

A Case of Follicular Atresia Triad Combined with Necrotising Fasciitis and Squamous Carcinoma of the Lower Limbs

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Abstract: Follicular atresia triad, also known as paradoxical acne (FOT), is a rare and serious clinical syndrome in dermatology, mainly manifested by coalescing acne, purulent perifolliculitis of the head, and suppurative sweating inflammation, and FOT combined with necrotising fasciitis of the lower limbs and squamous cell carcinoma is rare both at home and abroad. In this article, we share the clinical data and treatment of a patient with follicular atresia triad and necrotising fasciitis and squamous cell carcinoma of the left lower limb for your reference.

Keywords: follicular atresia triad, necrotising fasciitis, squamous cell carcinoma

Introduction

Follicular atresia triad (FOT), also known as paradoxical acne, is a recurrent, chronic, inflammatory, hereditary dermatological disorder due to follicular atresia resulting in involvement of the sebaceous units of the follicles and¹ is characterised by painful, deeply penetrating, inflammatory lesions followed by abscesses, sinus tracts and scarring. They mainly include head abscesses perifolliculitis, suppurative sweatitis, and coalescing acne vulgaris. Hyperkeratosis at the follicular funnel site may be important in the pathogenesis of FOT. Hyperkeratosis at the follicular funnel site causes blockage, swelling and rupture of the hair follicle.² Although the exact pathogenesis of FOT is unknown, genetics, endocrinology, bacterial infections, obesity, and smoking are considered to be risk factors for the development of the disease. Furthermore,³ miRNAs are thought to play a central role in ovarian follicular apoptosis.

Necrotising fasciitis is a rare but serious infection of the subcutaneous tissue and skin fascia.⁴ It can occur anywhere in the body, but the most common sites are in the perineum, lower extremities, postoperative wounds, and the abdomen, mouth, and neck.⁵ Trauma due to surgery, burns or soft tissue infections is a common cause of necrotising fasciitis, and other predisposing factors to infection include injection drug use, immunosuppression, diabetes, advanced age, peripheral vascular disease, obesity, alcoholism and malnutrition, all of which can play a role by increasing susceptibility to infection, and localised tissue damage, with diabetes being one of the most common predisposing underlying conditions.⁶ Necrotising fasciitis progresses rapidly and can develop into sepsis if not treated promptly. Early diagnosis, sensitive antibiotics, and thorough surgical debridement are the keys to treating necrotising fasciitis.

Squamous cell carcinoma of the skin is a common cancer of the skin in humans, and its incidence is increasing year by year.⁷ Risk factors for its development are currently recognised to include advanced age, male gender, immunosuppression, and a history of actinic keratosis.⁸ Surgery is by far the most common treatment for squamous cell carcinoma of the skin, but it is extremely mutated and survival rates drop dramatically when metastasis occurs.

The above three diseases are also very difficult to develop alone, and it is rare for all three diseases to occur in one patient at the same time, so I would like to share the following case for peer reference and discussion.

