# Weber-Christian disease, A Rare disease, and Successful Treatment Using Prednisolone and Colchicine:

## A Case Report from Nigeria and Literature Review

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**Abstract**

Weber Christian disease (WCD) is a rarely reported medical condition. It is an idiopathic lobular panniculitis, which is characterized by subcutaneous nodules, inflammatory cells in the fat lobules, and systemic symptoms. The literature has a handful of reports of WCD from different regions of the globe since the first descriptions by Pfeifer in 1892 and later in the 1920s by Weber and Christian. We report the first Nigerian case from the South East region of WCD. Being a rare entity, there were challenges with arriving at a diagnosis and successful treatment eventually with colchicine and low-dose prednisolone. Hence this report.

**Keywords:** Weber Christian Disease, Treatment, Colchicine, Prednisolone

**Traitement de la maladie de Weber-Christian par la prednisolone et la colchicine : à propos d'un cas au Nigeria et revue de la littérature**

**Résumé**

La maladie de Weber Christian (WCD) est une affection rare. Il s'agit d'une panniculite lobulaire idiopathique, caractérisée par des nodules sous-cutanés, des cellules inflammatoires dans les lobules graisseux et des symptômes systémiques. La littérature rapporte une poignée de cas de WCD provenant de différentes régions du globe depuis les premières descriptions par Pfeifer en 1892 et plus tard dans les années 1920 par Weber et Christian. Nous rapportons le premier cas de la région Sud-Est de la WCD du Nigéria Poser le diagnostic est difficile ainsi que sa prise en charge, d'où l'intérêt de notre cas qui a eu une évolution favorable avec la colchicine et la prednisolone à faible dose.

**Mots clés:** Maladie de Weber Christian, traitement, colchicine, prednisolone

## Introduction

Weber-Christian disease (WCD) was first mentioned in 1892 AD by Victor Pfeifer.[1] It was also described in 1925 by Weber[1] and later by Christian. It is an idiopathic lobular panniculitis, which is characterized by subcutaneous nodules, inflammatory cells in the fat lobules, and systemic symptoms. Weber-Christian disease is a rare condition in adults all over the world, and even rarer in Africans.

There are few reports of WCD. In one cohort,[2] a total of 13 WCD patients' data were analyzed. Of the thirteen patients diagnosed with WCD, the majority were female, male to female ratio was 2:11, with a mean patient age of 50.1 years.[2] White and Winkelmann's 1998 case record review of WCD at the Mayo Clinic found only 30 documented panniculitis cases in 28 years between 1960 and 1998.[3] There have been reports in the past of a lot of misclassifications of panniculitis.[2-5]

This rarity of reported cases may be due to poor understanding of WCD and failure on the part of previous investigators, medical practitioners, and authors to follow clear guidelines as originally described by Weber and Christian for diagnosis of WCD and thus inability to differentiate it from other

closely related panniculitis. There is still ongoing debate on whether WCD is a clinical entity or not. The work of White and Winkelmann made a significant attempt at a clearer uniform classification for this group of inflammatory disorders with primary inflammation of the subcutaneous fat as a common denominator.[3] However, none of their suggested classification or final clinicopathologic diagnoses fit into the original clinicopathologic description of WCD by Weber and Christian.

Wick also published an extensive summary attempt at the classification of the panniculitides because of these controversies surrounding Panniculitis.[5] However, he did not describe any finding of recurrent fever simultaneously with non-suppurative panniculitis in the patients. In that classification, none of the defined sub-classes of panniculitis fits into the original classification by Weber and Christian for WCD. From the report of Idiopathic Lipoatrophic panniculitis of children by Iliana et al,[6] it can be deduced that none of the subclasses of panniculitis, as described by Wick, fits the Idiopathic Lipoatrophic panniculitis of children in that case report, and can best be summarized as an attempt to rename WCD in a child. The combination of recurrent fever with other constitutional upset and idiopathic non-suppurative lipophagic panniculitis is the difference between erythema nodosa and WCD.

