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CASE REPORT

A Case of IgG4-Related Disease Presenting with Skin Lesions and Proptosis as Initial Manifestations

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Background: IgG4-related disease (IgG4-RD) is a rare chronic fibroinflammatory disorder. Elevated serum IgG4 levels and infiltration of IgG4-positive plasma cells into affected tissues are characteristic of it. It often involves multiple organs. However, initial presentations with cutaneous involvement are relatively rare. To better understand and treat the associated disease, we report this case.

Patients and Methods: We report a 39-year-old man who presented with a 3-year history of pruritic papules and nodules on the face, neck, shoulders, back, and lower extremities, along with progressive bilateral proptosis over the past year. He had a known history of allergic rhinitis. Previously diagnosed with "atopic dermatitis" at another hospital, he was treated with antihistamines and topical glucocorticoids, which produced minimal improvement. At our hospital, he underwent serum IgG4 testing,imaging studies,pathological examination, and multidisciplinary consultations involving dermatology, ophthalmology, and hematology, leading to a definitive diagnosis of IgG4-RD.

Results: Systemic glucocorticoids and methotrexate, along with topical medications,therapy resulted in marked clinical improvement in both skin and ocular symptoms, along with gradual normalization of serum IgG4 levels.

Conclusion: IgG4-RD can mimic a variety of diseases, through this case we found that this disease in addition to the reported diseases, but also mimic atopic dermatitis manifestations with intense itching makes it very easy to misdiagnose, missed diagnosis, which not only presents a complete multidisciplinary collaboration in the diagnosis and treatment of atopic dermatitis-like clinical diagnostic ideas of IgG4-RD, but also for the first time systematically reported the skin lesions of dermatoscopy and CT imaging features of skin, for clinical.

Keywords: IgG4-related disease, atopic dermatitis, proptosis, Dermoscopy

Introduction

IgG4-related disease (IgG4-RD) is a rare chronic fibroinflammatory disorder that has only recently been defined. It is characterized by elevated serum IgG4 levels and infiltration by IgG4-positive plasma cells, as well as tissue fibrosis. It can involve multiple organs, including the pancreas, salivary glands, lacrimal glands, skin, and kidneys. The disease is often underdiagnosed or misdiagnosed due to the variety of organs involved and poor specificity of signs and symptoms. This disease is easily confused with other similar malignant tumors. The consequences of misdiagnosis and subsequent inappropriate treatment are unimaginable. Furthermore, this disease frequently leads to lesions in various vital organs. Failure to diagnose it will allow the condition to progress, posing a significant threat to the patient's life and health. The diagnosis of this disease is based on a combination of clinical features, serum IgG4, imaging, and histopathology,[1,2] The diagnostic criteria for IgG4-related disease (IgG4-RD) have evolved through three major stages: The 2011 Boston Consensus laid the histopathological foundation for diagnosing IgG4-RD.[1] The 2019 ACR/EULAR Classification Criteria further integrated clinical, serological, and pathological findings, underscoring the importance of multidisciplinary team discussions.[2] The 2020 Revised Comprehensive Diagnostic Criteria were developed specifically for use in clinical trials, prioritizing high specificity to differentiate IgG4-RD from other conditions.[3]

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These criteria provide an essential framework for diagnosing IgG4-RD; however, clinical practice still requires individualized judgment based on each patient's presentation. Notably, several disorders—such as primary sclerosing cholangitis (PSC), type 2 autoimmune pancreatitis, inflammatory bowel disease (IBD), interstitial pneumonia, and plasmacytic penile inflammation—may exhibit elevated serum IgG4 levels or significant tissue infiltration by IgG4-positive plasma cells, yet lack the characteristic histopathological features of IgG4-RD. Similarly, lymphoproliferative disorders like Castleman disease and Rosai-Dorfman disease can also show abundant IgG4-positive plasma cells without meeting the typical histological criteria for IgG4-RD.[4] Therefore, early multidisciplinary diagnosis and management, coupled with proactive utilization of ancillary tests, are crucial to minimize misdiagnosis, enhance diagnostic accuracy, and improve the overall efficiency of patient care. And treatment often requires the systematic use of glucocorticoids and immunosuppressants.[5] In this report, we present a case of IgG4-RD initially manifesting as atopic dermatitis-like skin lesions and proptosis, and we describe the dermoscopic and skin CT features observed.

