

Massive Hyphaema Following Laser Iridotomy in a Patient on Dual Antiplatelet Therapy (Aspirin plus Ticagrelor)

Case report and literature review

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تخدمية جسيمة بعد بضع القرزحية بالليزر في مريض يتناول علاج ثنائي من مضادات تكتل الصفائح الدموية (الأسبرين بالإضافة الى التيكاجريلور) تقرير حالة ومراجعة للأدبيات

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ABSTRACT: Massive hyphaema presentation after a laser iridotomy is very rare. We report a 63-year-old man with ischaemic heart disease on dual antiplatelet therapy (aspirin plus ticagrelor) who was diagnosed as a primary angle-closure suspect and was to undergo a neodymium-doped yttrium aluminium garnet laser iridotomy at Centro Oftalmológico Virgilio Galvis, Floridablanca, Colombia in 2016. While performing the iridotomy in the left eye, active bleeding occurred that finally filled approximately 75% of the anterior chamber. Intraocular pressure (IOP) increased to 62 mmHg. Mannitol and a topical dorzolamide/timolol were used to control the increase in IOP. The hyphaema slowly resolved over the following week without *sequelae*. This case revealed that massive hyphaema can complicate laser iridotomy in patients on dual antiplatelet therapy, although this is rare. Therefore, if patients are taking aspirin and ticagrelor, it would be advisable to stop the second medication if possible. In addition, sequential application of photocoagulation and photodisruption lasers might diminish the risk of significant bleeding.

Keywords: Iridectomy; Nd-YAG Laser; Hyphema; Platelet Aggregation Inhibitors; Angle-Closure Glaucoma; Ocular Hypertension; Case Report; Columbia.

المخلص: حصول تخدمية جسيمة بعد بضع القرزحية بالليزر هو امر نادر جداً. نعرض هنا حالة رجل يبلغ من العمر 63 عاماً مصاب بمرض نقص تروية القلب ويتلقى علاج ثنائي من مضادات تكتل الصفائح الدموية (الأسبرين بالإضافة إلى التيكاجريلور) والذي تم تشخيصه كمشتبه مصاب بزرق إسداد الزاوية الأولي وخضع لعملية بضع القرزحية بالليزر العقيقي الذي يستخدم إيتريوم الألومنيوم المنشط بالنيوديميوم وذلك في مركز فيرجيليو غالفيس لطب العيون، فلوريدابلانكا، كولومبيا في عام 2016. أثناء إجراء عملية بضع القرزحية في العين اليسرى، حدث نزيف نشط ملأ حوالي 75% من الغرفة الأمامية للعين. وزاد الضغط داخل العين إلى 62 مم زئبق. تم استخدام مانيتول ودورزولاميد/تيمولول موضعياً للسيطرة على زيادة الضغط داخل العين. وزال نزيف العين في الأسبوع التالي دون مضاعفات. كشفت هذه الحالة أن التخدمية الجسيمة يمكن أن تحدث كمضاعفة لعملية بضع القرزحية بالليزر في المرضى الذين يتلقون علاج ثنائي من مضادات تكتل الصفائح الدموية، رغم أن هذا الأمر نادر الحدوث. بناء على ذلك إذا كان المريض يتناولون الأسبرين والتيكاجريلور من المستحسن إيقاف العلاج الثاني إن أمكن ذلك. بالإضافة إلى ذلك، الاستخدام المتتالي لليزر التخثير الضوئي وليزر التفتيت الضوئي قد يقلل من خطر حدوث نزيف حاد.

الكلمات المفتاحية: بضع القرزحية؛ ليزر Nd-YAG؛ تخدمية؛ مثبطات تكتل الصفائح الدموية؛ زرق إسداد الزاوية؛ ارتفاع ضغط العين؛ تقرير حالة؛ كولومبيا.

SIGNIFICANT HYPHAEMA AS A COMPLICATION of laser iridotomy has rarely been reported.¹⁻⁴ Massive hyphaema may cause secondary acute elevation of intraocular pressure (IOP) and corneal blood staining which may lead to serious visual morbidity. Laser iridotomy is a common procedure since currently it is performed prophylactically on most patients with narrow anterior chamber angles; the prevalence of this condition in adults varies according to race, from 0.7% in Brazil to 10% in China.⁵⁻⁷ Given the wide use of antiplatelet drugs in preventing thrombotic diseases and the increased frequency of patients taking

anticoagulant agents, the number of such patients requiring a laser iridotomy while concomitantly being on antiplatelet therapy is increasing.