Clinical Information

The patient is a 31-year-old man with “nodules, papules, and cysts with pain on the head, face, neck, and back of the shoulders for 10 years, aggravated for 2 years”. Admission. The patient started to have scattered nodules, papules and cysts on the forehead and chest with mild pain 10 years ago without any obvious triggers, and after using topical medication by himself (details unknown), the treatment effect was not good, and the rashes were progressively aggravated and increased rapidly, spreading to the head, behind the ears, the back of the shoulders, and the neck, with symmetrical distribution, accompanied by pain, and some of the rashes were fused, and pus appeared at the cysts, which then formed a scar, and the patient was repeatedly treated at the local hospital in Chaozhou, and was diagnosed with Acne vulgaris was diagnosed as “acne vulgaris” and was treated with traditional Chinese and western medicine (details unknown); the rash was stable during the medication period, but repeated after the medication was discontinued. 7 years ago, scattered subcutaneous nodules, plaques, and pustules began to appear in both axillae of both axillae without any obvious triggering factors, and the surface of the skin began to break down, pus flowed and fistulae, ulcers, and stripes appeared, accompanied by pain, and he went to the Second Affiliated Hospital of Sun Yat-sen University for medical treatment. The Second Affiliated Hospital of Sun Yat-sen University, diagnosed as “follicular atresia triad”, and given “methylprednisolone 16mg / d ((details unknown), combined with isotretinoin capsule (10mg tid)” treatment for 3 years, the rash is basically stable, with occasional new eruptions. In 2019, the patient discontinued his medication on his own, but his condition was largely stable 2 years ago, no obvious cause of the original rash site once again appeared similar rash, at the same time the trunk, bilateral groin once again appeared nodules, papules, cysts, accompanied by pain, the local rupture appeared pus, and then the formation of scarring, did not carry out standardized treatment, all to the traditional Chinese medicine taken orally (specifics are not available), the rash did not improve, the pain is obvious, so in order to seek further treatment by the clinic in order to “Follicular atresia triad” was admitted to our hospital on 16th November, 2023. The patient had a history of abnormal blood glucose during the hormone therapy regimen, and had taken oral metformin and acarbose for blood glucose control at the local hospital (details unknown). The patient noticed a new coin-sized erythema on the left calf about 10 days prior to admission, which rapidly increased in size and was well defined, with several pusheads visible on the erythema, elevated skin temperature, and effusion of pus. We performed a specialist examination of the patient after his admission to the hospital. Multiple follicular papules, elongated nodules and light red cysts with smooth and tense surfaces were seen on the posterior occipital region, with peripheral fistulas and pus discharge when pressed, and hair loss at the lesions; multiple depressed keloids and keloidal scars were seen on the face, neck, and back of the shoulders, and scattered nodules on the back, some of which were covered with pus dots; multiple hard subcutaneous nodules were seen on the axillae and groins of the bilaterals and striated proliferative scarring, clustered and fused into a sheet, on which fistulae and submerged irregular ulcers were visible. A large infiltrative erythema is visible on the left calf, well demarcated, with scattered pusheads on it. Pain VAS score: 7. The patient denied previous medical history of hypertension, coronary artery disease, nephropathy, infectious diseases such as hepatitis, tuberculosis, surgical history and blood transfusion. The patient’s maternal grandfather and uncle had a history of diabetes mellitus, and denied any other family history of hereditary diseases and tumours.

Aspects of the Follicular Atresia Triad (FOT)

Abscessive Exfoliative Perifolliculitis of the Head

Scattered deep folliculitis and perifolliculitis occur in the hair area, showing inflammatory nodules, cysts and abscesses, which penetrate and penetrate each other under the scalp, forming sinus tracts, accompanied by pus overflow and bleeding, and by squeezing a lesion, pus may flow from many sinus tracts in the form of sieve holes (Figure 1).

Polymerised Acne

Unlike Acne vulgaris, Acne vulgaris occurs on the cheeks, back and buttocks. It starts slowly with pimples, papules, pustules and cysts; the lesions gradually merge and become cysts, which are soft and fluctuating to the touch, and when they burst, they may discharge foul-smelling pus or mucous slurry, forming sinus tracts, which communicate with each other underneath the skin, and forming atrophic or hyperplastic scars on the skin (Figure 2). A biopsy of the dorsal skin tissue was performed after admission to the hospital (Figure 3).



Figure 1 (A) Scattered folliculitis, small cysts on the head.(B) Sieve-like sinus tract in the neck.



Figure 2 (A) Facial acne vulgaris lesions.(B) Scattered atrophic scarring on the back.