Case Report

A 39-year-old man presented with erythema, papules, and nodules on his lower limbs that had persisted for 3 years without an obvious cause, accompanied by severe pruritus. He had not received regular medical evaluation or treatment during this period. The skin lesions gradually spread to the bilateral shoulders, face, and neck, both lower limbs (Figure 1). He was previously diagnosed with atopic dermatitis at an outside hospital and was prescribed topical corticosteroids and antihistamines, but the symptoms did not improve. One year before admission, bilateral proptosis accompanied by visual deterioration was noted (Figure 2). Since the onset of the disease, the patient has not reported any systemic abnormalities such as dry mouth. He presented to the ophthalmology department of our hospital, where a multidisciplinary evaluation involving dermatology and rheumatology was arranged. He underwent various ancillary tests and examinations, revealing the following immunoglobulin and complement quantitative measurements: Total IgE antibody: 4911kU/L, Serum IgG: 424.60 g/L, Absolute eosinophil count: 1.14×10^9/L. Orbital CT showed symmetrical striated soft-tissue shadows, and cervical lymph node ultrasound revealed multiple enlarged cervical lymph nodes, Dermoscopy and skin CT (Figure 3a and b), shoulder and lower leg lesion histopathology (Figure 4a and b) showed

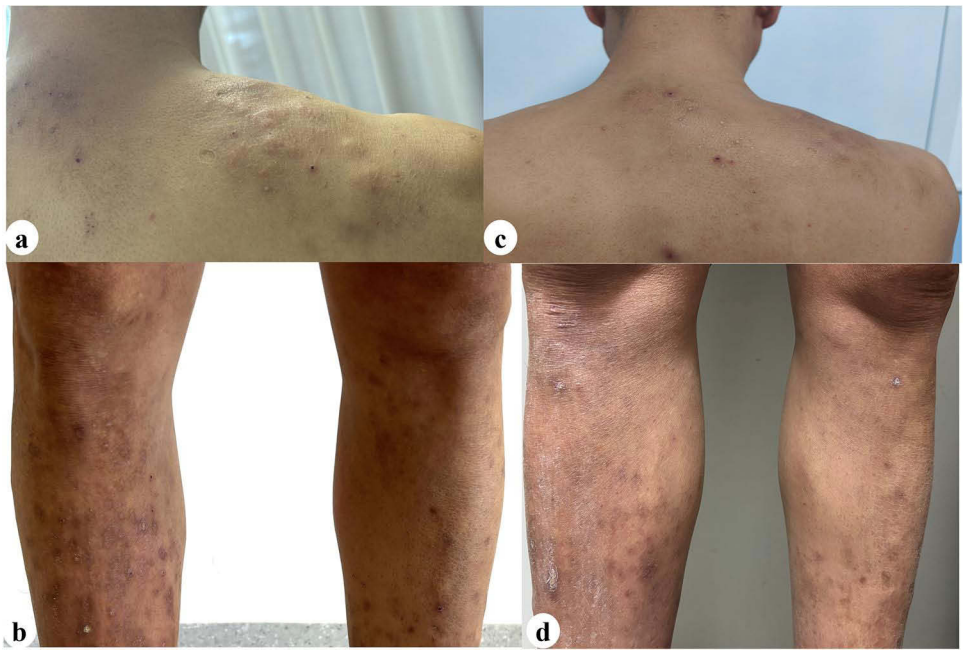

Figure 1 (**a**) Before treatment, thickening of skin texture on the shoulder and neck, scattered nodules, papules, erythema, hyperpigmentation, visible small number of papules broken and crusted, some nodules fused into a piece of patchy protrusion; (**b**) Before treatment, scattered papules, nodules, scales, hyperpigmented patches on both lower limbs, visible scattered scratches, no blisters, pustules, etc. (**c**) After treatment, a small number of nodules and papules were scattered on the shoulder and neck, reduced significantly compared with the former, and Scattered erythema and papules. (**d**) After treatment: scaly, hyperpigmented spots visible on both lower limbs, no erythema, breakouts, etc.

