Pfeifer-Weber-Christian Disease: A Case Report and Review of Literature on Visceral Involvements and Treatment Choices

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ABSTRACT: Pfeifer-Weber-Christian disease (PWCD) is a rare idiopathic disease characterized by lobular panniculitis of adipose tissue with systemic symptoms and multiple organ involvement. Even though the systemic involvement is rare, it is life-threatening and represent a treatment challenge for the clinicians. We report a case of PWCD characterized by hepatic, hematologic, and renal involvement, with good response to mycophenolate mofetil and prednisone treatment. A 47-year-old female presented several months’ history of painful subcutaneous nodules, fever and lymphadenopathy with recent appearing of microcytic hypochromic anemia, leucopenia with neutropenia, and increase in transaminase. Skin biopsy showed lobular panniculitis with lymph-histiocytic and neutrophilic infiltrates with necrosis of adipocytes. A combination therapy of corticosteroid with mofetil mycophenolate was effective. Moreover, we discuss the clinical manifestation and the therapeutic choices in PWCD, from classical immunosuppressive drugs to new biotechnological agents, and we provide a comprehensive review of the available literature.

KEYWORDS: Pfeifer-Weber-Christian disease, hematologic dyscrasia, nonalcoholic fatty liver disease, pleural effusion, liver biopsy, mycophenolate mofetil

Introduction

Pfeifer-Weber-Christian disease (PWCD) is a rare illness of unknown etiology, with a higher prevalence in female. It is characterized by recurrent fever associated with the appearance of single or multiple nonsuppurative nodules, sometimes tender, due to an inflammatory process associated with subcutaneous tissue necrosis.1 In many cases, further lesions subsequently appear elsewhere in the panniculus adiposus.2 Several cases with hepatomegaly or splenomegaly and changes in liver function have been published.3-7 Systemic symptoms and signs such as relapsing fever episodes, fatigue, and polyarthralgia are also frequent. On the contrary, hematological abnormalities and visceral involvement of organs including lungs, heart, intestines, spleen, kidneys, and adrenal gland are rarely described.2,5,8-11 We report herein a case of a patient with PWCD showing hepatic (nonalcoholic fatty liver disease [NAFLD]), hematological, renal, and serosal involvement, which were resolved by the administration of prednison and mycophenolate mofetil. This case report is presented after informed and signed consensus of the patient in study.

Case report

A 47-year-old Caucasian woman was admitted to our Rheumatology Unit, complaining a 6-month history of progressive appearance of tender ill-defined hard swellings on the right leg and the abdominal wall with severe erythema in overlying skin, associated with intermittent fever up to 39°C, not relieved by antipyretics and antibiotics.

The patient had fever up to 39°C, multiple tender erythematous swellings on abdomen wall and right leg, and several palpable lymphadenopathies on abdomen, neck, and right groin during admission to our Unit. She denied drug abuse, recent travel, or use of nonsteroidal anti-inflammatory drugs. Complete blood count revealed microcytic hypochromic anemia with hemoglobin 9.8 g/dL, mean corpuscular volume 69 fl, and leucopenia with neutropenia (WBCs 1.3 × 10^3/L; N 48.3%, L 43.8%, M 3.8%, E 0.4%, B 2.2%).

Thrombocytopenia (up to 67 000/µL) had been briefly observed during the recovery period. There was an increase in alanine transaminase (ALT) 104 IU/L (normal range, 2-40) and aspartate aminotransferase (AST) 91 IU/L (normal range, 2-40), with an AST/ALT ratio < 1 and an increase of gamma GT 67 IU/L (normal range, 7-38). A slightly high serum lipid profile (triglycerides, total cholesterol, and low-density lipoprotein) was observed. Erythrocyte sedimentation rate (ESR) was 17 mm/h, C reactive protein (CPR) was 0.05 mg/dL. Normal immunoglobulin assay except high levels of IgM 443 mg/dL (n. 40-230) and of IgE 857 mg/dL (n. 2-200) was noticed. Complement 3, complement 4, cryoglobulin levels, serum lipase, serum amylose, α-1 antitrypsin, procalcitonin, haptoglobin, creatine phosphokinase, creatinine, azotemia, serum glucose concentration, bilirubin and bilirubin fraction, serum

