Bilateral Purtscher-like retinopathy associated to mixed connective tissue disease

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ABSTRACT

Introduction: Purtscher-like retinopathy (PuR) is a rare vaso-occlusive retinopathy that can be associated with an autoimmune inflammatory process. In this case report we describe the clinical presentation of a patient with bilateral PuR with previously undiagnosed mixed connective tissue disease (MCTD). Case Report: A 64-year-old female with recently diagnosed hypertension, hypothyroidism, and osteoarthritis presented to our clinic complaining of blurred vision in both eyes of three weeks duration. At initial presentation, visual acuity was count fingers in both eyes. On dilated fundus exam the patient presented with bilateral peripapillary and macular hemorrhages associated to medium sized cotton-wool spots and Purtscher flecken along arcades limited to Zone 1. Review of systems revealed a self-limited episode of severe arm pain associated to bluish discoloration of the overlying skin six months prior, followed by progressive digit necrosis in upper and lower extremities. Work up was consistent with a diagnosis of MCTD. The patient was treated with intravenous (IV) methylprednisolone and mycophenolate mofetil. Conclusion: Diagnosis of bilateral PuR in the setting of MCTD is a rare presentation and warrants further study of potential screening in symptomatic patients as well as treatment regimen upon PuR diagnosis.

Keywords: Mixed connective tissue disease, Purtscher, Retinopathy

INTRODUCTION

Purtscher retinopathy is an occlusive microvasculopathy associated with trauma first described by Omar Purtscher in 1910 and is usually a sequela of head or chest trauma; initially described in a 62-year-old man who complained of bilateral vision loss after head trauma [1]. Ophthalmoscopic examination of the patient revealed cotton-wool spots, retinal hemorrhages, and areas of retinal whitening, later recognized as pathognomonic of the condition and called Purtscher flecken [2]. When fundus-exam findings are consistent with Purtscher, but the findings are not associated with trauma, the correct nomenclature is Purtscher-like retinopathy (PuR). Purtscher and PuR is a clinical diagnosis, characterized by sudden vision loss associated with cotton-wool spots, intraretinal hemorrhages, and pathognomonic Purtscher flecken as described by Omar Purtscher. Purtscher retinopathy is estimated to occur in 0.24 individuals per...
million per year [1]. Even though ophthalmologists have identified this condition as a vaso-occlusive retinopathy, there is still little evidence regarding its pathogenesis due to the scarcity of cases. The most supported theory involves vascular embolism, which leads to vascular occlusion and bilateral or unilateral vision loss [3]. Reports have mostly focused on cases that arise following trauma, thus there is still little knowledge with regard to its association with pancreatitis, autoimmune disease, retrobulbar injections, and other nontraumatic causes.

On the other hand, mixed connective tissue disease (MCTD) is an autoimmune overlapping syndrome that exhibits characteristics of multiple autoimmune diseases [4–6]. It commonly presents with positive anti-uridine-rich-ribonucleoprotein (U1-RNP) antibody, systemic lupus erythematous (SLE), arthralgias, Raynaud’s phenomenon, and other organ specific manifestations [7]. Due to its heterogeneous clinical presentation, MCTD incidence and prevalence is not well established.

The lack of understanding of PuR pathophysiology makes management a challenge [3]. Currently, physicians focus on the possible role of steroids as treatment, but evidence has only shown mixed results [4]. In this report, we describe the case of a 64-year-old Hispanic female with bilateral PuR secondary to previously undiagnosed mixed connective tissue disease. The lack of specific management of the disease and the need for further understanding of its pathophysiology highlight the importance of further research with regard to this rare condition.

CASE REPORT

A 64-year-old Hispanic female with past medical history of hypothyroidism, osteoarthritis, and recently diagnosed hypertension presented with a three-week history of progressive bilateral loss of vision that she described as “seeing through fog” and associated mild photophobia. Seven months before, she had an episode of sudden onset, severe left arm pain associated with bluish discoloration of the skin that resolved spontaneously after approximately 30 minutes. One month later the patient developed slowly progressive bilateral distal finger necrosis associated with episodes of pain and bluish discoloration of overlying skin. At that time, the patient underwent evaluation by a general physician outside our institution who ordered upper extremity Doppler that was within normal limits according to the patient. Review of systems was negative for recent fever, viral illness, myalgia, unintentional weight loss, scalp tenderness, jaw claudication, or behavioral changes. She travels to Florida, United States once a year and has a dog. The patient had a history of heavy smoking since she was 18 years of age, but reports quitting one month before our evaluation, for a total of 24 pack years. Family history is notable for rheumatoid arthritis in her mother.