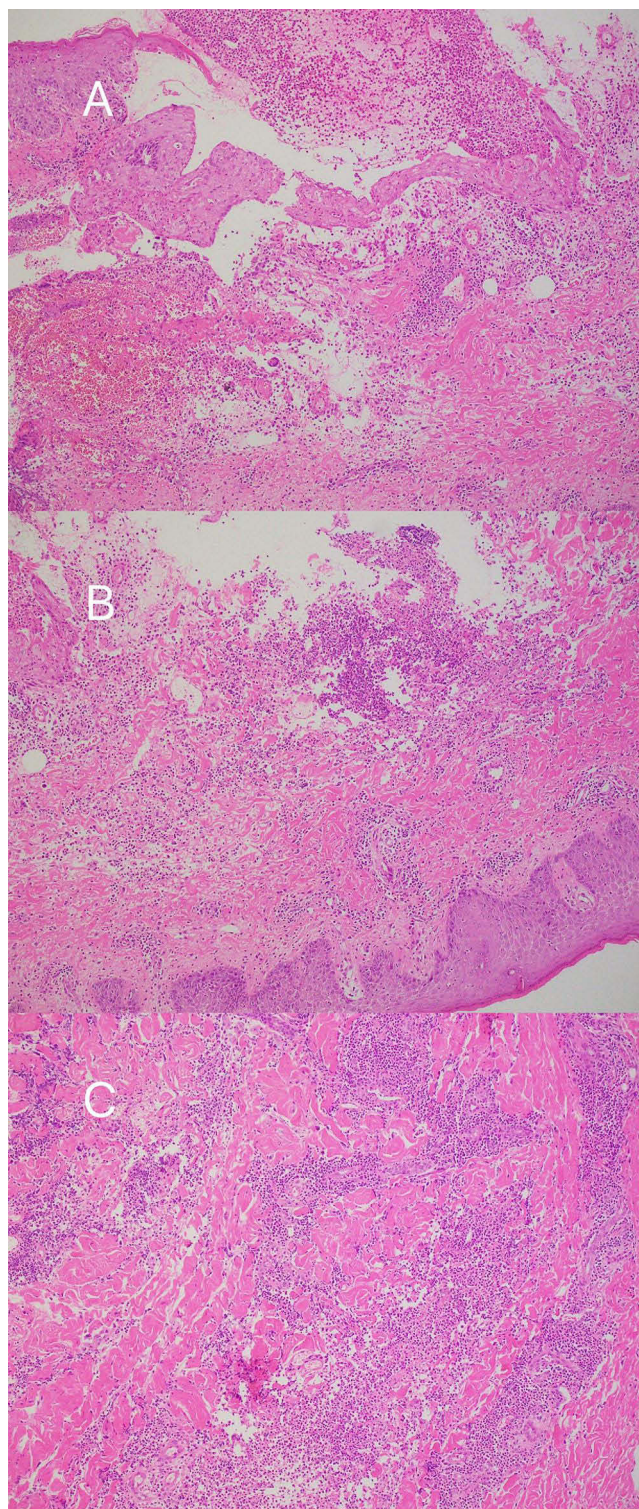


Figure 3 (A–C) (Dorsal skin mass) The skin tissue was sent for epidermal hyperkeratosis and hyperkeratosis, hypertrophy of the stratum spinosum, spongy oedema, infiltration of inflammatory cells such as lymphocytes, plasma vesicles, and neutrophils in the dermis and around the appendages, and abscess formation was seen.

Hidradenitis Suppurativa

It occurs most often in areas where sweat glands are distributed, such as the axilla, anus and around the external genitalia, and may involve the buttocks (Figure 4A and B). The causes of HS are complex and are thought to be related to factors



Figure 4 (A and B) Localised erythema and swelling with paradoxical severe pain in the left leg.

such as obesity, abnormal blood sugar levels, genetics, and other drug triggers.⁹ Follicular occlusion followed by follicular rupture has been shown to be crucial to HS development, leading to immune response activation, and resulting in typical clinical HS lesions. Chronic suppurative sweating adenitis is characterised by deep abscesses draining pus outwards through sinus tracts, skin breakdown and formation of irregular scarring, especially around the pustule, anus and external genitalia with many abscesses, sinus tracts, pus and blood discharge, and a high degree of swelling of the soft tissues;¹⁰ the sinus tracts may merge into a sheet, with extensive subcutaneous necrosis and ulceration of the skin, which can be extended to the perianal area, scrotum, labia, sacrococcygeal area, buttocks, lumbar area and femoral area, and often leads to Sclerosis and scar formation (Figure 4C).

Necrotising Fasciitis Aspects

Necrotising fasciitis (NF) is a rare and serious infection of the skin and fascial tissues, characterised by widespread and rapid infection of the subcutaneous soft tissues, which can spread throughout the body within a short period of time, and in severe cases, it can lead to systemic inflammatory response syndrome, shock and death. Before the patient was admitted to the hospital, there was a skin lesion on the left lower leg, which was not consistent with the skin lesion manifestation of intense pain and rapid progression of the disease made us highly suspicious of necrotising fasciitis (Figure 5), although the patient came to the hospital for the treatment of follicular atresia trichotillomania, but the skin lesion of the left lower limb was suspected to be necrotising fasciitis, and the disease progressed quickly, the condition was urgent and serious, and even serious or even life-threatening, so priority was given to the treatment of necrotising fasciitis, and the treatment of necrotising fasciitis was postponed for a while.