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corrected calcium, and alkaline phosphatase were within normal range. Antithrombin was mildly elevated, 165% (normal range, 70-130). Severe hypofibrinogenemia (40 mg/dL [normal range, 200-450]) with high levels of D-dimer (37 201 µg/mL [normal range, 0-500]) were detected. The 24-hour urinary sample showed moderate proteinuria (1.6 gm/24h). An increase of lactate dehydrogenase (LDH) 500 IU/L (n. 40-250) and beta-2 microglobulin 7.34 µg/mL (normal range, 0.8-2.7) was revealed. Partial thromboplastin time (PTT) was shorter. Prothrombin time and iron profile were normal. Albumin level was 3.2 gm/dL. A hypergammaglobulinemia (23.78%) was noted by protein electrophoresis. Serum and urine immunofixation were negative for free light chains. TORCH screening, tuberculosis screening, Coxsackie IgM, Brucella IgG and IgM, Borrelia IgG and IgM, and Parvovirus B19 were negative. The antinuclear antibodies, lupus anticoagulant antibodies, antineutrophil cytoplasmic antibodies, cryoglobulin, and antiphospholipid antibodies were negative. Viral hepatitis, autoimmune hepatitis, metabolic factors and in-born or hereditary disorders (Wilson disease, lypodystrophy), drug and toxins associated to malignancies.

A mild hepatosplenomegaly with widespread lymphadenopathy and left pleural effusion were detected using sonography and confirmed by neck, chest, and abdomen computed tomographic scan. The echocardiography detected a small pericardial effusion, with normal eject fraction and preserved systolic function. The endocrine and genital organs and the breast showed no clinical abnormalities.

Surgical skin sample showed lobular panniculitis with a lymph-histiocytic and neutrophilic infiltrates with necrosis of adipocytes, as seen in PWCD. Bone marrow biopsy displayed a discrete hypercellular bone marrow with an increase of megakaryocytic proliferation and low grade of dysmophia of myeloid cells. A widespread boost of stromal fibers was noticed at silver impregnation. The marrow changes were reactive and did not reflect a myelodysplastic syndrome.

Axillary lymph-node biopsy confirmed a reactive lymphadenopathy. The hematological specialist excluded hematological malignancies.

The liver biopsy evidenced a macro-vesicular steatosis with hepatocytes ballooning, as in NAFLD. Spotty necrosis, scattered mixed neutrophilic-lymphocytic inflammation, Mallory hyaline, and perisinusoidal fibrosis were absent.

On admission, levofloxacin (750 mg daily) and minocycline (200 mg daily) were empirically started and discontinued after 8 days for negative blood cultures. Mycophenolate mofetil (MMF) (2 gm daily) and prednisone (1 mg/kg daily, tapered to 5 mg daily in 3 months) were started. At 1-month follow-up, the improvement of skin lesion, the remission of fever, and complete normalization of blood count, proteinuria, and liver enzymes were recorded. A complete remission state, with just slightly hyper-pigmentated skin scares, was recorded at sixth month follow-up.

Of note, considering the prompt remission of proteinuria after prednisone and mycophenolate mofetil treatment, the kidney biopsy was not more performed.

Discussion

PWCD is an inflammatory disease characterized by a wide spectrum of clinical manifestations, ranging from skin lesions and adipose tissue abnormalities, to systemic involvement.

The skin-limited form of the PWCD, also known as “relapsing febrile non-suppurative nodular panniculitis”, well describes the principal clinical triad of pyrexia which varies widely in degree, panniculitis, and the tendency to relapsing course. It is rarely lethal and in most of the cases, it is described as a spontaneous remission.

Systemic PWCD frequently affects the liver, the bone marrow, and the kidneys, sporadically the serosa, spleen, lungs, heart, and intestines. It could be life-threatening, representing a treatment challenges for clinicians.

Systemic symptoms and signs such as relapsing fever episodes, fatigue, and polyarthralgia are also commonly encountered in both skin-limited and systemic PWCD form.

An electronic literature search on PWCD visceral involvement and treatment choices was conducted using Google Scholar, Scopus, and PubMed. Case reports published up until 2019 were evaluated (Table 1).

