



Case report

Bilateral exudative retinal detachments due to thrombotic microangiopathy associated with intravenous abuse of Opana ER

Fazila Aseem^a, Brian G. Zamora^a, Levi Kauffman^a, Peter J. Miller^b, Vishak J. John^{a,*}^a Department of Ophthalmology, Wake Forest School of Medicine, 1 Medical Center Blvd, Winston-Salem, NC 27157, USA^b Department of Internal Medicine, Sections on Hematology and Oncology, and Pulmonary, Critical Care, Allergy and Immunologic Medicine, Department of Anesthesia, Section on Critical Care, Wake Forest School of Medicine, 1 Medical Center Blvd, Winston-Salem, NC 27157, USA

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ABSTRACT

Purpose: To report the only known case, to our knowledge, of bilateral exudative retinal detachments in the setting of thrombotic microangiopathy associated with intravenous abuse of extended-release oxycodone (Opana ER).

Observations: A 35-year-old male presented with headaches and acute, painless vision loss in the context of daily IV abuse of crushed oral Opana ER. The patient was found to have microangiopathic hemolytic anemia (MAHA), acute kidney injury in conjunction with hypertensive crisis and bilateral exudative retinal detachments.

Conclusions and importance: Bilateral exudative retinal detachments are rare ophthalmic complications that have been reported with thrombotic thrombocytopenic purpura (TTP). Non-TTP thrombotic microangiopathy, initially described as a “TTP-like illness” consisting of MAHA and thrombocytopenia, has been associated with the IV abuse of Opana ER. We report a case of bilateral exudative retinal detachments due to thrombotic microangiopathy in the setting of IV abuse of Opana ER.

1. Introduction

Bilateral serous retinal detachments are a rare but reported ocular complication of thrombotic thrombocytopenic purpura (TTP).^{1–3} TTP is a life-threatening thrombotic microangiopathy caused by severe deficiency of the von Willebrand factor-cleaving protease, ADAMTS13. It is characterized by small blood vessel platelet-rich thrombi that cause microangiopathic hemolytic anemia (MAHA), defined by thrombocytopenia with schistocytosis and reticulocytosis, and end organ damage, including neurological, renal, gastrointestinal, cardiac and visual symptoms. With similar presentation to TTP and relatively normal ADAMTS13 activity, thrombotic microangiopathies can also occur secondary to infection, complement activation, pregnancy, HIV, and various drugs, including cocaine and IV Opana ER abuse.^{4–6} Pathophysiologically, thrombotic microangiopathies induce vascular endothelial damage, which can trigger the formation of platelet and fibrin thrombi, causing arteriolar and capillary occlusions.

Reported ocular complications from TTP and other thrombotic microangiopathies are dependent on which blood vessels of the eye are damaged, but can include choroidal vascular occlusion, vitreous hemorrhage, diffuse retinal ischemia, optic disk neovascularization, optic atrophy, and exudative retinal detachments.^{1–3} Here, we present the

first report, to our knowledge, of a severe ocular manifestation of a drug-induced thrombotic microangiopathy (DITMA) from the IV abuse of crushed oral Opana ER—bilateral exudative retinal detachments. This case highlights the potentially vision threatening complications of repeated IV abuse of Opana-ER, and points to the potential reversibility of this vision loss with cessation of Opana and through supportive treatment of the systemic manifestations of the Opana-induced thrombotic microangiopathy.

2. Case report

A 35-year-old male presented to our hospital as a transfer from an outside hospital with headaches, leukocytosis, severe hypertension, acute kidney injury, and acute, painless vision loss. He reported a 3-day history of complete vision loss in his right eye, and blurry vision with a new floater in the superior visual field of his left eye. He denied photopsias and had no other ocular history. He endorsed a two-day history of mild headache, nausea, and subjective fevers. His past medical history was significant for IV drug abuse, hepatitis C and infective endocarditis. He reported current, daily usage of 80–100 mg oral Opana ER, which he crushed and injected intravenously. His most recent injection was the day prior to presentation. The patient denied prior

* Corresponding author. Department of Ophthalmology, Wake Forest School of Medicine, 1 Medical Center Blvd, Winston-Salem, NC 27157, USA.
 E-mail address: vishakjohn@vistareye.com (V.J. John).



Fig. 1. Exudative retinal detachment. Color fundus images of patient's right (A) and left (B) eye showing retinal hemorrhages and retinal detachment in his inferior retina bilaterally. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

history of hypertension and kidney disease, and reported that his only medication was gabapentin 300 mg three times daily for muscle cramps and anxiety.

At the outside facility, the patient had a leukocytosis of 16,800 WBCs/uL, thrombocytopenia of 67,000 platelets/uL, and was markedly hypertensive with systolic of blood pressure of 210–220 mmHg. At presentation to our facility, the patient was afebrile, but remained significantly hypertensive (190/110 mmHg) and was tachycardic at 116 bpm. On ophthalmic examination, visual acuity was 20/200 OD and 20/70 OS with +rAPD OD. He had normal intraocular pressures and full extraocular motility. Slit lamp examination of the anterior segment was normal. Fundus examination revealed scattered intraretinal hemorrhages, focal areas of subretinal hypopigmentation in the posterior pole, and bilateral bullous exudative detachments inferiorly, which were more prominent in his right eye compared to his left (Fig. 1A and B).

