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Clinical Characteristics of Granular Parakeratosis Caused by Benzalkonium Chloride: A Retrospective Case Series

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Background: Granular parakeratosis (GP) is a rare keratinization disorder. Recent studies have suggested a possible association with exogenous irritants such as benzalkonium chloride (BAK); however, the clinical features of related cases have not yet been systematically characterized.

Aim: To analyze the clinical features, histopathological findings, and treatment outcomes of patients with GP induced by BAK exposure, with the aim of enhancing clinical recognition and management of this etiological subtype of GP.

Methods: A single-center retrospective study was conducted on eight patients diagnosed with BAK-associated GP confirmed both clinically and histopathologically, who presented between June 2024 and June 2025. Demographic data, clinical manifestations, histopathological changes, and treatment outcomes were collected and analyzed.

Results: Among the eight patients, six were male, with ages ranging from 4 to 43 years; four were children. Lesions were primarily distributed over the groin, trunk, neck, and upper chest, all presenting as erythematous-brown patches with characteristic parchment-like scaling. Histopathological examination in all cases revealed parakeratosis and retention of basophilic granules within the stratum corneum. Following definitive diagnosis and cessation of BAK exposure, combined with the use of emollients, complete resolution of lesions was achieved within 2 weeks to 1 month.

Conclusion: BAK can induce GP, which presents with certain characteristic features, notably the presence of parchment-like scaling that serves as a valuable clue for differential diagnosis. Early identification and elimination of the causative irritant are key to effective treatment. Pediatric patients may be more susceptible, and the development of GP may be related to individual predisposition and cumulative BAK exposure, warranting further investigation.

Keywords: granular parakeratosis, clinical characteristics, benzalkonium chloride

Introductions

Granular parakeratosis (GP) is a relatively rare, benign disorder of keratinization. It typically presents clinically as scaly erythema or brownish hyperkeratotic papules and plaques, predominantly occurring in flexural or intertriginous areas of the body. GP was first reported by Northcutt et al in 1991, who described a case series of four patients with similar axillary lesions. All patients exhibited pigmentation and bright red plaques in the axillary regions. Histopathological examination revealed compact parakeratosis with abundant retained keratohyalin granules within the stratum corneum. The condition was presumed to be associated with the use of antiperspirants/deodorants and was thus termed axillary GP.[1] Subsequently, similar lesions and histopathological patterns have been reported by different researchers in other intertriginous and non-intertriginous areas of the body, such as the groin and inframammary skin.[2,3] As a result, the term "axillary" is no longer used in the nomenclature of this condition.

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Cases of GP have been reported worldwide, with an estimated incidence of approximately 0.004%–0.005%, and no significant racial predilection. It predominantly affects adults, especially middle-aged and elderly women.[4,5] However, due to limited awareness of the condition among dermatologists, GP is often underdiagnosed or misdiagnosed in clinical practice, which may lead to underestimation of its true incidence. One study estimated that the average time from onset to diagnosis is 19.2 months.[4] In recent years, with increasing public hygiene awareness, reports of GP induced by disinfectants containing BAK have significantly increased.[6,7] BAK is a quaternary ammonium compound with antimicrobial and preservative properties, and is widely used in products such as shampoos, moisturizers, wet wipes, antiseptic cleansers, and contact lens solutions.[6]

However, given that dermatologists currently have insufficient understanding of this disease, missed and incorrect diagnoses are often encountered in clinical practice. Current reports on BAK-associated GP remain limited, and its clinical characteristics have yet to be systematically summarized. This study aims to retrospectively analyze a series of BAK-associated GP cases, elucidating the clinical features and epidemiological patterns, with the inclusion of pediatric cases to enhance clinical recognition of BAK-related GP and provide references for future standardized diagnosis and treatment approaches.

Methods

This retrospective study was approved by the independent ethics committee of the Second Affiliated Hospital of Wenzhou Medical University and Yuying Children's Hospital. Given the retrospective nature of the study and the use of de-identified patient data, the requirement for informed consent was waived by the IRB. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and its later amendments.