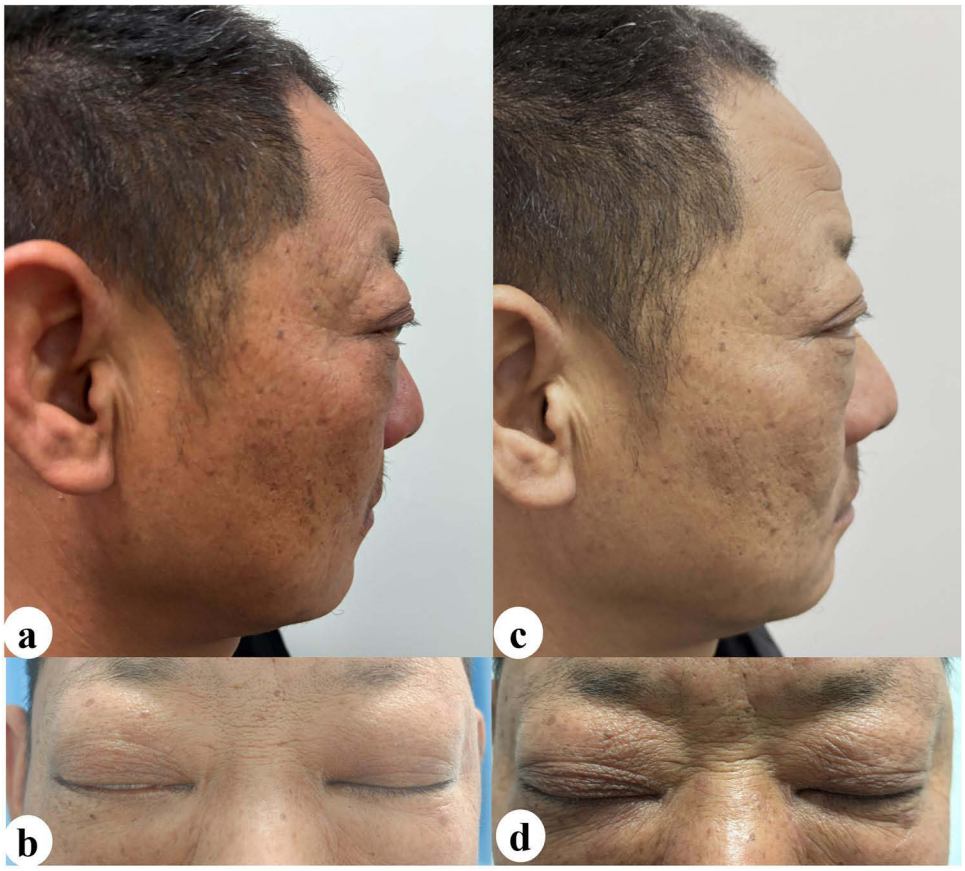

Figure 2 Ocular signs (**a** and **b**) Before treatment: Both eyes were seen to be protruding with incomplete closure; (**c** and **d**) After treatment: The protruding eyes were more strongly and significantly relieved, and no incomplete closure was seen.

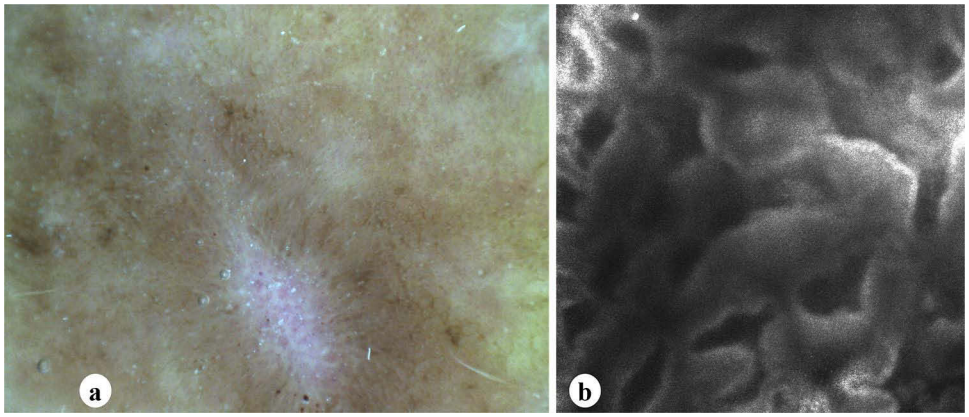

Figure 3 Dermoscopy with skin CT. (**a**) Dermoscopy (polarized x20): white scar-like structures with scattered punctate and bulbous blood vessels are seen in the center of the lesion, surrounded by brown hyperpigmented patches. (**b**) Dermatological CT: focal edema of the stratum spinosum, irregular hyperextension of the epidermal protuberance, uneven refraction of the pigmented ring of the basal layer, unequal amounts of medium to high refractive inflammatory cell infiltration visible in the dermal papillae.