Liver Manifestation

The liver is one of the most frequent organs involved in systemic PWCD. The liver manifestation consists principally in liver enlargement, moderate to severe increase of aminotransferase and LDH levels, and rarely in jaundice. Some cases of variceal bleeding due to extrahepatic portal hypertension from mass effect of fat necrosis and liver fibrosis have also been described. The most common histopathologic finding reported is the different degree of macro-vesicular steatosis (sometimes contained foam cells), with or without hepatocyte necrosis and mononuclear cells infiltration. In some cases, the presence of Mallory bodies has been evidenced. Oram and Cochrane first hypothesized that occasionally gross fatty metamorphosis can take place in the liver as well as in other organs and give rise to considerable enlargement, reporting a case of 63-year-old woman with hepatomegaly, steatosis (revealed by means of biopsy), and fever. Now, PWCD is recognized among the metabolic abnormalities associated with NAFLD and nonalcoholic steatohepatitis (NASH). Wasserman et al evidenced the difference between the NASH due to PWCD, characterized by an active inflammatory state and the elevation of the aminotransferase and especially the LDH levels and NASH due to obesity and diabetes mellitus. Enlargement of the portal area accompanied by inflammatory...
| NO. OF PATIENTS (AGE); DISEASE DURATION | SYSTEMIC SYMPTOM; VISCERAL INVOLVEMENT; COMORBIDITY | BLOOD COUNTS | BONE MARROW BIOPSY | LIVER BIOPSY | TRANSAMINASE | COAGULATION | KIDNEY DISFUNCTION | TREATMENT | OUTCOME |
|----------------------------------------|--------------------------------------------------|--------------|-------------------|-------------|-------------|-------------|------------------|-----------|---------|
| 1 f (16 y); 5 months                   | Fever; Lymphadenopathy; paratracheal and mesenteric lymphadenopathies (dilated sinusoids filled with macrophages and giant cells); Hemorrhagic pleural and peritoneal effusion | Anemia       | —                | —           | —           | —           | —                | —         | Exitus for severe hemorrhage from the biopsied region |
| 1 f (57 y); 13 months                  | Fever; left pleural and peritoneal effusion; pulmonary opacities | Pancytopenia | —                | —           | ↑ GOT and ↑ bilirubin (6-8 mg/100 mL) | —           | Prednisone (80 mg/d with tapering) | Exitus    | —       |
| 1 f (19 y); 24 months                 | Gastrointestinal and subcutaneous hemorrhages | —           | —                | ↑ Fbg, ↓ factor XIII levels ↑ PFD, ↓ factor V, ↓ plasminogen levels | —           | Prednisolone at 90 mg/d with tapering, benzylpenicillin, tranexamic acid, apomorphine and heparin | Died from staphylococcal sepsis and intracranial hemorrhage |
| 1 f (21 y); 33 months                 | Fever, tarry stools, epistaxis, vein thrombosis. | Pancytopenia | —                | ↑ GOT and ↑ GPT and ↑ bilirubin | ↑ KPTT, ↓ PT, ↓ TT value, ↓ Fbg | Prednisolone (100 mg/d), blood transfusions and heparin iv | Well-controlled state |
| 1 f (7 y); 11 y                       | Fever; splenomegaly; Comorbidity: herpes genitalis, diabetes mellitus and hepatic cirrhosis, amyloid deposit in pancreatic islets | Hypochromic anemia, leukopenia | —                | —           | —           | —           | —                | —         | Exitus for liver failure |
| 1 f (32 yrs); 51 months               | Fever, hepatosplenomegaly. | Normal       | —                | ↑ GOT and ↑ GPT | —           | —           | Prednisolone, 60 mg/d | Recurrent |
| 1 f (27 y)                            | Fever; Lymphadenopathy; reactive changes; rectal bleeding, jaundice | Slightly anemia and neutropenia | —                | Mallory bodies | —           | —           | —                | —         | Exitus for liver failure |

