; PHY, Phymatous Rosacea; TLR-2, Toll-like receptor-2; VEGF, Vascular endothelial growth factor; UV, Ultraviolet.

Data Sharing Statement

No datasets were generated or analyzed during the current study.

Statement of Ethics

Written informed consent was obtained from the patient for the publication of any potentially identifiable images or data included in this article. The Ethics Committee of Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine has granted approval for this research and has consented to publish the pertinent information regarding this case.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest regarding the content of the manuscript.

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