A retrospective analysis was conducted on eight patients diagnosed with GP who presented to the Department of Dermatology at The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University between June 2024 and June 2025. All cases were clinically and histopathologically confirmed as GP, with documented histories of BAK exposure. BAK exposure was confirmed through both patient self-report and verification of product ingredients when available. Each diagnosis was independently reviewed and confirmed by two dermatologists. Clinical data collected included sex, age, lesion location, disease duration, lesion morphology, subjective symptoms, histopathological findings, treatment regimens, and prognosis. These data were systematically organized and analyzed.

Results

The clinical information of the eight patients is summarized in Table 1. Among the eight diagnosed cases of GP, six were male and two were female, with ages at presentation ranging from 4 to 43 years; four of the patients were children. Three of the eight patients were from the same family, indicating familial clustering, while the remaining five were sporadic cases from unrelated households. The duration of BAK exposure prior to onset ranged from one month to over two years, and the disease course varied from two weeks to nearly two years.

Table 1 Clinical Information of Patients

Case	Gender	Age (Years)	Disease Course	Duration of BAK Exposure Prior to Onset of Symptoms	Previous Diagnoses Prior to Confirmation of GP
1	Female	43	1 month	More than 2 months	Contact dermatitis
2	Male	32	6 months	3 months	Tinea cruris
3	Male	6	Nearly 2 years	About half a year	Pustular psoriasis, contact dermatitis, atopic dermatitis
4	Male	34	More than 3 months	More than two years	Tinea cruris
5	Female	33	More than 2 months	More than two years	/
6	Male	4	More than 1 month	Nearly 3 months	Inverse psoriasis, contact dermatitis
7	Male	7	2 weeks	1 month	Paederus dermatitis, photosensitive dermatitis
8	Male	16	3 weeks	More than 4 months	/

The clinical features of the eight patients are detailed in Table 2, and representative skin lesions are shown in Figures 1 and 2. Lesions most commonly involved the groin, trunk, neck, and upper chest (50%), followed by the axillae (37.5%). The buttocks, perineum, and extremities were also affected in 25% of cases. All patients presented with symmetrical, map-like or reticulated erythematous or brownish patches accompanied by parchment-like brown scales (Figure 3). Wrinkling of the skin was observed in five patients (62.5%). Subjective symptoms included pruritus in 50% of cases, stinging in 25%, and burning sensations in 12.5%; 37.5% of patients reported no significant discomfort.

A total of nine skin lesions from the eight patients underwent histopathological biopsy (Figure 4). All specimens demonstrated parakeratosis, retention of basophilic granules within the stratum corneum, and superficial perivascular

Table 2 Clinical Characteristics of Patients

Characteristics	Total Cases	
	n	%
Anatomic site		
Axillae	3	37.5
Groin folds	4	50.0
Buttocks/perineum	2	25.0
Trunk	4	50.0
Neck/upper chest	4	50.0
Extremities	2	25.0
Morphology		
Erythematous/brownish patches	8	100.0
Parchment-like scales	8	100.0
Wrinkling of the skin	5	62.5
Erythematous papules	3	37.5
Pustules	2	12.5
Symptoms		
Pruritus	4	50.0
Stinging	2	25.0
Burning sensation	1	12.5
Asymptomatic	3	37.5
Pathological features		
Hyperkeratosis	6	75.0
Parakeratosis	8	100.0
Retention of basophilic granules in the stratum corneum	8	100.0
Epidermal hyperplasia	2	25.0
Epidermal atrophy	1	12.5
Irregular acanthosis	3	37.5
Perivascular lymphocytic infiltration in the superficial dermis	8	100.0
Perivascular neutrophilic infiltration in the superficial dermis	3	37.5
Accumulation of neutrophils within the stratum corneum	2	12.5
Vacuolar degeneration of keratinocytes	2	25.0
Treatment regimens (Including prior interventions)		
Immediate cessation of BAK-containing products/Disposal or repeated washing of BAK-contaminated clothing	8	100.0
Topical corticosteroids	4	50.0
Topical antifungal agents	2	25.0
Topical antibiotics	4	50.0
Topical retinoids	1	12.5
Topical emollients	8	100.0
Oral corticosteroids	3	37.5
Oral antibiotics	1	12.5
Oral antihistamines	4	50.0

