Weber-Christian Disease in a 12-year-old Filipino Female: A Case Report

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ABSTRACT

Weber-Christian Disease (WCD), or relapsing febrile nodular panniculitis is a rare form of subcutaneous fat inflammation commonly affecting women aged 40-75 years old. It is rarer in children with only 1 previously reported case in the Philippines. It presents as erythematous nodules, frequently affecting the lower extremities. There is no standard treatment, but reportedly improves with steroid therapy, cyclosporine, and immunomodulators.

This is a case of a 12-year-old-female, who presented with a 4-month history of palpable facial nodules, thigh pains, and recurrent fever. Work-up for hypersensitivity reaction, autoimmune condition, hematologic problem, or infectious etiology yielded unremarkable findings, and corresponding management had no significant response. Patient developed firm lesions on the abdomen which was sent for biopsy and showed results consistent with WCD. Steroid, hydroxychloroquine, and topical indomethacin were then started and noted gradual improvement of the lesions. Patient was then discharged improved with lesions noted to progressively decrease in size and with no appearance of newer lesions upon follow-up.

WCD is a rare form of nodular panniculitis, more so in the younger age group. It is characterized by presence of cutaneous lesions associated with systemic symptoms. Skin biopsy is necessary to confirm its diagnosis. Visceral organ involvement and failure to respond to treatment may result to poor prognosis, and occasionally leads to death.

Keywords: Weber–Christian Disease, panniculitis, relapsing febrile nodular panniculitis, case report

INTRODUCTION

Weber-Christian Disease (WCD), also known as *Pfeifer–Weber–Christian disease* or *idiopathic lobular panniculitis* or *relapsing febrile nodular panniculitis*, is a form of lobular panniculitis of unknown etiology. It was first described by Pfeifer in 1892 and was established in 1980s by Weber and Christian.[1] The documented cases are rare in adults and even rarer in children. The reported cases are commonly in the fourth to seventh decade of life, 75% of which comprises women.[2] In the pediatric population, a study in Brazil showed that only 6 out of 30 cases fulfilled the criteria for WCD in a 20-year review.[3] Only two cases are documented in the Philippine Pediatric Registry from January 2006-January 2025.[4]

The disease is characterized by presence of erythematous, occasionally tender subcutaneous nodules, frequently seen on the lower extremities. It is associated with systemic symptoms. The commonly reported symptoms are recurrent episodes of high fever, general malaise, arthralgia or myalgia.[5-8] Organ involvement may also occur with WCD. In a study by Rotondo et al., among adult patients with WCD, liver is one of the frequent organs involved. Heart, lungs, orbits and intestines may also be affected. Inflammation in the

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visceral organs causes significant morbidity and mortality in the patient.[6] A skin biopsy of the cutaneous lesion is needed to confirm its diagnosis where an infiltration of lymphocytes in the subcutaneous tissue is noted. There is currently no standard treatment for this disease. Systemic steroids have been used which showed promising result. Other treatment options include cyclosporin, mycophenolate mofetil, immunomodulators, and fibrinolytic agents.[7-10]

We report a case of a 12-year-old female, who presents with a 4-month history of palpable facial nodules, thigh pains, and recurrent febrile episode on admission. On the course of the hospital stay, patient developed palpable nodules on the abdomen with histologic findings consistent with panniculitis, and is currently treated with systemic steroids.

CASE PRESENTATION

This is a case of a 12-year-old Filipino female, who was admitted for a 4-month history of recurrent fever as high as 39°C. This was associated with the presence of bilateral periorbital swelling and thigh pain. Patient has no known history of allergy nor family history of atopy or malignancy. Prenatally, mother had regular check-ups with private physician. Patient was born term with unremarkable past medical history. Symptoms persisted despite antipyretics (Paracetamol) and antibiotics (Co-Amoxiclav). Considering a hypersensitivity reaction, she was given anti-histamines (Cetirizine and Desloratidine), which also afforded no relief. Though the anti-nuclear antibody (ANA) was negative, the erythrocyte sedimentation rate (ESR) was elevated at 50 mm/h and complete blood count (CBC) showed leukopenia at 2.9 x 10^3 /uL (differential count of neutrophil 44%, lymphocyte 49%, monocyte 6%) with otherwise normal hemoglobin, hematocrit, and platelet count. An autoimmune cause could not be totally ruled out so prednisone was provided for five days and later shifted to dexamethasone for an additional five more days. There was noted improvement of the periorbital edema, however, it recurred after discontinuation of steroid therapy.