(Continued)
| No. of Patients | Age (yrs) | Disease Duration | Symptom | Visceral Involvement | Comorbidity | Blood Counts | Bone Marrow Biopsy | Liver Biopsy | Transaminase | Coagulation | Kidney Dysfunction | Treatment | Outcome |
|----------------|----------|------------------|---------|---------------------|-------------|--------------|-------------------|--------------|---------------|-------------|------------------|------------|---------|
| Hotta et al. | 20 | 1 f (23 y); 3 y | Fever | —— | — | ↑ GOT and ↑ GPT | Normal | Normal | AZA (150 mg/d) | Remission |
| Dupont et al. | 13 | 1 f (54 y); 23 months | Fever | Anemia | — | Normal | Normal | Proteinuria (membranous glomerulonephritis) | No treatment was instituted | Spontaneous remission |
| Kirch et al. | 21 | 1 m (31 y); 23 months | Arthralgia, fever, and fatigue | Leukocytosis | — | — | Normal | Normal | Cyclophosphamide (200 mg daily) | Remission |
| Yoshimura et al. | 11 | 1 f (42 y); 8 y | Fever, muscular pain, multiple joint pain, Lymphadenopathy: swelling of cervical and inguinal lymph nodes, dermatopathic lymphadenitis, Comorbidity: Hashimoto thyroiditis. | Anemia and thrombocytopenia | — | Enlargement of the portal area accompanied by small round cell infiltration, piecemeal necrosis, bile duct proliferation and edema as well as fibrosis around the bile ducts were observed. Thickening and cell infiltration of branches of the hepatic artery suggestive of vasculitis were also found. | Normal | Normal | Proteinuria due to proliferative glomerulonephritis | Prednisolone (20 mg/d), cyclophosphamide (50 mg/d) | Death due to gastrointestinal bleeding |
| Erik et al. | 22 | 3 (55 y, 58 y, 49 y); 10 months | Fever, 2 pts also had inflammatory lesions in their retroperitoneal fat (assessed by magnetic resonance imaging) | Normal | —— | —— | Normal | Normal | MMF (2 g/d) in addition to prednisolone, Failure of AZA (1.5 mg/kg per d) and MTX (50 mg/wk) | Complete remission of skin and retroperitoneal lesions. |
| Wasserman et al. | 14 | 1 f (27 y); 5 y | Recurrent fevers | Leukocytopenia | — | Moderate centrilobular macro-vascular steatosis with hepatocyte necrosis and mononuclear cell infiltration. Portal fibrosis and centrilobular pericellular fibrosis were observed | ↑ GOT, ↑ GPT and ↑ γ GT | Normal | Normal | AZA 125 mg daily and prednisone 20 mg/d | Good response with just 2 relapse episodes (AZA 50 mg/d) |
| Bajana et al. | 1 f (45 y); 10 months | Fever, malaise, and arthritis, Comorbidity: peptic ulcer and depressive syndrome. | Hypochromic and microcytic anemia | — | — | — | Normal | Normal | MMF (2 g/d), (Failure of prednisolone 1.5 mg/kg per d) | Complete remission |

(Continued)
| NO. OF PATIENTS (AGE); DISEASE DURATION | SYSTEMIC SYMPTOM, VISCERAL INVOLVEMENT, COMORBIDITY | BLOOD COUNTS | BONE MARROW BIOPSY | LIVER BIOPSY | TRANSAMINASE | COAGULATION | KIDNEY DISFUNCTION | TREATMENT | OUTCOME |
|----------------------------------------|--------------------------------------------------|-------------|-------------------|-------------|--------------|-------------|-----------------|-----------|---------|
| Hojo et al. | 1 m (73 y); 9 months | Fever | Anemia | 3.4% blasts. Several erythroid cells with two nuclei, neutrophils with Pelger-Hüet–like nuclei or without granules, and megakaryocytes with multisegmental nuclei or multiple nuclei (refractory anemia) | — | ↑ GPT, ↑ GPT and ↑ γ GT | — | Renal failure (creatinine 2.7 mg/dL) | Prednisolone at 40 mg/d with tapering | Remission of anemia, liver and kidney dysfunction |
| Amarapurkar et al. | 1 f (47 y); 19 months and half | Fever; right pleural effusion and ascites. Psoriasis | Normal | — | Diffuse fatty change with mild inflammation. Laparoscopy: multiple areas of fat necrosis. | ↑ GPT, ↑ GPT, ↑ LDH | Normal | Normal | Prednisolone (30 mg/d) and MMF (500 mg twice a d) | Remission |
| Miranda-Bautista et al. | 1 f (42 y), 24 months | Right exophthalmos, due to a significant enhancement of the soft tissue in the right orbit, ileocolonic involvement | Pancytopenia | — | — | Normal | Normal | Normal | IFX (5 mg/kg, repeated at wk 2, 6 and then every 8 wk) | Remission |
| Hagag et al. | 1 m (2 y and 9 months) (14 months) | Fever, hepatosplenomegaly | Microcytic hypochromic anemia | — | — | Normal | Normal | Normal | Corticosteroid treatment (2 mg/kg/d for 3 wk) and CsA (5 mg/kg/d) for 6 months. | Complete remission |