dense infiltration of lymphocytes, and part of eosinophilic granulocytes infiltrated in the tissue, and immunohistochemistry (Figure 5a and c) demonstrated dermal fibroplasia with approximately 120–150 IgG4-positive plasma cells per high-power field (HPF), IgG4+/IgG+ plasma cell ratio >40% (Figure 5b and d). The patient had a history of allergic rhinitis and no notable family history.

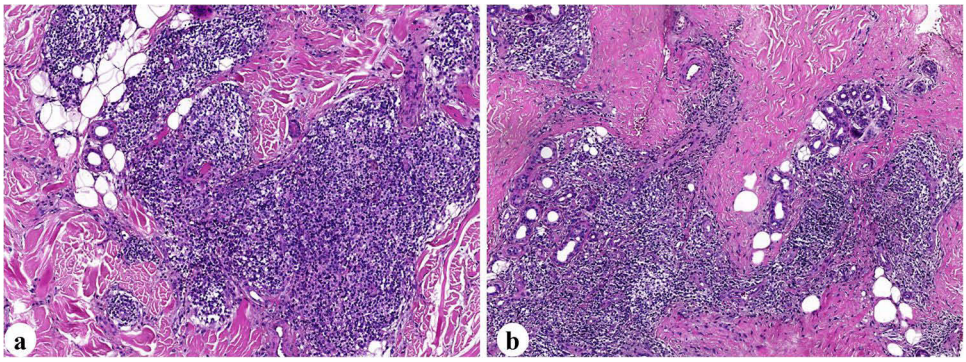

Figure 4 Histopathological examination of the skin (50×). (**a**) Shoulder lesion: mild hyperkeratosis of the epidermis, dilated capillaries within the dermis, peritubular lymphoid cells, and histiocytes were seen in a focal infiltration. Lymphoid cells, histiocytes, and some eosinophils are seen in a patchy infiltration in the subcutaneous fat lobules; (**b**) Lower leg lesion: the epidermis is approximately normal, with capillary endothelial cell hyperplasia and thickening of the walls of the capillaries in the dermis, and a focal infiltration of lymphoid and histiocytes in the peritubular area. A small amount of subcutaneous adipose tissue was seen, and lymphoid cells, histiocytes, and some eosinophils were seen in a sheet-like infiltration in its fat lobules.