Figure 5 (A) Chronic suppurative sweating in the axilla and formation of hyperplastic scarring. (B) Chronic suppurative sweating on the inner thighs. (C) Multiple sinus tracts and scar formation on the buttocks.

Therefore, priority was given to the treatment of necrotising fasciitis, and the treatment of the follicular atresia triad aspect was postponed. We immediately improve the blood sampling, skin biopsy, MRI of the affected limb, the left calf biopsy suggests (Figure 6). Immunofluorescence results: C3(-), IgA(-), IgG(-), IgM(-). MR (3.0T) scanning of the soft tissue of the left lower leg suggests: 1 Multiple abnormal signal shadows in the bone marrow cavity of the left upper and lower tibia and the inner and outer condyles of the femur, consider femoral infarction; 2. Oedema of the subcutaneous fat plus interstitial space in the middle and lower portion of the left lower leg, consider an infectious lesion, combine with the clinic please. After excluding the possibility of other infections such as cellulitis, the intraoperative exploration and debridement were perfected as soon as possible in the first instance, which revealed a dark grey fascial swelling, dilute exudate without obvious suppuration, as well as an easy separation of the tissue level by blunt dissection. This further validated our diagnosis and intraoperative bacterial and fungal cultures as well as histological examination were refined for further evidence support. In the meantime, an empirical antibiotic regimen was used, along with multidisciplinary cooperation by requesting an endocrinology consultation to adjust the glucose-lowering regimen, a dietetics consultation to guide the nutritional regimen, and a pharmacy department consultation to guide the use of antibiotics. After several debridement procedures and VSD negative pressure suction, the infection was controlled and finally epidermal graft repair was performed (Figure 7).

Squamous Cell Carcinoma Aspects

Squamous cell carcinoma of the skin is one of the common malignant tumours of the skin, and its specific pathogenesis has not yet been clarified,¹¹ with common triggers such as genetic factors, ultraviolet irradiation, and repeated inflammatory stimulation, etc. Due to its increasing incidence and high recurrence rate, it has attracted more and more attention from the public. On November 27, 2023, intraoperative histopathology of necrotizing fasciitis in the left calf (Figure 8) suggested that highly differentiated squamous cell carcinoma is considered. There is no family history of