During initial evaluation, the patient presented with elevated blood pressure >180/100 with an adequate pulse and no fever. Examination of hands and feet revealed bilateral upper and lower extremity distal necrosis and skin discoloration (Figure 1).

Ophthalmic examination revealed visual acuity of counting fingers at 2 feet and counting fingers at 3 feet in the right and left eye, respectively. Intraocular pressure by applanation (Goldman) was within normal limits in both eyes. On slit lamp examination, mild anterior chamber inflammation with occasional cells in right eye and cells +1 in left eye were seen, with no iris nodules or keratic precipitates identified. Additionally, pupils were round, isochoric, and reactive to light without an afferent pupillary defect. Nuclear cataracts were noted in both eyes, and there was no vitreous inflammation. Dilated fundus exam revealed bilateral and symmetric peripapillary and macular hemorrhages, medium-sized cotton-wool spots (localized retinal nerve fiber layer infarcts) and Purtscher flecken (areas of deep retinal whitening located between 50 µm from retinal arteries or venules) following superior and inferior retinal arcades limited to Zone 1 with clear periphery (Figure 2).

The patient was diagnosed at that moment with PuR, after the patient denied any recent significant body trauma. She was started in anti-hypertensive medication and laboratory tests as well as brain and chest imaging ordered in attempt to find a systemic association or etiology for the retinal findings.

Chest X-ray (CXR; Figure 3) revealed confluent reticular opacities in both lower lung fields concerning for underlying pulmonary infiltrates and a thoracic computer tomography (CT) was sent. Laboratory findings revealed a normal complete blood count (CBC), mild elevation
A B2 glycoprotein I immunoglobulin M >150 U/mL and (SM) >8.0 AI and also positive lupus anticoagulant with speckled pattern, positive antibodies to Smith antigen was recommended by rheumatology service. The patient benign lesion.

mass had the typical characteristics of an adenoma, a stenosis. The abdominal MRI revealed that the adrenal gland was found. Purtscher-like retinopathy has been reported in association to neoplastic process and adrenal gland was found. Purtscher-like retinopathy has been reported in association to neoplastic process and abdominal lymph nodes. Incidentally, a mass in the left adrenal gland was found. Purtscher-like retinopathy has been reported in association to neoplastic process and thus an abdominal magnetic resonance image (MRI) was scheduled for a better characterization of the adrenal mass. A brain MRI was attempted but was degraded by motion artifact, however, nonspecific findings suggestive of elevated intracranial pressure were the only significant pathology present.

Figure 3: Chest X-ray showing confluent reticular opacities is noted in both lower lung fields without evidence of effusions or pneumothorax.

of liver enzymes, erythrocyte sedimentation rate (ESR) of 38 mm/h (normal after adjusted by age and sex), and C-reactive protein (CRP) of 18.6 mg/L (elevated). Venereal Disease Research Laboratory test (VDRL) results were positive, and confirmatory tests for syphilis were sent. Hepatitis profile and HIV testing results were negative, however, the patient had low complement levels (C3 in 36.00 mg/dL and C4 in 4.40 mg/dL).

Thoracic CT revealed fibrosing interstitial lung disease consistent with nonspecific interstitial pneumonia, diffuse dilation of the esophagus and enlargement of the mediastinal lymph nodes. Incidentally, a mass in the left adrenal gland was found. Purtscher-like retinopathy has been reported in association to neoplastic process and thus an abdominal magnetic resonance image (MRI) was scheduled for a better characterization of the adrenal mass. A brain MRI was attempted but was degraded by motion artifact, however, nonspecific findings suggestive of elevated intracranial pressure were the only significant pathology present.

A two-dimensional echocardiogram performed to rule out a thromboembolic etiology revealed no thrombus, no vegetations. The patient had severe concentric hypertrophy of the left ventricle despite adequate ejection fraction and normal motion consistent with hypertensive cardiomyopathy. Carotid duplex revealed a homogenous plaque with smooth surface in right common carotid with no visible plaque in the left carotid and less than 50% stenosis. The abdominal MRI revealed that the adrenal mass had the typical characteristics of an adenoma, a benign lesion.