Due to the recurrence of periorbital edema and persistence of the intermittent febrile episodes, a consultation with a pediatric nephrologist was sought for the possibility of nephrotic syndrome. Laboratory work-up showed persistence of leukopenia at 3.7 x 10^3 /uL and ESR increased further to 75 mm/h. A pediatric rheumatologist was also consulted since these findings along with the history of thigh pain could still indicate an autoimmune condition like juvenile dermatomyositis (JDM). She was evaluated for myopathies. Creatinine kinase-MM (CK-MM) though was within normal values, serum glutamic oxaloacetic transaminase (SGOT 1.5 x at 51 u/L) and lactate dehydrogenase (LDH 2.2 x at 545 u/L) were both elevated beyond their upper normal limits. Coombs test and peripheral blood smear were all normal. Naproxen was started at 11 mg/kg/day, which offered no relief. An x-ray of the paranasal sinuses and skull was done which showed unremarkable results. Her condition progressed with appearance of painful maxillofacial lesions. The patient was then advised admission for further evaluation to determine the underlying etiology of the periorbital edema, recurrent fever, and these new lesions.

On admission, the patient was noted to be febrile at 39.6°C with bilateral swelling of the periorbital area that was noted to be warm and tender. A firm, circular, movable, and tender mass was seen on both maxillofacial areas, about 3 x 3 cm on the left and 4 x 3 cm on the right. There was no history of weight loss or night sweats. The CBC showed leukopenia at 2.69 x 10^3 /uL. Chest x-ray was also done with noted normal findings. Due to the presence of elevated ESR, deranged CBC results, and febrile episodes, an infectious process could not be totally ruled out. Patient was co-managed with an infectious disease specialist. Ceftriaxone at 80 mg/kg/day and vancomycin at 40 mg/kg/day were started. Nasal swab gram stain, culture, and sensitivity yielded negative results. A hematologist-oncologist was consulted for the recurrent fever, palpable mass, and deranged CBC results. A magnetic resonance imaging with contrast of the brain showed non-specific inflammatory process in both periorbital and maxillofacial regions. Since the patient only had leukopenia, no further work-up on this consideration was pursued. On day 4 of antibiotics, there was noted hyperpigmentation on the periorbital area and maxillofacial region. She developed similar lesions on her abdomen. These were palpable, tender, warm nodules with indistinct borders (Figure 1). Computed tomography scan of the abdomen (Figure 2) showed hepatosplenomegaly and presence of increased density in the subcutaneous tissue of

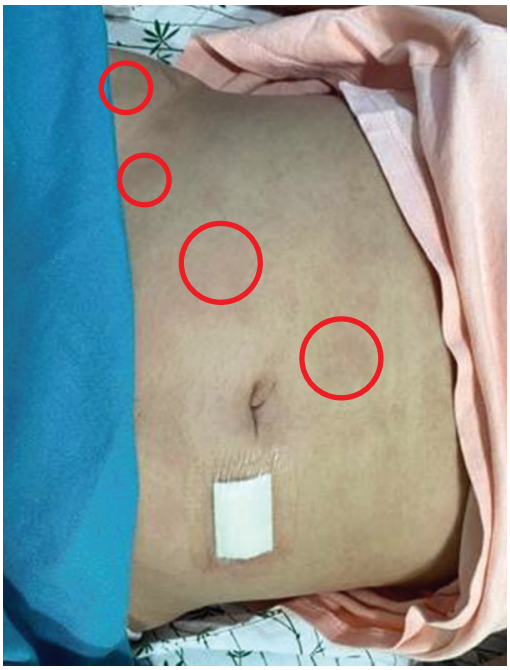

Figure 1. Nodules *(red circles)* on the abdomen.