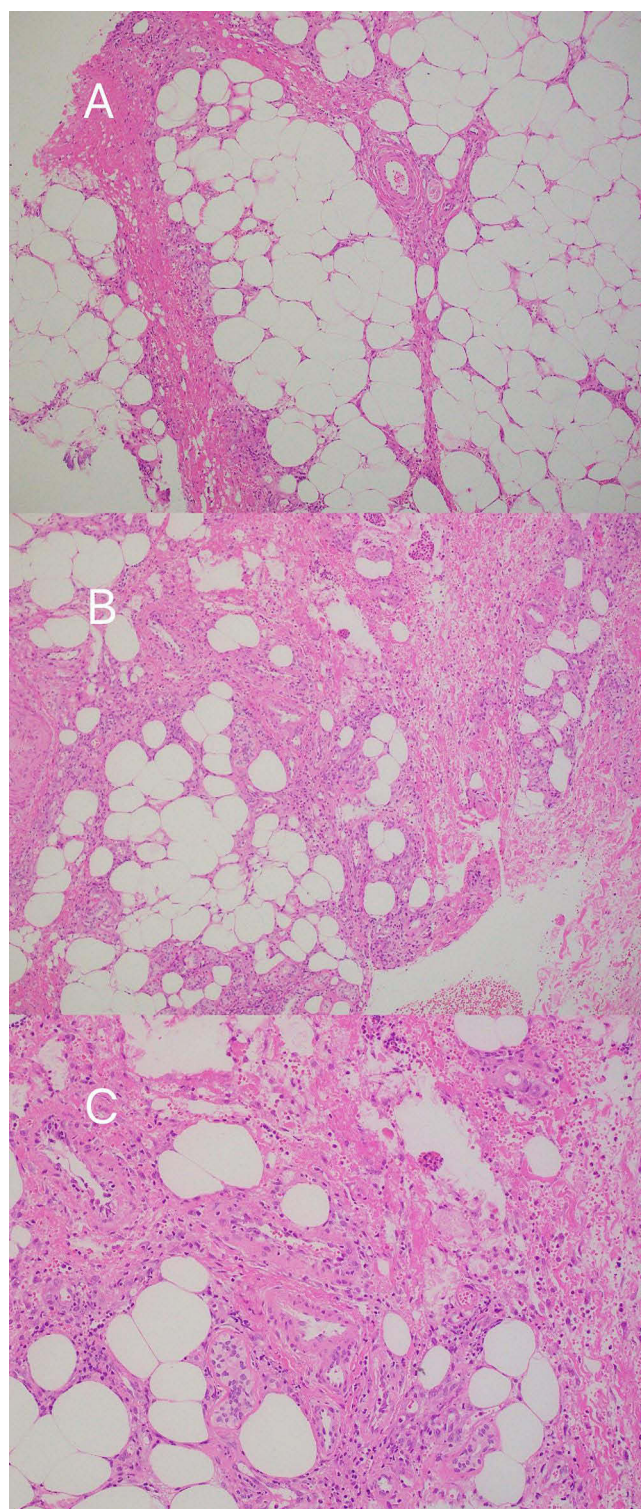


Figure 6 (A–C) (Skin tissue of the left lower leg) Sent skin tissue with epidermal hyperkeratosis and hyperkeratosis, hypertrophy of the stratum spinosum, spongiotic oedema, inflammatory cellular infiltration of lymphocytes, plasma cells, neutrophils and other inflammatory cells in the dermis and around the appendages.

squamous cell carcinoma in this patient. The exact cause of the patient's pathogenesis has not yet been clarified, and it is considered that it may be related to a state of immunosuppression due to prolonged chronic inflammatory stimulation of the FOT and prolonged oral hormone therapy.