Specific laboratory testing for an autoimmune process was recommended by rheumatology service. The patient had positive anti-nuclear antibody (ANA) test, 1:32 AI in speckled pattern, positive antibodies to Smith antigen (SM) >8.0 AI and also positive lupus anticoagulant with a B2 glycoprotein I immunoglobulin M >150 U/mL and a negative fluorescent treponemal antibody test (FTA-

ABS, confirmatory test for syphilis) all four associated with a diagnosis of lupus. In the tests sent, the patient also presented with positive U1-RNP >8.0 AI, associated to MCTD.

Given the patient’s physical exam findings, as well as imaging and laboratory results, the patient was diagnosed with mixed connective tissue disease. Rheumatology service recommended starting patient in mycophenolic acid and hydroxychloroquine at the time of diagnosis, however, the ophthalmology service expressed concern over the potential retinal toxicity from hydroxychloroquine, and instead a steroid pulse was started in an attempt to improve the patient’s vision. Methylprednisolone 60 mg IV daily was started but after one dose, the patient developed behavioral changes with associated visual and auditory hallucinations. Treatment was subsequently discontinued with complete resolution of the mental disorder and behavior back to baseline. The patient left the hospital against medical advice and was lost to follow-up.

DISCUSSION

After a clinical diagnosis of PuR is made, it can be confirmed by fluorescein angiography. Histopathological studies will typically reveal signs of retinal vascular occlusion with edema of the internal layers of the retina, subretinal cystoid space, and an abrupt transition to normal retina [8]. The pathogenesis of PuR is still uncertain. Several theories have been proposed that include microembolization secondary to fat emboli, protease activation or by complement activation and leukocyte aggregation [8–10]. This correlates with the associated etiologies of PuR as described by a Miguel et al. which are acute pancreatitis, Valsalva maneuver, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, pregnancy, and some autoimmune disorders [1].

Xia et al. reviewed the alternatives of treatment for PuR including the use of corticosteroids, bevacizumab, traditional Chinese medicine, hyperbaric oxygen treatment, and found no consensus as to which is the best treatment option for this condition. As documented in a review about PuR treatment, corticosteroids, bevacizumab, traditional Chinese medicine, hyperbaric oxygen treatment, among others have been suggested for Purtscher retinopathy and PuR with variable results, thus there is no consensus as to which is the best treatment for this condition [3]. The authors also found that retinopathy and vision improved regardless the patient received treatment or not, suggesting a self-limited condition [3]. Observation in PuR, after diagnosing and treating any systemic medical condition, would seem like a feasible option since in some cases risks may outweigh the benefits of treatment.

We presented a case of PuR associated to previously undiagnosed MCTD. Mixed connective tissue disease is
a systemic autoimmune disease that is diagnosed using clinical criteria and laboratory tests. This uncommon condition that, as its name states, presents with overlapping symptoms of different connective tissue disorders associated with the presence of U1-RNP antibody. Our patient in particular had a history of arthralgia with severe Raynaud’s phenomenon resulting in distal necrosis of her extremities, however, the reason to seek medical attention was her progressive loss of vision.

Both MCTD and SLE have been associated with deposition of immune complexes and anti-phospholipid syndrome, which promote a hypercoagulable state that could be the cause of their variable clinical presentation and possibly the relationship with our case [9]. Also, both conditions have been associated with mild retinopathy, however, there is limited evidence describing these diseases specifically with PuR. In the cases that have been reported, deposition of immune complexes leading to vascular occlusion serves as the most probable pathophysiologic mechanism [2].

This report establishes an uncommon presentation of an already rare disease (0.24 patients per million), PuR in the setting of underlying mixed connective tissue disease [1]. This case report may be beneficial to patients with MCTD as it can lead the discussion in the importance of potential screening and treatment. Further study is necessary to assess the role of steroid treatment, as well as the role of preventive or corrective bevacizumab therapy [11]. Additionally, the potential side effects of hydroxychloroquine therapy may need to be assessed in each patient individually based on their vision and retinal pathology findings, as therapy may be warranted for their underlying condition and may outweigh the risks of retinal toxicity [12].

CONCLUSION

This case establishes a correlation between PuR and MCTD. Any patient with diagnosed MCTD that presents with visual complaints should undergo screening for this uncommon retinopathy. Further studies are warranted to establish an etiology for this disease and thus obtain an effective treatment.

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Author Contributions

Mariam S Vila-Delgado – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Luis Serrano – Conception of the work, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Viviana Barquet – Conception of the work, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Alejandra Santiago – Conception of the work, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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