We looked at the available literature and the case reports and did a critique of the details of how the previous authors (that reported WCD) arrived at the diagnosis of WCD and found that many of these reported cases in literature still fitted into the original description of WCD. Thus, this eponym WCD is still relevant in the light of available literature and should still be used. The incidence and prevalence of WCD are unknown both in the United States and internationally. Many physicians worldwide have only seen one or a few cases in a lifetime[1,2] and older physicians in Nigeria said they have not made this diagnosis in their practice of more than 20 to 40 years (personal communication).

There are still challenges with proper evaluation, diagnosis, and treatment. There are currently no established treatment guidelines. We, therefore, decided to add to the available literature this interesting case of a young woman who had lots of diagnostic and treatment challenges. We believe this rare case that responded to Colchicine and low-dose prednisolone, rarely reported, merits report being the first to be reported from Nigeria. We also reviewed available literature and brought an update on the latest trend about WCD. Hence this case report and literature review.

## Case Summary

Our patient is a 21-year-old tertiary student from Imo State Nigeria, Igbo by tribe, whose first presentation to the University of Nigeria Teaching Hospital, Enugu (UNTH) was on the 5th of June 2014. She presented with vomiting, intermittent high-grade fever, fatigue, weight loss, anorexia, bilateral leg swelling, painful red macules, papules, and painful subcutaneous nodules on her arms, legs, buttocks, and anterior abdominal wall. The subcutaneous swelling started with the left arm, and then progressively spread over the hands, forearms, arms, ankle, abdomen, and lower limbs. There was transient redness over the sites of the painful subcutaneous swellings.

There was no history of cough, urinary symptoms, vaginal discharge, abdominal pain, diarrhea, sore throat, central nervous systems and other systems complaints. She is not known to have Hypertension, Diabetes mellitus, or Sickle cell disease. She had been seen by physicians earlier before her referral to UNTH. She was first reviewed and managed by the Dermatologist because she presented with fever and red painful swellings on the skin. Histology was done. Her working diagnosis was Panniculitis and treatment given was an escalated dose of prednisolone but no remission. She was thereafter referred to and reviewed by a musculoskeletal physician outside Southeast, Nigeria.

The working diagnosis was Dermatomyositis / Systemic lupus erythematosus and the tests requested were Antinuclear antibodies (ANA) screen, Extractible Nuclear Antibodies (ENA), Serum Creatine kinase, serum aldolase, and lactate dehydrogenase. Drugs commenced were firstly, escalated doses of Methotrexate, folic acid, and prednisolone but with no improvement. She had a later review via telemedicine and was started on Azathioprine 50mg thrice daily and Hydroxychloroquine 200mg daily. With this there

was no significant improvement in her clinical state, hence her referral to the Rheumatology clinic UNTH for further evaluation and management.

On examination, she was found to be chronically ill-looking and lethargic. She had pallor and bilateral pitting leg edema. She was febrile with a temperature of 38.6$^0$C. She had no jaundice or lymphadenopathy. Examination of the skin revealed discrete exquisitely tender plaques and subcutaneous nodules, scars, and a few superficial ulcerations on the forearms, buttocks, and thighs. She had tachycardia but her blood pressure was 110/50 mmHg. She had firm, mildly tender, smooth surface, hepatomegaly. The musculoskeletal system, nervous system, and chest examinations were normal. The working diagnosis was Panniculitis / Undifferentiated Connective Disease.

She had pulse IV methylprednisolone 500mg daily for 3 days, intravenous (I.V) antibiotics, and was started on Hydroxychloroquine and leflunomide. She showed remarkable improvement clinically and 2 weeks later was discharged home on oral low-dose prednisolone, Hydroxychloroquine, and leflunomide.