Abbreviations: AZA, azathioprine; CsA, cyclosporine A; d, day; f, female; FBG, fibrinogen; FDP, fibrin degradation products; IFX, infliximab; KPTT, kaolin partial thromboplastin time; LDH, lactate dehydrogenase; m, male; MMF, mycophenolate mofetil, MTX, methotrexate; PT, prothrombin time; TT, plasma thrombo-test (or thrombin time); wk, weeks.
cell infiltration, including plasma cells, piecemeal necrosis, bile duct proliferation (in some cases with disruption of the limiting plate), and edema as well as fibrosis around the bile ducts have been observed in liver biopsy. The evolution in centrilobular pericellular fibrosis is sporadically described. Suggestive signs of vasculitis, due to the presence of the thickening and cell infiltration of branches of the hepatic artery suggestive of vasculitis, were also found. The liver failure, until 1980, was among the main causes of death in systemic PWCD.

Hematological Manifestation
The clinical features of hematological involvement are anemia, pancytopenia, and thrombocytopenia. The findings of bone marrow aspirate varied from considerable retardation of the maturity of granulocytic series, to refractory anemia, characterized by several erythroid cells with two nuclei, neutrophils with Pelger-Huet-like nuclei or without granules, and megakaryocytes with multisegmental nuclei or multiple nuclei. The myelodysplastic syndrome (MDS) in PWCD is rarely reported.

Kidney Involvement
Kidney involvement is rarely described in PWCD. The proteinuria is the most common clinical signs encountered in PWCD. It is described, at immunochemistry, as the presence of granular immune deposits, containing IgG and IgM, on the epithelial side of the glomerular basement membrane, consistent with membranous glomerulonephritis. In another case, the proliferative glomerulonephritis with glomerular lobulation and partial double track of the glomerular basement membrane was evidenced by electron microscopy and marked coarse granular deposition of IgG and IgM and slight deposition of IgA and C3 along the glomerular capillary walls were observed by the direct immunofluorescence technique.

Coagulopathy
The hypofibrinogenemia, the reduction of factor XIII, factor V levels and plasminogen levels, the increase in fibrin degradation products (FDP), decreased activity of factors II, V and VIII, prolongation of the kaolin partial thromboplastin time (KPTT), prothrombin time (PT) and thrombin time (TT) are observed.

Many reports describe the tendency to hemorrhagic complications, consisting of internal organ bleeding and disseminated intravascular coagulation (DIC) in the PWCD patients, but the mechanism which might cause the development of consumption coagulopathy is still unknown. The possible role of the dysregulation of lipid metabolism, the destruction of the tissues and vascular wall eventually liberate tissue thromboplastin into the circulating blood, as well as active blood contact factors were taking into account. In addition, abnormalities in the micro-circulation, hypofunction of the reticuloendothelial system, and disfunction of the fibrinolytic system may also take part in the pathogenetic mechanism.

It is evidenced that the presence of thrombocytopenia and liver abnormalities could contribute to hemorrhagic diathesis in patients with PWCD.

Organ bleeding has been for several years the cause of death in many patients with PWCD.

Miscellaneous
Perivisceral fat involvement in pericardium, pleura, omentum, and mesentery is described. Abdominal involvement can include retroperitoneal panniculitis, nodular mesenteritis or retractile mesenteritis, and sterile splenic abscesses. Mesenteric panniculitis could be present as intestinal obstruction, abdominal fullness, and tenderness or abdominal and pelvic mass. A case of PWCD ileocolonic involvement with histologic findings of lobular lympho-histiocytic panniculitis lipophagic granulomas and a deep cecal ulcer surrounded by thrombosed vessels was reported. A macroscopic picture similar to Crohn’s disease with thickening of cecal and terminal ileum wall, a large cecal ulcer covered with fibrin and nodular, hyperemic and friable margins; ileocecal valve inflammation and stenosis is described.

Bone osteolytic lesions are also noted.

Treatment Choices
Effective therapeutic strategies to treat the systemic PWCD have not been identified yet and no data exist comparing the effectiveness of a therapy over another.

High doses of steroids had represented, for several years, the only treatment option. In the three last decades, the introduction of immunosuppressive agents permitted to spare the steroid dose and to obtain complete clinical remission.