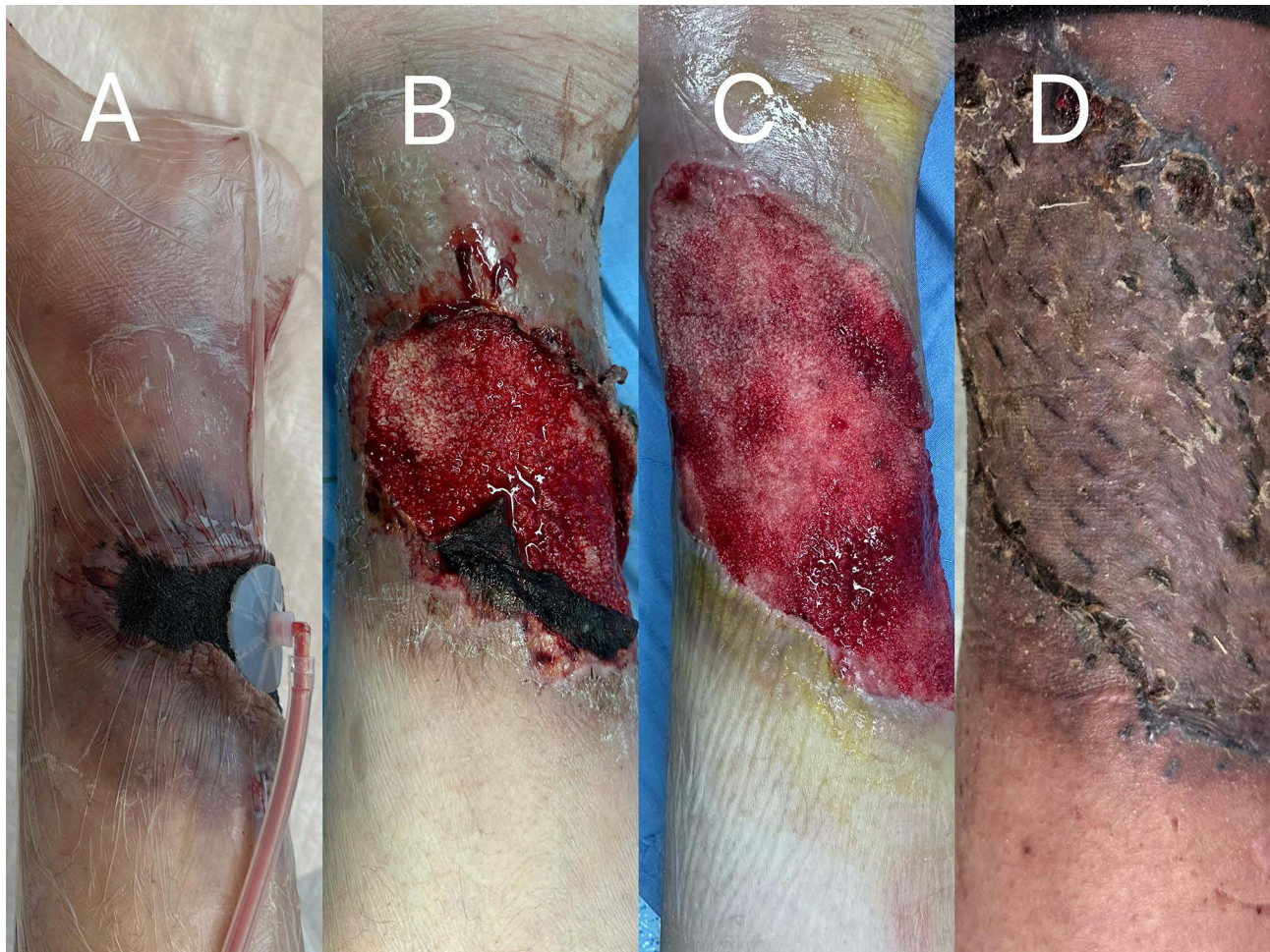


Figure 7 (A) VSD negative pressure suction therapy. (B) Removal of VSD negative pressure suction device. (C) post-traumatic surgery. (D) Recovery period after epidermal grafting.

On 4 December 2023, during the third debridement in again took 4 cut margins of the skin lesion upper, lower, left, right and the central basal part of the tissue was sent for examination, the pathology results (Figure 9) suggested that consistent with postoperative changes and did not see clear cancer residues.

Analysis and Discussion

Follicular atresia triad (FOT) and necrotizing fasciitis are rare but serious diseases, and the combination of these two diseases with squamous cell carcinoma is rare both at home and abroad. There is no uniform solution for FOT, and the treatment is difficult and prolonged, and the disease is recurrent and difficult to be relieved naturally in some patients, which can be prolonged for a long period of time,² and is easy to be combined with serious infections in high-risk groups such as diabetes mellitus.

With regard to necrotizing fasciitis, after the patient was admitted to the hospital, we clarified the diagnosis as soon as possible, empirically used broad-spectrum antibiotic regimen such as levofloxacin, and continuously adjusted the antibiotic regimen according to the results of the drug sensitivity test and changes in the condition, and at the same time, we invited the Department of Pharmacy, Orthopaedics, Endocrinology and other multidisciplinary cooperation to guide the specialised medication regimen. Despite the early surgical debridement and continuous improvement of antibiotic regimen, the patient still suffered from recurrent high fever after surgery, and the continuous inflammatory consumption and use of high-level antibiotics also led to the patient's poor appetite and the complication of hypoproteinemia, and the patient's condition was stabilised after several debridement surgeries and the use of antibiotics and