Case Report

A 63-year-old male patient with ischaemic heart disease, in whom a prophylactic laser iridotomy had been indicated, presented to Centro Oftalmológico Virgilio Galvis, Floridablanca, Colombia in 2016. At that time, he was taking two antiplatelet agents, ticagrelor and aspirin. Initially, a neodymium-doped yttrium aluminium garnet

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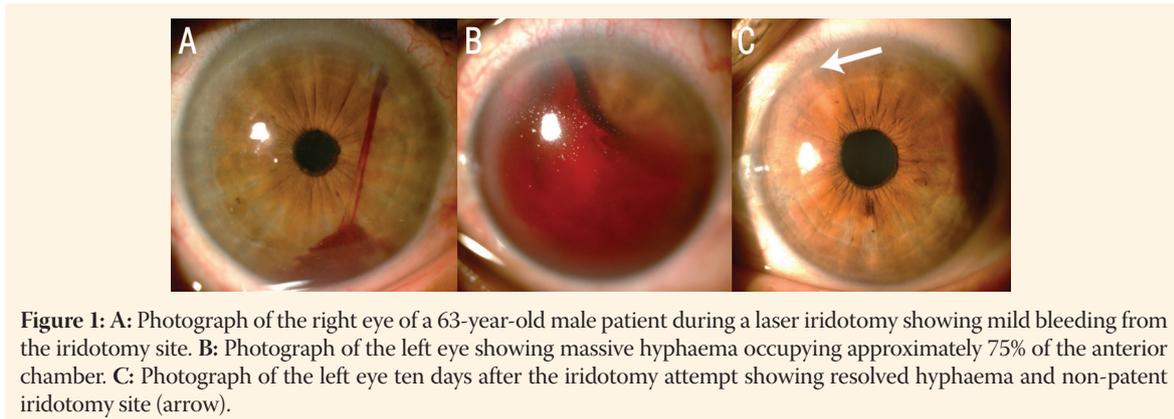


Figure 1: A: Photograph of the right eye of a 63-year-old male patient during a laser iridotomy showing mild bleeding from the iridotomy site. B: Photograph of the left eye showing massive hyphaema occupying approximately 75% of the anterior chamber. C: Photograph of the left eye ten days after the iridotomy attempt showing resolved hyphaema and non-patent iridotomy site (arrow).

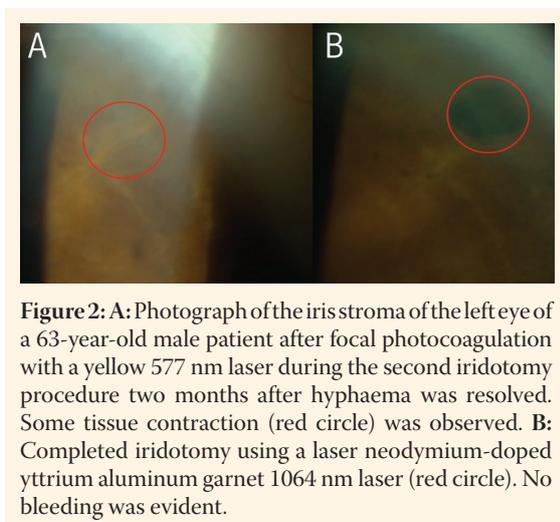


Figure 2: A: Photograph of the iris stroma of the left eye of a 63-year-old male patient after focal photocoagulation with a yellow 577 nm laser during the second iridotomy procedure two months after hyphaema was resolved. Some tissue contraction (red circle) was observed. B: Completed iridotomy using a laser neodymium-doped yttrium aluminum garnet 1064 nm laser (red circle). No bleeding was evident.

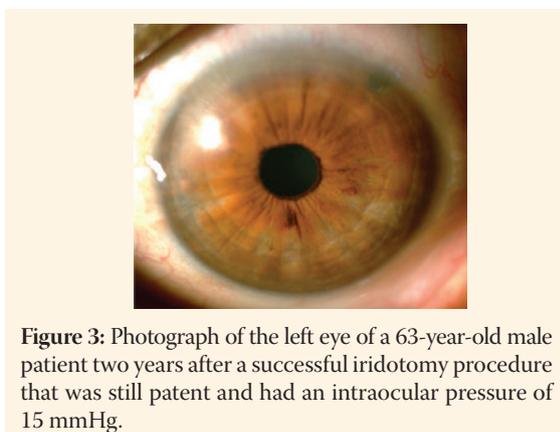


Figure 3: Photograph of the left eye of a 63-year-old male patient two years after a successful iridotomy procedure that was still patent and had an intraocular pressure of 15 mmHg.