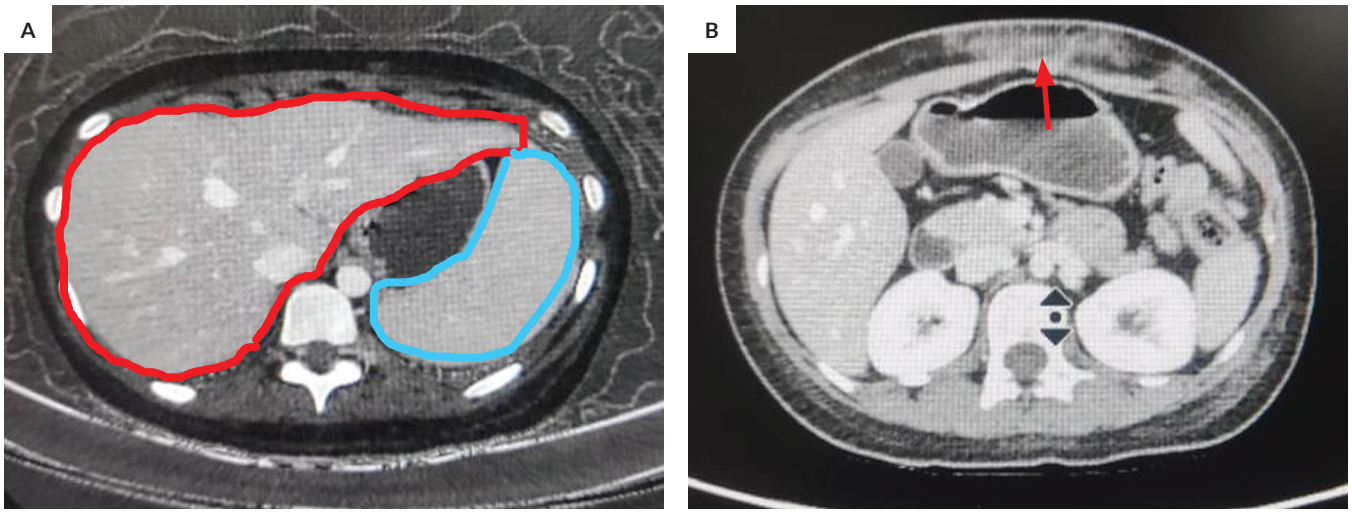

Figure 2. **(A)** CT-Scan of the abdomen showing hepatomegaly *(red outline)* and splenomegaly *(blue outline)*, and **(B)** increase density in the subcutaneous tissue *(red arrow)*.

the abdomen. A case of panniculitis was then considered. An incisional biopsy was done on the abdominal wall. The biopsy results then revealed histologic findings consistent with lobular panniculitis, with predominant histiocytic foam cells and lymphocytes (Figure 3) thus, a diagnosis of WCD was reached. The patient was started on methylprednisolone pulse therapy at 1 g/day once a day for a total of three days, hydroxychloroquine 4 mg/kg/day once daily, and topical indomethacin 1% gel was applied on lesions twice a day. There was gradual improvement of the patient's status (Figure 4), while no new lesions were noted upon the initiation of the treatment regimen and lysis of fever was noted. Patient was then discharged improved with prednisone 10 mg/tablet two tablets after breakfast and dinner plus one tablet after lunch (1 mg/kg/dose), hydroxychloroquine 200 mg/tablet one tablet once a day (4 mg/kg/day), Clindamycin 300 mg/capsule one capsule three times a day to complete seven days (18 mg/kg/dose), levocetirizine + montelukast 5 mg/10 mg one tablet once a day and topical indomethacin 1% gel was applied on lesions twice a day which she took with good compliance. Succeeding follow-ups revealed progressive resolution of the lesion. Repeat SGOT showed normal results at 20 u/L. There were no noted adverse reactions or untoward events. Prednisone was gradually tapered off upon resolution of symptoms and normalization of laboratory results. Lipid profile was taken and showed hypercholesterolemia at 221mg/dL and hypertriglyceridemia at 411mg/dL. Patient was advised for dietary modification (balanced diet with less fatty / oily food) and improved physical activities (daily exercises). Repeat lipid profile showed normal results. The patient is maintained on hydroxychloroquine with plans to discontinue once she remains asymptomatic for at least a year.

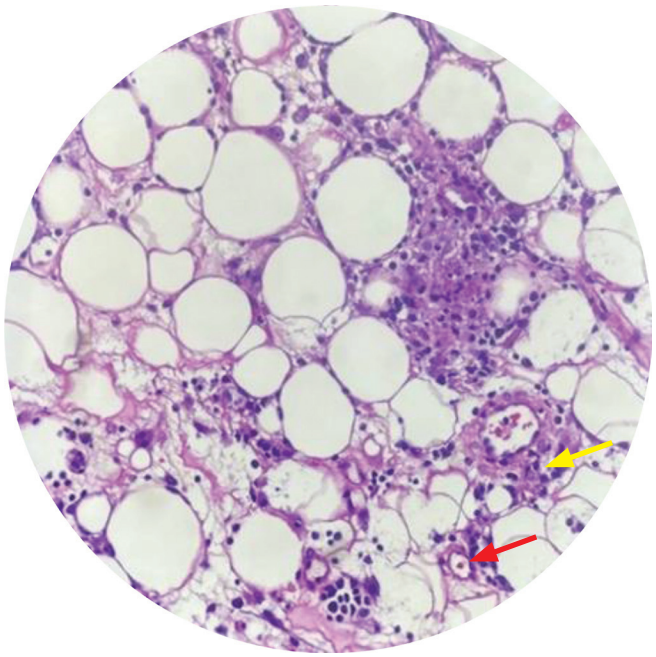

Figure 3. ***Histopathologic findings of abdominal mass.*** Lobular panniculitis showing histiocytic foam cells *(red arrow)* and lymphocytes *(yellow arrow)*.