Laboratory investigations revealed severe anemia (Hgb 7.5 g/dL), leukocytosis (13,500 WBCs/uL), and thrombocytopenia (76,000 platelets/uL). Peripheral blood smear was significant for 2 + schistocytes and 2 + anisocytosis on RBC analysis, and showed no WBC or platelet abnormalities—notably no giant platelets or platelet clumping was observed. LDH and reticulocytes were significantly elevated at 945 IU/L and 16.4%, respectively, consistent with a hemolytic anemia. Serum creatinine was 7.35 mg/dL and BUN was 51 mg/dL. Urine drug screen was positive for opiates.

His constellation of hematologic findings—thrombocytopenia, microangiopathic hemolytic anemia (MAHA)—along with headache and renal disease was consistent with thrombotic microangiopathy. Thrombotic microangiopathy secondary to drug abuse, unlike TTP, is not associated with decreased ADAMTS13 level.^{6,7} Given the significant history of IV Opana ER abuse, the working diagnosis of Opana-induced thrombotic microangiopathy was made.

The patient was treated with supportive measures for his hypertension, acute kidney injury and leukocytosis. Patient was started on antihypertensive medications, and due to fluid overload, was eventually started on hemodialysis. As his blood pressure and lab values normalized over his hospital course, his visual acuity and visual symptoms significantly improved. On hospital day 3, visual acuity was 20/40 OD and 20/25 OS and subjectively, patient felt like vision was back to base line with interval decrease in visual symptoms. The patient was discharged on hospital day 12 with systolic blood pressures in the 150–160 mmHg range on oral amlodipine 10 mg daily, hydralazine 20 mg TID, and clonidine 0.2 mg BID. Platelets improved to 271,000 cells/uL and hemoglobin showed slight improvement to 7.8 g/dL. Serum creatinine at discharge was 6.51 mg/dL and the patient was scheduled for outpatient hemodialysis. On ophthalmologic examination prior to discharge, the exudative RD in the right eye was significantly improved and in the left eye, the exudative RD was resolved. Visual acuity

remained at 20/40 OD and 20/25 OS and the patient was scheduled for outpatient follow up in Ophthalmology clinic. Unfortunately, the patient failed to return to clinic and has since been lost to follow up.

3. Discussion

The clinical presentation of this patient—microangiopathic hemolytic anemia (MAHA), thrombocytopenia, acute kidney injury in conjunction with hypertensive crisis, and bilateral exudative retinal detachments—is consistent with a thrombotic microangiopathy. Given the history of daily intravenous injection of crushed extended-release oxymorphone pills, we suggest our patient developed a drug-induced thrombotic microangiopathy (DITMA) in response to repeated IV abuse of Opana ER, which ultimately contributed to the development of bilateral exudative retinal detachments.

Drug-induced thrombotic microangiopathy (DITMA) is an acquired condition resulting from exposure to a drug that either causes formation of drug-dependent antibodies or direct tissue toxicity, resulting in the formation of platelet-rich thrombi in small arterioles or capillaries.^{8–11} Kidneys appear to be especially susceptible, often resulting in hypertensive emergency. Mechanistically, animal studies suggest that the inert additives used to make oxymorphone tablets crush-resistant, which includes high molecular weight polyethylene oxide (PEO), can directly cause hemolytic anemia and thrombocytopenia, and therefore may mediate the toxic effects of IV Opana ER abuse in humans.^{4,12}

Bilateral exudative retinal detachments are a rare but reported complication of TTP. To our knowledge, this is the first reported case of bilateral exudative retinal detachment associated with thrombotic microangiopathy from IV abuse of Opana ER. Shah and Cherney were the first to report a case of intravenous Opana ER abuse associated with vision loss.⁵ They described a patient with diffuse retinal ischemia and postulated that Opana induces arteriolar and capillary thrombotic microangiopathies and endothelial damage, leading to vision loss. Our case involves bilateral vision loss with bilateral exudative retinal detachments in the setting of a severe DITMA from concomitant IV abuse of Opana ER. Likely contributing to this unique presentation was the hypertensive emergency component. While the patient's extremely elevated blood pressure was likely a sequela of his thrombotic microangiopathy, we cannot fully rule out the possibility that the retinal detachments were due, at least in part, to severely uncontrolled blood pressure. However, there are reports in the literature of exudative retinal detachments in thrombotic microangiopathies that were unrelated to systemic hypertension, substantiating the possibility that our patient's retinal detachments were likely a result of his Opana ER-induced thrombotic microangiopathy and should be managed accordingly.^{13–15}

Opana ER-induced thrombotic microangiopathy can be managed with supportive measures. Therapeutic plasma exchange is the mainstay initial treatment for TTP. However, drug-induced thrombotic

microangiopathy patients recover with supportive care if the drug is discontinued.^{7,16} Therefore, plasma exchange can safely be deferred and Opana-induced thrombotic microangiopathy cases can be managed with supportive measures when Opana is discontinued.

4. Conclusions

We present the first reported case of bilateral exudative retinal detachment in the setting of a thrombotic microangiopathy from the IV abuse of crushed extended-release oxycodone pills. This unique case suggests that microangiopathy associated with IV abuse of Opana ER plays a significant role in vision loss either directly through PEO and the development of microthrombi in Opana-induced thrombotic microangiopathy, or more indirectly through a mechanism of hypertensive emergency, which is also a direct complication of Opana-induced thrombotic microangiopathy. It is our assertion that IV abuse of Opana ER can directly and in concert with hypertension lead to significant vision loss through the development of bilateral exudative retinal detachments and should be considered in patients with decreased vision in the setting of IV Opana ER abuse.

Patient consent

Personal identifying information has been removed from this report because consent to publish such information was not obtained.

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Conflict of interest

The following authors have no financial disclosures: FA, BGZ, LK, PJM and VJJ.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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