(Nd:YAG) laser iridotomy (VISULAS[®] YAG III, Carl Zeiss Meditec AG, Jena, Germany) was performed in the right eye (four laser shots each containing 6 mJ of power). A small amount of bleeding was noted but was stopped under digital pressure on the Abraham lens [Figure 1A]. When performing the second shot in the left eye, however, the iridotomy site started to bleed and the blood flow did not stop despite applying digital pressure. Over the subsequent ten minutes a hyphaema formed, filling approximately 75% of the anterior chamber and the IOP increased to 62 mmHg [Figure 1B].

Given the patient's medical history of ischaemic heart disease, he was sent to the emergency department. Internal medicine advised to give an intravenous injection of mannitol (2 g/kg) over one hour and to discontinue the antiplatelet therapy. Topical treatment was started with prednisolone acetate (1%) four times a day and dorzolamide/timolol twice a day. By the next day, IOP had decreased to 14 mmHg. By the fourth day post-procedure, the blood clot filled approximately 25% of the anterior chamber. Following the evaluation by the cardiologist, the patient resumed antiplatelet therapy.

Ten days after the iridotomy attempt, the anterior chamber of the left eye was free of blood and IOP was 18 mmHg. The iridotomy site in that eye was not patent [Figure 1C]. Two months later, after the patient's cardiologist had temporarily suspended antiplatelet therapy, a new iridotomy was performed in the patient's left eye without complications. This session used a sequential application of a yellow 577 nm laser (Pascal Streamline 577, Topcon Medical Systems Inc., Oakland, New Jersey, USA) in order to photocoagulate the tissue and an Nd:YAG laser was used to create the perforation (VISULAS[®] YAG III) [Figure 2]. At the last check-up visit two years later, the iridotomy was open and IOP was 15 mmHg [Figure 3].

Discussion

Preventative laser iridotomies are currently performed in most patients with narrow anterior chamber angles; the prevalence of this condition in adults varies from 0.7–10% depending on race.^{7–10} In addition, given the growing frequency of patients taking antiplatelet or anticoagulant agents, the number of patients requiring a laser iridotomy is increasing. Both photocoagulating (Argon laser: 514 nm or Nd:YAG frequency-doubled laser: 532 nm) and photodisrupting lasers (Nd:YAG: 1064 nm) have been used to perform laser iridotomies; the use of the latter has become more common in the past three decades. Bleeding at the iridotomy site that stops under digital pressure on the Abraham lens has

been reported in a wide range of cases, from 3% to approximately 50%.^{2,8–14} However, massive hyphaema has been rarely reported as a complication of Nd:YAG laser iridotomies in patients with uveitis or rubeosis and in some patients without apparent risk factors.^{1,2,4} Bleeding seems to be less frequent with photocoagulating lasers because of the thermal coagulation effect. However, at least one case of significant hyphaema following peripheral iridotomy using an Argon laser has been reported.³ The sequential use of two different types of laser—photocoagulating and photodisruptive—has also been reported to diminish the risk of bleeding.^{13,14}

Antithrombotic medications are widely used to prevent both arterial or venous thromboembolisms, which can cause cerebrovascular or cardiovascular disease (e.g. myocardial infarction, ischaemic stroke and peripheral arterial disease leading to limb gangrene) usually related to arterial thrombosis or deep vein thrombosis that can result in pulmonary embolism.¹⁵ Aspirin is the most commonly used antiplatelet medication which inhibits platelet cyclo-oxygenase-1 therefore blocking the synthesis of thromboxane A₂. Another family of antiplatelet medications are the adenosine diphosphate (P2Y₁₂) receptor inhibitors, including thienopyridines (e.g. clopidogrel and prasugrel) and the newer class of cyclopentyl triazolopyrimidines (e.g. ticagrelor).^{15–18}

Newer antiplatelet agents, like ticagrelor, are frequently used in addition to aspirin in order to reduce the rate of major adverse cardiovascular events in patients with ischaemic heart disease. This approach has been advantageous in terms of preventing thrombotic and major adverse cardiovascular events in high-risk patients. However, these combined therapies are associated with increased risk of bleeding.^{16,19–21} In the Platelet Inhibition and Patient Outcomes trial, ticagrelor was compared with clopidogrel, both in addition to aspirin, revealing a similar association with total major bleeding. Nevertheless, ticagrelor exhibited higher and more consistent levels of inhibition of platelet aggregation across the dosing interval than clopidogrel and also a higher risk of both minor and major non-cardiac surgery related bleeding rates as well as during non-coronary artery-bypass-grafting.^{15,17,18,21}