DISCUSSION

Panniculitis comprises a broad spectrum of diseases characterized as inflammation of the subcutaneous fat that may preferentially affect the lobule or the septum. WCD is a form of panniculitis presenting as cutaneous lesion with systemic involvement.[11]

The etiology of WCD is unknown, however, an immune-complex mediated reaction is considered as some patients present with elevated levels of circulating immune

A B C D E F

Figure 4. ***The pictures show progressive resolution of swelling on the periorbital area and maxillofacial region.*** **(A)** Picture was taken prior to admission; **(B)** Picture shows progression of swelling with purplish discoloration of the surrounding area prior to starting of steroid therapy; **(C)** Picture shows improvement with ongoing therapy; **(D)** Picture shows follow-up after 1 week; **(E)** Picture was taken 12 weeks after initiation of therapy; **(F)** Picture was taken 32 weeks from initiation of therapy. Steroid therapy was tapered off.

complexes.[12] Other risk factors considered were physical, chemical or infectious agents. The infectious agent may be seen in the biopsy of the specimen and symptoms resolve after administration of appropriate antibiotics.[12] In the patient, there was no pathogen isolated nor did the symptoms resolve after antibiotic use. There was also no history of chemical or physical trauma.

Patients with WCD present with cutaneous lesions described as erythematous, occasionally tender subcutaneous nodules, that are symmetric in distribution affecting most commonly the thighs and legs. They appear and resolve during a period of weeks to months and leave an atrophic depressed scar. The epidermis overlying the affected area occasionally breaks down, and a brown liquid oil discharges from the lesions.[5-8] Periorbital area involvement is unusual.[12] In addition to the characteristic lesions, WCD is also associated with systemic symptoms such as fever, malaise, and arthralgia. Other symptoms such as vomiting, nausea, and abdominal pain may less commonly occur. In the adult population, there are also reported cases that involve the lungs, heart, intestine, spleen, and kidney. Liver involvement is frequently reported though in WCD. It usually presents with liver enlargement, increase in aminotransferases and LDH levels. Laboratory tests in WCD are usually normal. However, non-specific laboratory findings in WCD such as leukopenia, anemia, mild liver function impairment, elevation of serum LDH, and elevated CRP may also be seen in a patient.[12] The patient presented with tender nodules at the maxillofacial areas and hypogastric area. This was associated with recurrent fever, periorbital swelling, and hepatomegaly. On laboratory examination, she presented with leukopenia, mild liver function impairment, and elevated LDH. The lungs, may, although rare, may be involved in WCD. Chest imaging will show nodules on the chest. This was not seen in our patient.

The presentation of the patient may also be found in other diseases. It is however important that the other conditions that may present with lobular panniculitis such as systemic lupus erythematosus (SLE), factitious, pancreatic associated histiocytic cytophagic panniculitis have been excluded.[13]

Recurrent fever with periorbital swelling was initially seen in our patient. Preseptal cellulitis was considered, however, there was no noted improvement in the periorbital swelling despite antibiotic use. Angioedema was also considered, however, patient did not complain of pruritus on the affected area and swelling did not subside with anti-histamines. A hematologic cause was also considered, but there was no history of weight loss nor family history of malignancy. Though the CBC of the patient showed leukopenia, a hematologic malignancy would have shown a decrease in at least 2 cell lines, so no further work-up on this consideration was pursued. SLE was considered due to age, gender, and presenting symptom of periorbital swelling which may be a manifestation of kidney involvement. There was also the associated recurrent febrile episodes and myalgia. In addition, laboratory work-up demonstrated leukopenia with elevated inflammatory markers, but ANA was negative. A nephrotic syndrome was also considered, however, renal work-up showed normal results. JDM was also considered due to history of thigh pain. Although patient presented with elevated LDH and SGPT, she had normal CK-MM and no pathognomonic skin lesion (heliotrope rash, Gottron's papules) consistent with JDM.