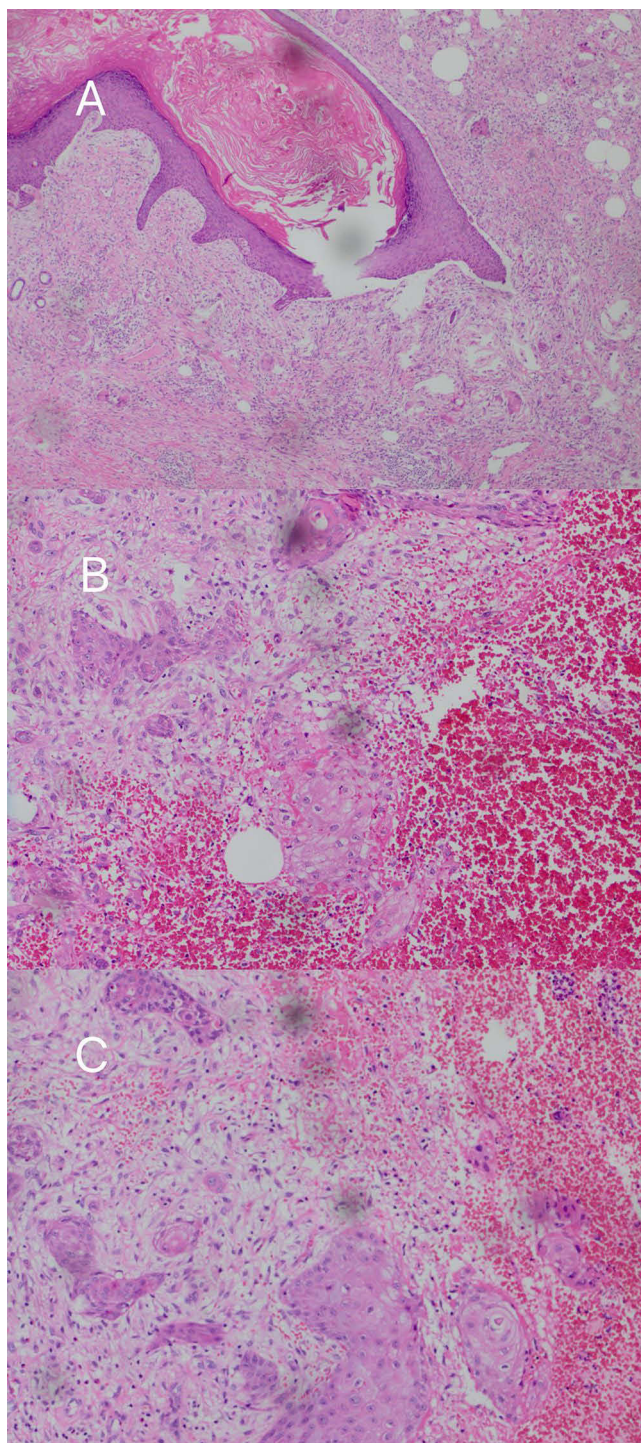


Figure 8 (A–C) (Skin of the left lower leg) Focal epidermoid cyst rupture with infection and multinucleated giant cell reaction was seen in the skin sent for examination, focal squamous epithelial infiltrative growth, scattered cellular nests were seen in the interstitium, and mild cellular heterogeneity was seen.

nutritional supportive therapy. Postoperative drug sensitivity tests and culture of pathogenic bacteria did not identify the causative organisms, and the cause of recurrent hyperthermia was not clearly identified, so the patient was temporarily considered to be an outbreak of postoperative inflammatory storm.

In the case of follicular atresia triad combined with necrotising fasciitis, the treatment of FOT was suspended due to the rapid progression and severe condition of necrotising fasciitis. On the one hand, the antibiotic regimen used in the