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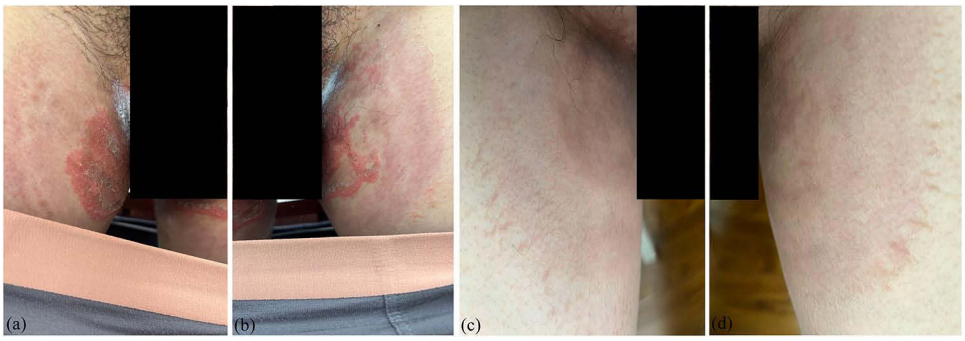

Figure 1 (**a** and **b**) Groin lesions of Patient 2 before treatment; (**c** and **d**) Groin lesions of Patient 2 after treatment.

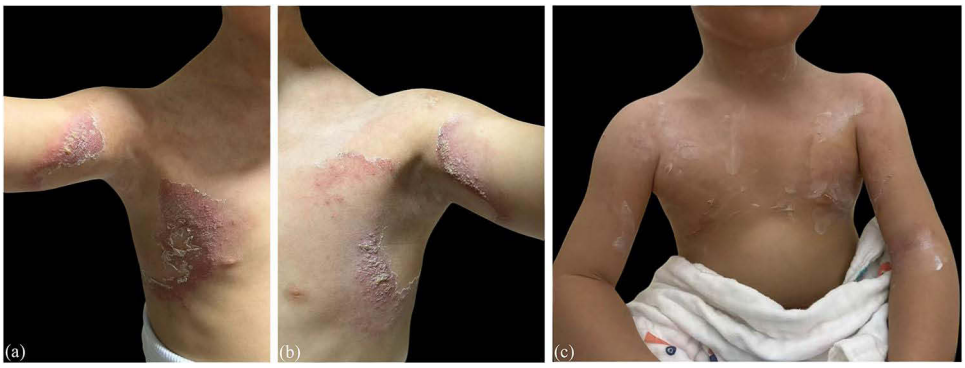

Figure 2 (**a** and **b**) Lesions on the upper chest and upper limbs of Patient 3 before treatment; (**c**) Lesions on the upper chest and upper limbs of Patient 3 after treatment.

lymphocytic infiltration in the dermis. Hyperkeratosis was also observed in 75% of the cases. Biopsies from pustular lesions in Case 3 and Case 6 additionally revealed intra-stratum corneum aggregation of neutrophils and superficial perivascular neutrophilic infiltration in the dermis.

Among the eight patients, five were initially misdiagnosed with other dermatological conditions and had received various treatments, including topical corticosteroids, antibiotics, antifungal agents, retinoids, as well as oral corticosteroids and antibiotics. However, clinical improvement was limited. Case 3, a pediatric patient with extensive pustules, was treated with oral cefuroxime axetil, but the pustules persisted. Patients with pruritus experienced significant symptomatic relief after taking oral antihistamines, though little improvement was observed in the primary lesions. Upon definitive diagnosis of BAK-associated GP, all patients were instructed to discontinue use of BAK-containing products and either discard or thoroughly wash previously contaminated clothing. Following the application of topical emollients, complete resolution of lesions was achieved within 2 weeks to 1 month.

Discussions

GP clinically presents as discrete, clustered, or reticulated brownish-red hyperkeratotic papules or plaques, or red to brownish patches, which may be accompanied by scaling or crusting. Lesions can be unilateral or bilaterally symmetrical, and may be associated with pruritus, burning sensations, or pain. In this study, all eight patients with BAK-associated GP exhibited the characteristic feature of parchment-like brown scaling. This finding is consistent with previous reports,[7,8] suggesting that this lesion morphology is a strong clinical indicator of BAK-related GP and warrants particular attention from dermatologists.