Based on the results of a prospective controlled trial, Golan *et al.* suggested that there was no indication for discontinuing antiplatelet or anticoagulant treatment before an Nd:YAG laser iridotomy.¹² However, Golan *et al.*'s study only included patients taking either aspirin, warfarin sodium or clopidogrel, with no patients on a dual antiplatelet therapy. None of the patients experienced massive hyphaema, yet the incidence of minor bleeding from the iridotomy site was comparable with and without the antiplatelet therapy (34.6% in both groups).¹² However, there were five cases (4.8%) of grade two bleeding

—defined by the authors as not controlled by light pressure on the lens but no macroscopic hyphaema—in the group of patients treated while taking antiplatelet agents, and only one case (1%) in the group of patients treated two weeks after discontinuing the medication. Although Golan *et al.* found this difference to be not statistically significant ($P = 0.14$); however, calculations made by the current authors based on the data published by Golan *et al.* and using a one-tailed Z score to compare the two population proportions, revealed the results to be significant ($P = 0.046$).

In 2012, the evidence-based clinical practice guidelines of the American College of Chest Physicians advised that interrupting aspirin before non-cardiac surgeries may be reasonable for patients at low risk of cardiovascular events due to the low benefit-to-risk ratio of continuing it perioperatively.²² On the other hand, in patients at moderate-to-high risk of perioperative adverse cardiovascular events, it may be preferable to continue the aspirin perioperatively.

With regard to dual antiplatelet therapy in patients who require a coronary artery bypass graft, the guidelines indicated that perioperative continuation of dual antiplatelet therapy has been related to an increased risk of bleeding. However, it was not clear whether there was a similarly increased risk for serious bleeding with perioperative continuation of dual antiplatelet therapy in patients having non-cardiac surgery and procedures.²² Kong and Khan stated that although dual antiplatelet therapy increases the likelihood of bleeding in ophthalmic procedures, this complication is generally less significant than major adverse cardiac events in patients with coronary stents. Therefore, they advised that antiplatelet therapy should be continued in patients with coronary stents undergoing eye surgery.²³

Based on the joint consensus of several European and Asiatic scientific societies, Thachil advised stopping the second agent in dual antiplatelet therapy if the bleeding risk of a non-cardiac procedure was low.²⁴ Similarly in a recent multidisciplinary consensus from Spain, Vivas *et al.* concluded that in patients receiving dual antiplatelet therapy and scheduled for an elective procedure, the first step should be to consider postponing the procedure if the patient has a moderate-to-high risk of thrombosis until the risk is lower. Once the risk is low, they recommend maintaining aspirin, unless contraindicated (e.g. in neurosurgery) and withdrawing the second antiplatelet agent. If the thrombotic risk remains high, the decision to stop dual antiplatelet therapy will depend on the bleeding risk associated with the procedure. If the bleeding risk is low, they do not suggest stopping dual antiplatelet therapy but cases of moderate-to-severe risk of bleeding are more controversial and they advocate evaluating patients on a case-by-case basis within a multi-disciplinary team.²⁵

Although the current patient was hypertensive and diabetic, he did not have renal failure. There were no signs of diabetic retinopathy and the iris did not show rubeosis. It is therefore difficult to state that a comorbidity could have played a role in the hyphaema development. On the other hand, suspicion that the origin of the haemorrhage had not been the iris was rejected since when performing a laser iridotomy, the risk of causing a lesion to other vascularised intraocular structures such as the ciliary body, has never been reported and is almost non-existent since a space separates the iris from more posterior structures and the laser energy acts focally. However, in view of the current case, it is important to note that there was no significant bleeding in the first eye treated in the patient and it is therefore not possible to establish a direct link between the dual antiplatelet therapy and massive bleeding during the peripheral iridotomy.

Conclusion

Massive hyphaema is a very rare complication following Nd:YAG laser iridotomy, which may occur in patients on dual antiplatelet therapy, as shown in the current case. The bleeding risk with a laser iridotomy is low; however, to avoid this potentially vision-threatening complication in patients on dual antiplatelet therapy, it is suggested to consult with an internist/cardiologist in order to evaluate the option of temporarily discontinuing the two or at least the second anticoagulant, while continuing aspirin, for patients with low thrombotic risk. In patients with a high risk of thrombosis, a case-by-case analysis should be undertaken with a cardiologist where the risk of bleeding during the procedure is weighed against the risk of developing a cardiovascular thrombotic event. In addition, as sequential use of photocoagulating and photodisrupting lasers has been shown to have a lower risk of iris bleeding, this approach would be preferable in these patients. However, these recommendations are based on the limited evidence of this case report.

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