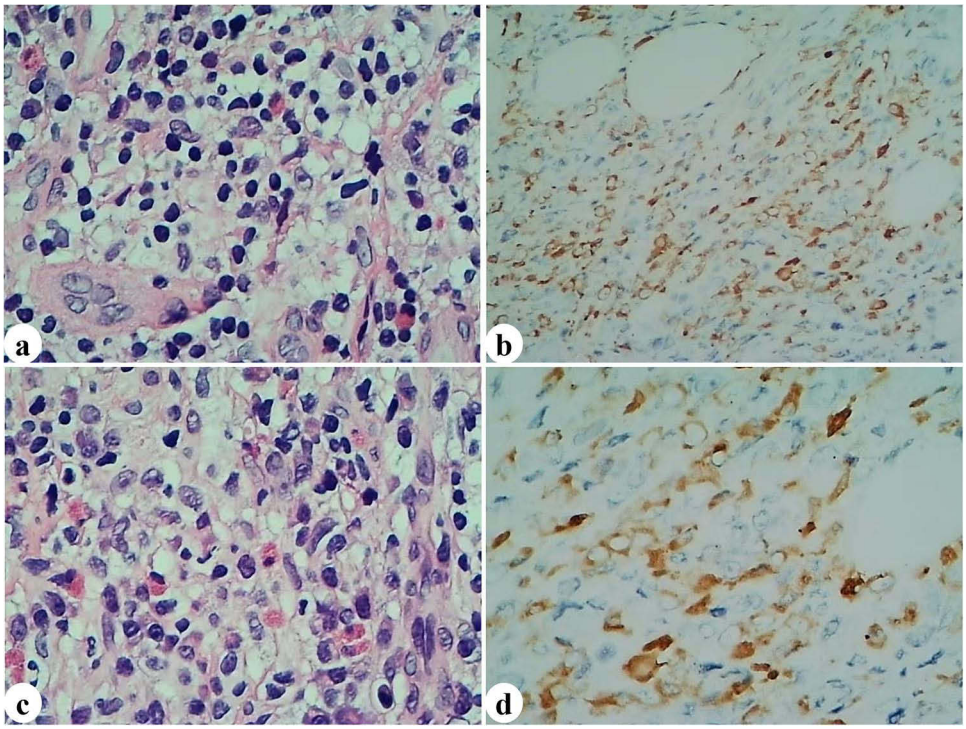

Figure 5 Immunochemical staining of skin tissue. (**a** and **b**) (20×), (**c** and **d**) (40×), Skin biopsy samples from the "shoulder": epidermis shows no abnormality, dermal fibroplasia, some small lymphocytes, plasma cells, and scattered eosinophils are seen around the blood vessels, and the number of IgG4-positive cells is about 120–150/HPF, IgG4+/IgG+ plasma cell ratio >40%.

Dermatologic specialist examination revealed generalized xerosis, with multiple scattered papules, nodules, follicular eruptions, scaling, and hyperpigmentation on the scalp, face, neck, back, and limbs. No blisters or pustules were observed (Figure 1a and b). Ophthalmologic examination showed incomplete eyelid closure in both eyes (Figure 2a and b) and conjunctival congestion (++), with no other abnormalities.

Diagnosis: Based on the 2011 Japanese Comprehensive Diagnostic Criteria for IgG4-Related Disease, the patient meets the criteria for a definite diagnosis. Clinical features include cutaneous nodules and orbital involvement. Serologic testing revealed elevated serum IgG4 levels (≥135 mg/dL). Histopathological examination demonstrated dense lymphoplasmacytic infiltration and dermal fibrosis, with IgG4-positive plasma cells exceeding 50 per high-power field (HPF) and an IgG4+/IgG+ plasma cell ratio greater than 40%. Malignancy and other immune-related disorders were confidently

excluded through comprehensive laboratory and imaging investigations. The final diagnosis is IgG4-Related Disease (IgG4-RD).

Differential Diagnosis: See the Discussion section for details.

Treatment: Systemic treatment: prednisone acetate 45mg orally qd, according to the patient's review results, it has been gradually reduced to prednisone acetate tablets 5mg qd; methotrexate 10mg orally qw. Topical treatment: cyclosporine eye drops, instilled in both eyes four times a day; polyethylene glycol eye drops, instilled in both eyes four times a day. The patient's ophthalmic symptoms improved significantly. The patient's ocular symptoms improved significantly. The patient's ocular symptoms improved significantly. The patient was also treated with topical hormone cream (Desonide Cream) twice a day. Therapeutic effect: After 4 months of treatment and follow-up, clinically, the cutaneous lesions on the shoulder, neck, and lower limbs were substantially reduced (Figure 1c and d), and the patient's proptosis symptoms improved significantly (Figure 2c and d). Besides, serum IgG4 levels returned to normal, decreased from an initial level of 24.60 g/L to 2.78 g/L, indicating significant remission of the condition. Maintenance treatment programme: Prednisone acetate tablets 5mg (1 tablet) each time, once daily. Subsequent adjustment of the treatment regimen based on review.

Discussion

The main manifestation of this case was atopic dermatitis-like skin lesions for 3 years and proptosis for 1 year, and the patient had a history of allergic rhinitis, so the diagnosis of atopic dermatitis was made in an outside hospital. At our hospital, the patient's serum IgG4 was found to be elevated, and orbital imaging suggested fibrotic lesions in the eye. Thyroid and other systemic diseases were excluded through appropriate testing. Combined with skin histopathology, immunohistochemistry, and multidisciplinary exhibition consultation, a diagnosis of IgG4-RD was established. The following is a discussion of the differential diagnosis for this case.