In Case 3, the pediatric patient developed millet-sized pustules scattered over erythematous patches and had previously been misdiagnosed with pustular psoriasis over an extended period. Additionally, due to the presence of erythematous papules and pruritus in the antecubital and popliteal fossae, the patient was also diagnosed with concurrent atopic dermatitis. Case 7 initially presented with a solitary, linear erythematous lesion and was misdiagnosed with

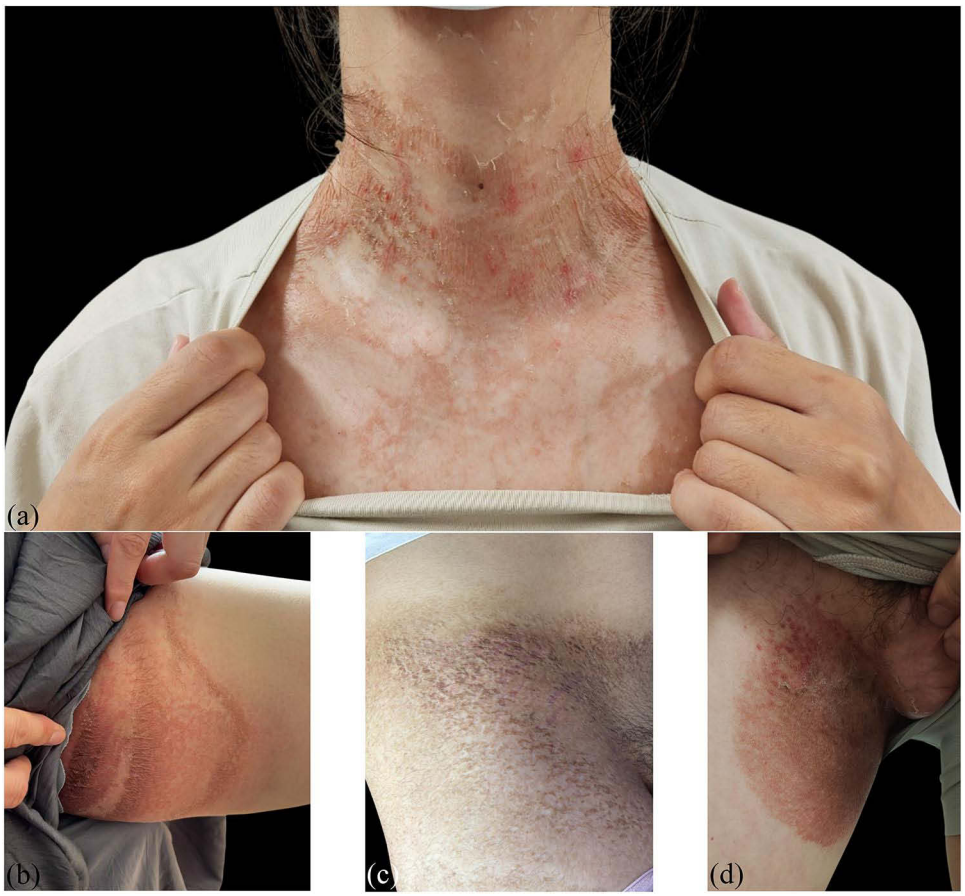

Figure 3 Clinical presentation of "parchment-like scaling" in patients with GP; (**a**) cervical and upper chest lesions in Patient 5; (**b**) groin lesions in Patient 1; (**c**) groin lesions in Patient 8; (**d**) groin lesions in Patient 4.