The diagnosis of WCD is based on clinical manifestations and biopsy results consistent with the condition. The characteristic pathologic finding of WCD is nodular inflammatory pattern of the fat lobules. Histologically, three stages can be seen in Table 1.

Table 1. Histopathologic stages of WCD[14]

Stage 1	Stage 2	Stage 3
Early rapid phase where fat lobules are replaced with neutrophil, lymphocyte and histiocyte	Granulomatous inflammation where macrophage migrate and phagocytose degenerated fat	Fibrosis of affected tissue

The histopathology result of our patient is consistent with lobular panniculitis with histiocytes and lymphocytes, thus classifying it to stage 1. Early recognition of the disease is crucial to prevent visceral organ involvement.

Currently, there is no standardized treatment for WCD. However, several medications were reported to have been able to improve the condition of patients. This include cyclosporin, fibrinolytic agents, mycophenolate mofetil, immunomodulators, and systemic steroids. Systemic steroids are found to be effective in suppressing acute exacerbations. Supportive treatment such as NSAIDs may also be used to alleviate fever and pain.[7-10] Our patient improved gradually after initiation of steroid therapy (methylprednisolone and prednisone), immunomodulators (hydroxychloroquine), and NSAID (naproxen and indomethacin).

Prognosis of patients with WCD will depend on the organ involvement and its severity, as well as, if the patient will respond to provided treatment. Significant morbidity and mortality may occur in patients with inflammation involving visceral organs. In a review of literature on organ involvements among adult patients with WCD,[6] the liver is one of the most commonly involved. The common manifestations include liver enlargement[6], moderate to severe increase of aminotransferase and LDH levels, and rarely in jaundice. Involvement of the kidneys is rare in WCD. The most clinical signs encountered is proteinuria. Patients with WCD also have tendency to hemorrhagic complications[6] due to derangement in the coagulation factors. This includes hypofibrinogenemia and reduction of factors XIII, V, and plasminogen levels. There was also noted prolongation in PT and APTT. Organ bleeding has been the cause of death in many patients with WCD. The skin-limited form, which is described by pyrexia, panniculitis, and the tendency to relapsing course, is rarely lethal and in most cases achieve spontaneous remission. Younger age group typically has a milder course. Clinical monitoring is significant if they would become symptomatic and develop complications requiring prompt intervention. The patient had cutaneous manifestations with elevated SGOT and hepatosplenomegaly. The cutaneous lesions gradually improve since the start of the treatment. Repeat laboratory tests also showed normal results.

Although the recognition, diagnosis, and management of WCD is still challenging, awareness of its occurrence even among children is a positive step towards helping those afflicted with it.

CONCLUSION

WCD is rare among children. This is the second documented case in the Philippines. Etiology is unknown. It is characterized by the development of painful subcutaneous nodules associated with fever, myalgia or arthralgia. The patient presented with these symptoms except arthralgia. Laboratory tests showed leukopenia, elevated inflammatory markers, and elevated liver enzymes. Other laboratory tests demonstrated normal results. A biopsy is needed to confirm its diagnosis. The patient's biopsy showed a nodular inflammatory pattern of the fat lobules with prominent infiltrate of histiocytes and lymphocytes which is consistent with WCD. There is no standard treatment in WCD. Systemic steroid, immunomodulators, and NSAIDs, however, were found to have improved the condition of the patient. Prognosis depends on disease severity, organ involvement, and treatment response. The patient had cutaneous manifestation and hepatosplenomegaly, but with significant treatment response that resulted to resolution of her clinical manifestations. Repeat laboratory tests on succeeding follow-ups were also noted to be normal.

Ethical Consideration

The research was conducted upon the approval of the Chong Hua Hospital Research Ethics Committee in accordance with the ethical principles set out in the Declaration of Helsinki 2015 WHO guidelines, International Conference on Harmonization – Good Clinical Practice. This study likewise complied with principles stated in the National Ethics Guidelines for Health and Health-Related Research (NEGHHRR) 2017 Edition, specifically the Ethical Guidelines For Research Involving Minors or Children.

Patient Anonymity and Confidentiality

All personal information regarding the patient was kept in strict confidence in compliance with the Data Privacy Act of 2012 and its implementing rules and regulations in 2016. All patient identifiers (such as name, geographical location, date of birth, contact number, etc.) were removed from the manuscript and the presented images. Only the data relevant to this study were collected.

Informed Consent

Consent from the patient and mother were secured prior to the reporting of this case.

Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

Both authors declared no conflicts of interest.

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