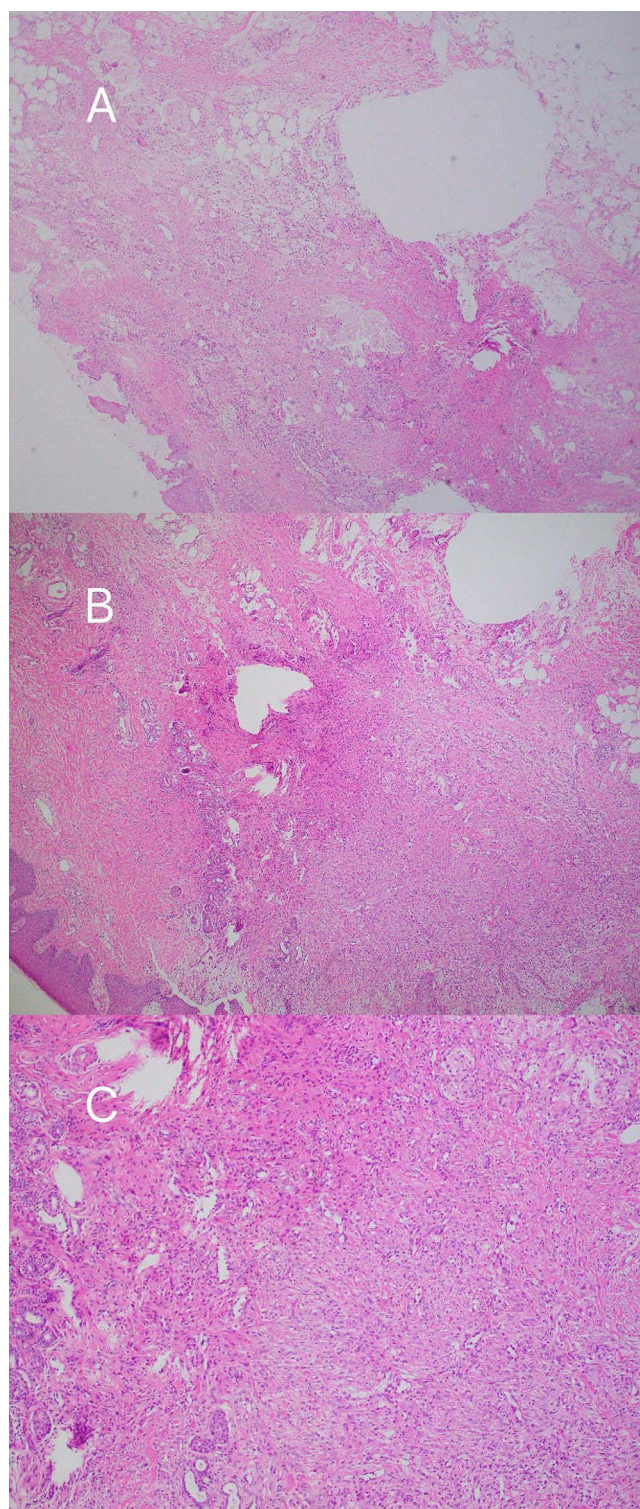


Figure 9 (A–C) (Medial left calf lesions (top) and (bottom), lateral left calf lesions (top) and (bottom), and central left calf lesion) The skin tissue sent for examination showed fibrotic tissue hyperplasia with inflammatory cell infiltration of lymphocytes, plasma cells, neutrophils, etc., and a multinucleated giant cell reaction was seen.

treatment of necrotising fasciitis can control the skin inflammation in the FOT aspect to a certain extent, and on the other hand, at the same time, we also use gentamicin irrigation and topical closure of tretinoin for sinus tracts and cysts with a lot of oozing pus.

For squamous cell carcinoma, after several surgical resections and sending specimens for pathological examination, although the pathological report of the last specimen did not report squamous cell carcinoma, the patient was young and had serious conditions in terms of FOT, with the presence of chronic inflammatory stimulation and the need for long-term oral hormone therapy, so a long-cycle follow-up should be established and the patient was advised to follow up regularly to keep an eye on the progress of the disease.

Conclusion

For this kind of long-term chronic inflammatory skin lesions and patients with the condition, we should be highly vigilant and improve the pathological examination in time to exclude the possibility of skin tumour. For patients with squamous cell carcinoma after excision, due to the possibility of jumping growth of squamous cell carcinoma, the recurrence rate has gradually increased in recent years, so we should establish a long-term follow-up and follow-up mechanism and pay attention to the exclusion of metastatic foci in other parts of the body. The pathogenesis of these three diseases is complicated, and there is no clear pathogenesis yet, and the simultaneous development of the three diseases is even more rare, and the existence of the same risk factors may be one of the triggers for the development of the disease, such as blood sugar abnormality. The appearance of FOT on the patients has caused great disturbance to their life, and it is a great challenge for us to help patients to repair their appearance affected by FOT, but the prerequisite for repairing the appearance of FOT is the patients themselves! However, the prerequisite for repairing FOT is that the patient's chronic inflammation is under control, and long-term oral hormone therapy has many side effects. Biologics are a hot direction in the treatment of skin diseases in recent years, and we are looking forward to the availability of suitable biologics to help patients with FOT to recover as soon as possible.

Ethical/Copyright Statement

The article has been approved by the institution (Guangdong Provincial Hospital of Traditional Chinese Medicine) for the record, and informed consent has been obtained from the patient for the disclosure and publication of all information.

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