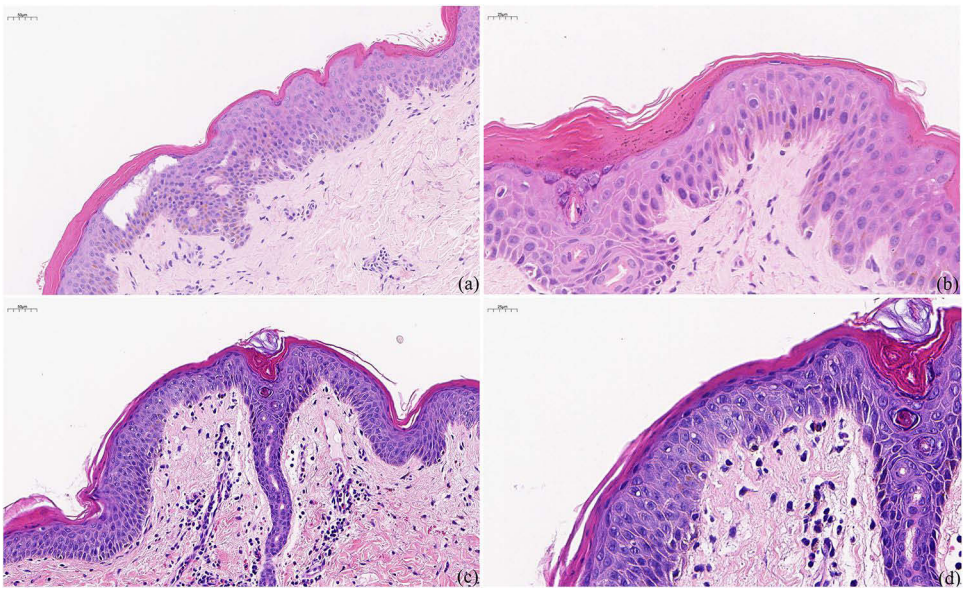

Figure 4 (**a** and **b**) Histopathological features of Patient 1, showing mild hyperkeratosis, parakeratosis, retention of basophilic granules within the stratum corneum, focal acanthosis, and superficial dermal lymphocytic infiltration. (**c** and **d**) Histopathological features of Patient 4, showing parakeratosis, retention of basophilic granules in the stratum corneum, dilation of superficial dermal blood vessels, and perivascular lymphocytic infiltration.

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Paederus dermatitis. As the lesions progressed to diffuse erythema and brownish patches on the neck accompanied by pruritus, photosensitive dermatitis was suspected. It was not until the appearance of skin wrinkling and characteristic parchment-like scaling that BAK-associated GP was considered. These findings highlight the clinical polymorphism of GP and the fact that lesions are not necessarily confined to the axillae or groin. Early recognition may be insufficient, leading to misdiagnosis. Dermatologists should enhance their awareness and diagnostic sensitivity to the key morphological clue of parchment-like brown scaling, especially in suspected cases of BAK-associated GP.

The pathogenesis of GP has not been fully elucidated. The currently prevailing hypothesis suggests that the disease is associated with a defect in profilaggrin metabolism, where parakeratosis and retention of keratohyalin granules within the stratum corneum result from impaired conversion of profilaggrin to filaggrin.[1,9] Metze et al demonstrated that the retained basophilic granules within the stratum corneum react positively with antibodies specific to filaggrin and its precursors.[9] Regarding BAK-associated GP, it has been proposed that BAK may exert pathogenic effects by disrupting keratinocyte membranes and inducing intracellular enzyme inactivation.[8] Furthermore, BAK has been shown to cause mitochondrial dysfunction and oxidative stress, which may also contribute to the development of GP.[10]

Currently, GP is no longer considered a distinct disease entity but rather a cutaneous reaction pattern with characteristic histopathological features.[2] A systematic review of punch biopsy specimens from 106 GP patients indicated that parakeratosis (91.5%) and retention of keratohyalin granules within the stratum corneum (97.2%) are the most characteristic findings. Other common features include hyperkeratosis and superficial dermal interstitial or perivascular lymphocytic infiltration.[3] The absence of spongiosis in GP histopathology supports its distinction from contact dermatitis.[5] In this study, all eight BAK-associated GP patients demonstrated these hallmark histological changes. However, it is noteworthy that Kumarasinghe et al[11] suggested that the histopathological features of GP may vary depending on the stage of disease progression. Parakeratosis and retained keratohyalin granules may not be consistently present. Therefore, they proposed that the term *hyperkeratotic flexural erythema* may be a more appropriate descriptor for this condition.