This improvement was short-lived and she represented 2 months later with another major flare with facial and lower limbs edema, reduction in urine output, crops of panniculitis lesions, pyrexia, anorexia, fatigue, abdominal pain, hepatomegaly, and elevated Blood Pressure. Her urinalysis showed proteinuria only and the renal function test showed mild azotemia. She was managed with pulse 2 weekly intravenous cyclophosphamide 500mg x 6 doses, pulse intravenous soluble methylprednisolone 500mg daily for 3 days, intravenous frusemide, and thereafter maintained on oral methylprednisolone, azathioprine, dapsone, and Hydroxychloroquine. She improved and was back on her feet.

However, in May 2015, she had another major flare with vomiting, intermittent high-grade fever, painful red macules, papules, and painful nodules on her arms, legs, buttocks, and anterior abdominal wall, fatigue, weight loss, and anorexia, and bilateral leg swelling. She was given a subcutaneous injection of Etanercept (Enbrel) 50mg weekly for three weeks in addition to oral Methotrexate 7.5mg weekly, folic acid 10mg weekly, and Prednisolone 15mg daily. Her clinical state improved but this was short-lived; in June 2015, after completing the last dose of Enbrel, she became very ill again.

The decision to repeat the serology tests and repeat the biopsy for histology was made. Serologic tests (Rheumatoid Factor, Anti-Cyclic Citrullinated Peptide, ANA / CTD screen, ANCA) and serum lipase tests came out negative and normal respectively, but the histology was highly suggestive of Panniculitis. Hence the diagnosis of Idiopathic lobular Panniculitis (Weber-Christian disease; WCD) was made. She was started this time only on Colchicine and 10mg daily of oral prednisolone and calcium and vitamin D supplements and all other previous medications were withdrawn.

She had a sustained remission of WCD to date. She later developed end-stage renal failure that required haemodialysis in 2020 and had a successful kidney transplant in Europe in 2022. Figures 1,2 and 3 show the pictures of the patient: spared face and healing panniculitis on both arms, patient's both healing active panniculitis on the right arm, and patient's active panniculitis on the left arm respectively.

## Discussion

Weber-Christian disease is a rare disease. It is one of the diseases that share a common denominator, panniculitis. Panniculitis is a term for localized inflammation within the subcutaneous fat tissues. Distinctively it is called Weber-Christian disease when it is an idiopathic, non-suppurative aggregate of inflammatory cells within the fat lobules in the subcutaneous tissues and with constitutional symptoms, particularly fever.

Weber-Christian disease is rarer in children. At least two studies suggested its rarity in the population.[6,7] In Brazil, over 20 years (1983-2002) only 35 pediatric and adolescent cases of panniculitis were found, with only 6 cases met the description for Weber-Christian disease.[6] White and Winkelmann's 1998 case record review of Weber-Christian disease at the Mayo Clinic found only 30 cases in 28 years between 1960 and 1998.[3] However, at a critical review, many were found not to be definite WCD, but other diagnoses such as factitious panniculitis, erythema nodosum, and leukemia.

We presented a young woman, 21 years old, who developed symptoms which were suggestive of WCD but because of the rarity of this WCD, it was not thought of at the outset despite visits and reviews by many physicians. The onset was earlier than most reported cases in adults. The skin manifestation usually makes consult to a dermatologist an early consideration which was the case with our patient. This diagnosis was missed because constitutional symptoms were not considered. We conducted a thorough review of the literature for Nigerian cases and did not find any reported cases. Additionally, discussions with experienced physicians yielded no recollection of encountering or managing cases of WCD in Nigeria. This case may represent the first reported instance of WCD in Nigerians.

Weber-Christian disease is characterized by cutaneous lesions that appear in crops and constitutional symptoms that may resolve within weeks to months[6]. The skin lesions are often symmetric in distribution, and the thighs and legs are most commonly involved. Individual nodules may regress over a few weeks. The most commonly reported constitutional symptoms are fever, malaise, weight loss, arthralgia, and myalgia. Where the skin lesions appear over or around a joint, the patient may report arthralgia; and lesions over the thighs could be reported as myalgia.