Azathioprine (AZA), a purine analogue, whose metabolites inhibit nucleotide conversions and de novo purine synthesis, impeding the DNA, RNA, and protein synthesis, has been used as first immunosuppressive agent in PWCD, by Hotta et al in 1981. At high dose, AZA is effective in skin, hematological and liver manifestation of PWCD. However, it is described that AZA failed to reach complete remission in 2 cases. Cyclophosphamide (CyC), a synthetic alkylating agent, which metabolite forms irreversible DNA interstrand crosslinks, leading to cell apoptosis.
used CyC (200 mg/daily) in a patient with hematological and liver involvement and glomerulonephritis, describing a treatment discontinuation due to the occurrence of leucopenia and thrombocytopenia. Martin et al. used CyC (75 mg/day) in a 40-year-old patient with nodular lesions. They observed an improvement of skin lesion but the appearance of colitis induced a temporary discontinuation of CyC.44

Cyclosporine A (CsA) is able to block the transcription of cytokine genes in activated T cells. Hagag and Barakat24 reported a good efficacy of CsA (5 mg/kg/die for 6 months) in a child with hematological and hepatosplenomegaly. CsA (5 mg/Kg/day) had been used with success in an 8-year-old boy with skin lesion and small vessels vasculitis.45 Of note, CsA is, also, proved to be very effective in cytophagic histiocytic panniculitis, considered a severe variant of PWCD. It is characterized by lobular panniculitis with T helper cells infiltrated, and histiocytes containing blood cell fragments, and by severe systemic features with multiorgan failure, hypertriglyceridemia, and coagulopathy, which may lead to death.45,46

MMF is the 2-morpholinoethyl ester of mycophenolic acid (MPA). After assumption, it is rapidly hydrolyzed to its active metabolite, MPA. MPA potently, selectively, and reversibly inhibits inosine monophosphate dehydrogenase, interfering in the de novo pathway of purine synthesis and finally in lymphocytes activity.47 MMF has been first approved for the treatment of acute renal graft failure in transplant patients and then widely used as immunosuppressive agent in various autoimmune and inflammatory disorders.47 Enk and Knop22 first described the efficacy of MMF (2 g/day), in addition to prednisolone, in 3 patients with WDC with skin and retroperitoneal lesions, after failure of AZA and methotrexate. Başkan et al48 reported rapid and good therapeutic response to MMF in a patient with PWCD with skin lesions, fever, systemic symptom, anemia, and arthritis. In our case, the presence of slight systemic arterial hypertension led to choose treatment with MMF rather than CsA.

Methotrexate (50 mg/daily) and hydroxychloroquine (400 mg daily) seem to not be valid treatment options in PWCD.22,21

With regard biotechnological drugs, few data are available. Infliximab good response is described in a patient with subcutaneous lobular panniculitis,48 in a PWCD patient with sclerosing mesenteritis,49 and in a PWCD patients with orbital, mesenteric, and ileocolonic involvement.9 In a PWCD patient with subcutaneous and orbital panniculitis, a long-term good response to adalimumab, after a dramatic response to infliximab discontinued for hypersensitivity, was reported.50 It is evidenced that TNFα is produced by T-cells and TNFα-high affinity receptors are prevalently expressed by adipose tissue, liver, muscle, gut, and kidney. T-cells seem to be involved in the early stage of PWCD, so could be reasonable to use anti-TNFα drugs to treat it. No scientific evidences are available on the use of others biotechnological drugs (rituximab, abatacept, and tocilizumab) in PWCD patients.

Conclusion
The etiology of PWCD remains unknown and the PWCD diagnosis is possible just after the exclusion of all known causes. Until 3 decade ago, the systemic involvement of PWCD was life-threatening. Liver failure and organ bleeding were the main causes of death. Recently, the published evidences of successful treatment with immunosuppressive agents are growing. As a result, a pathogenetic role of immunologically mediated reaction to diverse antigenic stimuli and T-cell dysregulation hypothesized. It is also possible that rapid, aggressive institution of immunosuppression might avoid irreversible organ injury if diagnosis is prompt. The use of CsA and MMF seems to be safe and effective compared with other immunosuppressive drugs, in a wide spectrum of PWCD systemic manifestations. Further study would be necessary to establish the usefulness of biotechnological drugs in PWCD.

Author Contributions
Rotondo C and Corrado A treated the patient, wrote and revised the paper; Mansueto N and Cici D collected the data; Corsi F and Pennella A supervised for the description of pathology; Cantatore FP made the decision of the treatment for the patient.

Ethical Approval
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Patient’s Consent
Written informed consent was obtained from the patient for publication of this case report.

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