We reported eight cases of BAK-related GP, and the histopathological findings supported that it was a distinct cutaneous reaction pattern rather than a form of irritant contact dermatitis, despite the fact that lesions resolved following cessation of BAK exposure. Given evidence suggesting that the pathogenesis of GP may involve impaired profilaggrin-to-filaggrin conversion, and considering that not all individuals exposed to BAK develop the condition, it suggests a contributory role of genetic susceptibility and keratinocyte dysfunction. In this study, the time from initial BAK exposure to disease onset ranged from one month to over two years, indicating that cumulative exposure may be contribute to symptom development. The specific mechanisms of this study warrant further investigation. In the future, large-scale, multicenter cohort studies are required to better elucidate the epidemiological characteristics and risk factors of BAK-related GP. A prospective study design incorporating standardized exposure assessment and quantitative BAK concentration analysis will enhance the accuracy of causal inference.

All the GP patients reported in this study were triggered by laundry disinfectant containing BAK. The duration of BAK exposure prior to disease onset varied widely (from 1 month to over 2 years), suggesting individual differences in BAK tolerance. However, these variations were also influenced by differences in usage patterns, such as the dilution concentration of BAK and the duration of garment soaking. Furthermore, this study reports a 25% co-occurrence rate of GP among parents of pediatric patients. Specifically, Case 3 involved a child patient, while Cases 4 and 5 were his parents. The entire family began using BAK-containing disinfectants for undergarment sanitation over two years prior to disease onset. The child developed lesions approximately six months after initial exposure, with seasonal exacerbations each summer, whereas the parents did not develop symptoms until more than two years of exposure had elapsed. Cases 6, 7, and 8 were pediatric patients whose family members also used BAK-containing disinfectants, yet none of the adult family members manifested the condition. These findings suggest that, under comparable BAK exposure conditions, children may be more susceptible to developing GP than adults. This may be attributable to their relatively weaker skin barrier function and reduced metabolic capacity to detoxify BAK. However, these findings should be interpreted cautiously due to the limited sample size and single-center design of this study.

Currently, there is no universally established treatment protocol for GP. Literature reports have described the use of topical corticosteroids, vitamin D analogs, retinoids, and systemic therapies such as oral corticosteroids and antibiotics, with variable outcomes. Some cases of GP have even been noted to resolve spontaneously.[2,3] For patients with BAK-

induced GP, once an accurate clinical diagnosis is made, they are typically advised to discontinue exposure to the offending irritant. In such cases, spontaneous resolution of lesions often occurs within several months. In this study, all eight patients achieved complete lesion resolution approximately one month after eliminating contact with BAK-contaminated clothing. Prior to the removal of the causative agent, neither systemic nor topical treatments proved effective in alleviating the lesions. To date, for cases of GP with clearly identified contact-related triggers—such as BAK—disease control is typically achieved through elimination of the causative factor. However, for GP of other or unknown etiologies, treatment reports remain limited and cannot currently support evidence-based therapeutic recommendations.

Our study demonstrates that BAK-induced GP is largely preventable through appropriate patient education. Clinicians encountering the characteristic "parchment-like" brown scaling should routinely inquire about BAK-containing product use (eg, wipes, disinfectants, personal hygiene items). Particularly in pediatric populations and individuals with sensitive skin, educating patients to read ingredient labels and avoid prolonged BAK exposure can significantly reduce disease incidence.

This study has several limitations. The small sample size and single-center design restrict the generalizability of the findings. Additionally, the retrospective study design partially relied on patients' recall of product usage, which may introduce recall bias in assessing BAK exposure. Furthermore, we were unable to verify the components of all products, so some exposure data were solely based on patient reports. Future studies could incorporate patch testing for relevant components to improve diagnostic accuracy.

In conclusion, benzalkonium chloride (BAK) can induce granular parakeratosis (GP), which manifests as the characteristic "parchment-like" brown scaling lesions. The development of GP may be associated with cumulative BAK exposure and individual susceptibility, with children exhibiting heightened vulnerability—a finding warranting further investigation. Early identification and removal of causative factors are pivotal in managing GP. Clinicians should enhance recognition of characteristic lesions to avoid misdiagnosis, reinforce patient education regarding avoidance of long-term BAK-containing products, particularly in children and individuals with sensitive skin.

Data Sharing Statement

Data are available on request from the corresponding author.

Ethics Statement

All patients provided informed consent for the publication of their clinical data and photographs, and no information that could potentially identify individual patients will be disclosed.

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Disclosure

Fan Lin and Yingwei Wang contributed equally to this work and should be considered co-first authors. The authors declare that they have no conflict of interest.

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