This is often a cause of confusion and may lead to the generation of a strong differential diagnosis of more common causes of arthralgia and myalgia such as Systemic lupus erythematosus and dermatomyositis. This was the case with our reported patient. She historically led us initially into thinking it was arthralgia and myalgia. However, a careful examination of the skin and musculoskeletal revealed the tenderness was from the involved skin as in panniculitis which has remarkable non-tenderness of non-involved skin. Nodules may also appear, which are usually symmetric and measure approximately 1-2 cm, in the lower and upper limbs and less frequently trunk and face.

Our patient presented with involvement of both her upper and lower limbs, with more pronounced severity in the arms. The lesions appeared in crops, and resolved, with residual depressed scars. Some authors have reported brown oily liquid discharge from the lesions[8] but this is absent in our patient. Such oily discharge has been attributed to liquefaction necrosis in the subcutaneous fatty layer of the skin. Abdominal pain, hepatomegaly, splenomegaly, and evidence of renal system impairment may be seen in patients with visceral involvement. These features were seen at a time in our patient and we believed then it was a manifestation of visceral involvement.

Verrilli et al[9] reported a case of a 20-year-old woman with WCD that presented with severe bilateral ocular inflammation. There are other reports of ocular affectation though extremely rare.[10] Our patient did not have a visual impairment history and was not examined comprehensively for this. Some authors have suggested ocular evaluation.[10]

Though lung involvement has been reported,[11] our patient had no evidence of lung involvement. Weber-Christian disease can also present with central nervous system manifestations. In a case report by Mangiardi et al,[12] one patient exhibited WCD presenting as a dural mass causing the signs and symptoms of increased intracranial pressure.

Skin biopsy plays a critical role in the diagnosis of panniculitis. The most common histopathologic approach to diagnosis relies on the differentiation between predominantly septal or lobular panniculitis, as well as making a distinction between lesions with and without vasculitis. It is also very important to submit a part of the skin biopsy for microbiological analysis and for T-cell clonal expansion if T-cell lymphoma is suspected. Pathologically, the panniculitis of WCD is typically lobular with a mononuclear or pleomorphic cellular infiltrate, fat-laden macrophages, and varying degrees of giant cells.[1,13]

The diagnosis of WCD is based on relapsing fever, systemic inflammation, histological demonstration of panniculitis that is lobular, and an early neutrophilic infiltrate with fat degeneration, foamy histiocytes, and giant cell formation. It is different from erythema nodosum in which the panniculitis is septal and there are no febrile and other constitutional symptoms. The differential diagnoses for WCD are many.[13]

Great care is required to exclude the differentials and to reach a diagnosis of WCD. The list of differentials includes SLE, alpha-1-antitrypsin deficiency, pancreatitis, erythema nodosum, malignancies, Rheumatoid arthritis, dermatomyositis, and vasculitis. The patient we reported had tests at different times in the course of evaluation. There were lots of diagnostic challenges and many tests were done looking for a definitive diagnosis. The auto-antibodies were all negative and thus made unlikely Rheumatoid arthritis, SLE, and connective tissue diseases. The serums Lactate Dehydrogenase, Creatine Kinase, and aldolase were almost normal thus excluding biochemical evidence of muscle inflammatory damage and could not account for her symptoms.

The histopathology report by the pathologist was that of reception of a cuboidal-shaped skin biopsy specimen measuring 2cm x 1.5cm x0.5cm with a solid cut surface and was yellow. The microscopy revealed a section of skin showing atrophy of the skin and increased fibrocollagenization of the papillary and reticular dermis. The subcutis showed necrosis with chronic inflammatory cells which form follicles in some areas. Multinucleate giant cells were also seen. These are typical features of idiopathic lobular panniculitis and exclude vasculitis and erythema nodosum.