First, this case presented with chronic, progressive atopic dermatitis-like lesions accompanied by pruritus and a history of allergic rhinitis. Histopathology showed spongiosis, hyperkeratosis, epidermal hyperplasia, and inflammatory cell infiltration, which are consistent with Zhang's diagnostic criteria for adult atopic dermatitis.[6] However, typical atopic dermatitis does not present with proptosis, and the absence of significant IgG4-positive plasma cell infiltration in such cases further differentiates it from the current case. Some cases of IgG4-RD are also often associated with allergic rhinitis.[7]

Moreover, the proptosis observed in this case could easily be mistaken for Graves' ophthalmopathy (GO).[8] Both GO and IgG4-related ophthalmopathy (IgG4-ROD) can involve ocular symptoms, including eyelid swelling, extraocular muscle hypertrophy, and proptosis of the eyeballs etc. However, GO is primarily characterized by inflammatory changes in the extraocular muscles and orbital fat, which are typically associated with thyroid dysfunction—a condition excluded in this case. In contrast, orbital imaging and histology in this patient supported the diagnosis of IgG4-related orbital disease (ROD).

Additionally, the involvement of cervical lymph nodes and eosinophilia in this case has similarities with many hematologic diseases (eg, lymphoma, Castleman's disease, Erdheim-Chester disease, etc).[9] However, this patient exhibited no hematological abnormalities, and serum IgG4 levels in hematologic conditions are typically normal or only mildly elevated. Furthermore, lymphomas are characterized by lymphocyte proliferation, and plasma cell tumors by plasma cell infiltration, both of which differ histologically from the findings in this case. The patient's positive therapeutic response and prognosis further support the exclusion of hematologic malignancies.

Currently, the etiology of IgG4-RD remains unclear, although genetic predisposition and immune dysregulation are likely contributing factors. Various immune components—including autoantigens, B cells, T cells, macrophages, IgG4, and complement- are involved in its pathogenesis. The disease can mimic a variety of diseases, including malignant tumors, infections, and autoimmune diseases. It can involve multiple organs at the same time, such as the pancreas, salivary glands, lacrimal glands, and kidneys. In contrast, the involvement of the skin and the eye is relatively rare, which makes the disease more complicated to diagnose in the early stages of the disease.[10] Treatment options include glucocorticoids, immunosuppressants, and biologics (B-cell depletion therapy), and so far, glucocorticoids are still considered the first-line therapy for IgG4RD. However, this disease is prone to recurrence, and maintenance strategies remain a challenge. Some studies suggest that immunosuppressant-only regimens may reduce recurrence and side effects compared with steroid monotherapy.[11] In this case, the use of glucocorticoids combined with immunosuppressive therapy led to clinical improvement and normalization of serum IgG4. Notably, Close follow-up is necessary to monitor for relapse.

In summary, this case represents a typical early-stage presentation of IgG4-RD with predominantly nonspecific lesions in the skin and eyes. When multiple organs are involved, clinicians should conduct a thorough evaluation and consider early multidisciplinary consultation to ensure accurate diagnosis. To our knowledge, this is the first reported case describing the dermoscopic and skin CT manifestations of IgG4-RD lesions. But its primary manifestations are nonspecific and resemble those of other inflammatory dermatoses. Further accumulation of dermatoscopic and CT imaging data from a larger number of IgG4-RD skin lesions is necessary to systematically evaluate whether these modalities can offer disease-specific diagnostic clues. Such efforts may ultimately provide new perspectives for the diagnosis of this condition.

Conclusion

IgG4-RD can mimic a variety of diseases, through this case we found that this disease in addition to the reported diseases, but also mimic atopic dermatitis manifestations with intense itching makes it very easy to misdiagnose, missed diagnosis, This case not only comprehensively presents the clinical diagnostic approach for IgG4-related disease (IgG4-RD), characterized primarily by skin lesions and ocular symptoms, but also reports for the first time the dermatoscopic and skin CT imaging features of the affected skin areas. Although these features lack distinct specificity, they offer novel research perspectives for clinical investigations into this condition. The sharing of this case highlights that dermatologists encountering patients with multiorgan involvement should adopt a comprehensive approach and prioritize multidisciplinary collaboration to enhance diagnostic and therapeutic efficiency.

Ethics Approval and Consent to Participate

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images. Institutional approval for the publication of anonymized case details was granted by the First Affiliated Hospital of Kunming Medical University. This study was performed in accordance with the Declaration of Helsinki.

Consent for Publication

We have obtained written informed consent from the patient for the publication of this case series and associated images. All authors have reviewed and approved the final manuscript for submission.

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Disclosure

No potential conflict of interest was reported by the authors.

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