Her serum lipase level was also normal, which was strongly against pancreatitis. Alpha-1-antitrypsin deficiency was not done because of unavailability; however, the presence of high fever and characteristic histology made further pursuit of this diagnosis unnecessary. A radiograph of the affected joint showing calcification within the necrotic subcutaneous fat nodules has been described in WCD[14]. This may help subtly to differentiate WCD from other causes of inflammatory arthritis.

The aetiology of WCD is unknown. Pongratz et al suggested it could be due to dysregulation in T cells because they found that the reported patient only responded to a calcineurin inhibitor; cyclosporine A.[15] However, others have found responses to different drug classes suggesting different aetiopathogenesis. The episodic fever, discrete localized inflammatory lesions, and response to colchicine in some cases suggested auto-inflammatory disorder.

Treatment of WCD has remained hugely challenging. This is evident in the management of this patient in which many medications were tried. Many medications have been tried in the past for the treatment of WCD which include corticosteroids, antimalarial, colchicine, cyclosporine, mycophenolate, NSAIDS, tetracycline, thalidomide, and amphotericin B. Many medications have been reported effective in patients with WCD.[10,15-28] Some case reports concluded that cyclosporine A and corticosteroids have the best evidence of remission in WCD.

Pongratz G et al[15] reported the rare case of a 64-year-old male patient, with WCD who had background Rheumatoid arthritis which responded to corticosteroids and different disease-modifying drugs (Leflunomide, Sulphasalazine, methotrexate). However, the manifestation of WCD persisted. Switching to Ciclosporin A led to the resolution of symptoms of WCD.[15] Weber Christian disease was reported by Wang Y et al in a patient who had lung nodules that dramatically improved with corticosteroid and cyclophosphamide therapy.[11] They were found effective during the following 27 months. Mavrikakis et al reported a case of Orbital lobular panniculitis in WCD.[10]

The orbital affectation did not respond to conventional synthetic disease-modifying anti-rheumatic drugs. Ocular lesions are noted to have sustained response only to anti-TNF treatment and thus the use of anti-TNF blockers is recommended for them.[10] Baskan et al[25] reported an intractable case of idiopathic nodular panniculitis–with failed response to corticosteroid therapy, and this had to be discontinued because of serious adverse effects.

Our patient however had a remarkably rapid and good therapeutic response to mycophenolate mofetil (MMF) monotherapy. Subash et al in 2019 reported a case of a 66-year-old Caucasian who eventually had successful treatment of WCD using Mycophenolate.[26]Another success story with MMF was reported earlier by Enk A H et al.[18] However, more research is necessary to determine the long-term safety and effectiveness of these

pharmacological treatments for individuals with idiopathic nodular panniculitis. The treatment reported by Mangiardi et al was only surgical excision. Even though the skin lesion was highly suggestive of lobular panniculitis, no comment on the drug for the WCD was made in this report.[12]

There are currently no effective methods of prevention and the prognosis is highly variable. The clinical course may be characterized by exacerbations and remissions of the cutaneous lesions for several years before the disorder resolves. Patients with severe systemic disease have high mortality.

In conclusion, Weber-Christian disease is still rarely reported and can pose serious diagnostic and thus management challenges. A high index of suspicion in patients with recurrent fever and panniculitis is required. Awareness of this rarely reported disorder should be created hence this case report and literature review.

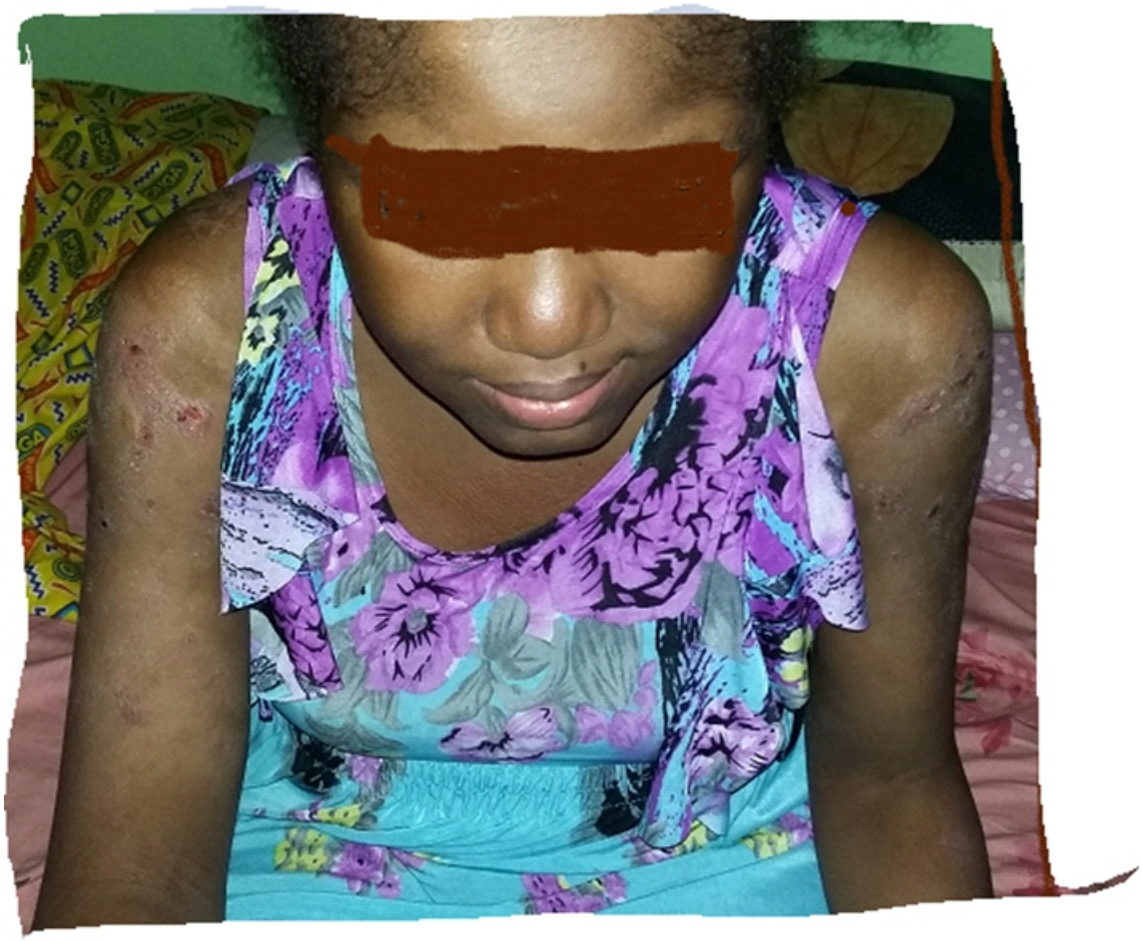

**Figure 1: Shows the patient's spared Face and healing panniculitis on both arms (original)**

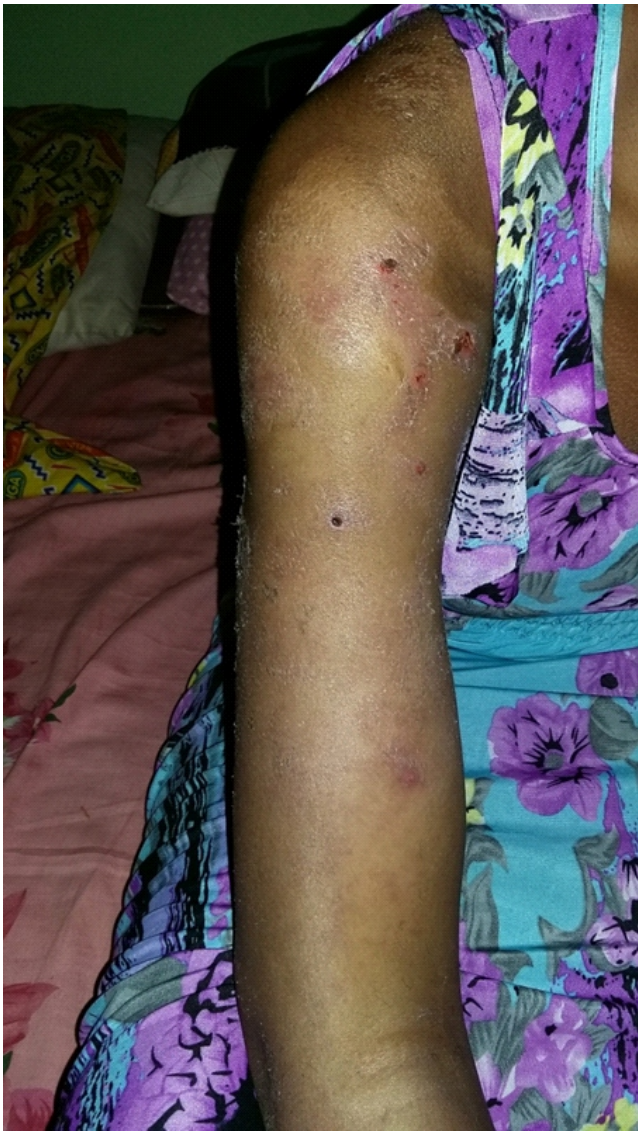

**Figure 2: Shows the patient's healing active panniculitis on the right arm (original)**

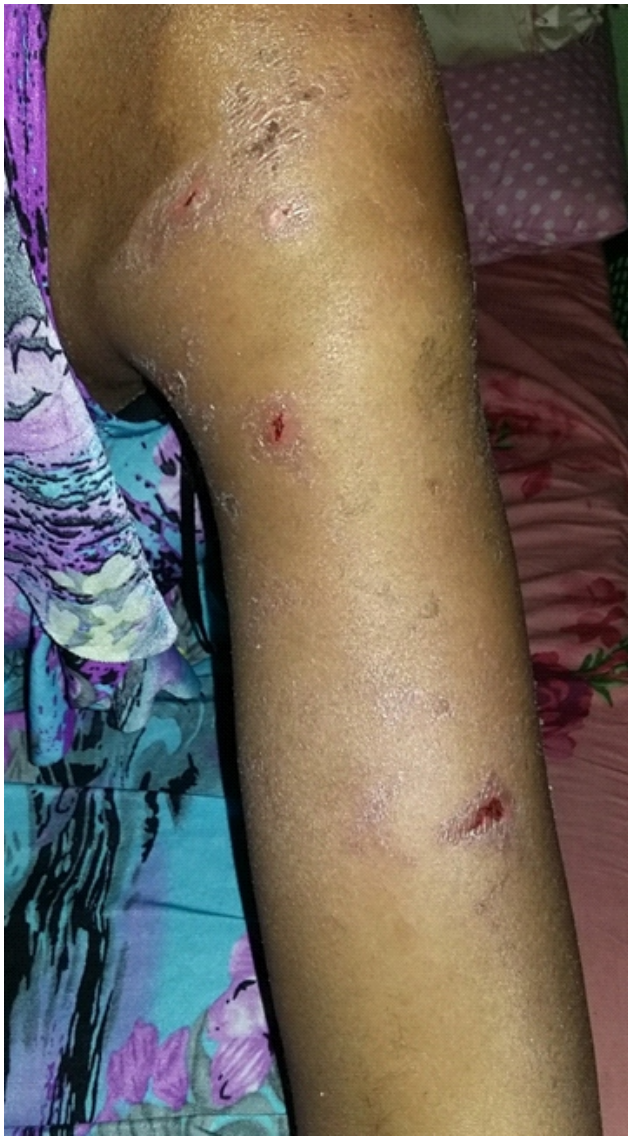

**Figure 3: Shows the patient's active panniculitis on the left arm (Original)**

## Learning Points

- Weber-Christian disease is a rare disease with challenging diagnosis and management
- can occur in blacks
- Diagnosis requires a high index of suspicion

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