Retinal Pigment Epithelial Tear after Intravitreous Triamcinolone Acetonide Injection for Fibrovascular Pigment Epithelial Detachment

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A 78-year-old woman was diagnosed with fibrovascular pigment epithelial detachment (PED) associated with age-related macular degeneration (AMD) affecting both eyes. Due to decreased vision in her left eye (20/2000) and disease progression, the patient received 4 mg of triamcinolone acetonide (TA) by intravitreal injection into her left eye. There were no immediate post-injection complications in the left eye. However, one week later, a retinal pigment epithelial (RPE) tear, temporal-inferior to the fovea in the left eye, was noted and confirmed by fundus photography, fluorescein angiography and optical coherence tomography. In contrast, there no similar RPE tear occurred in her right eye after treated several times by intravitreous bevacizumab injection. Not only anti-vascular endothelium growth factor agents, but also intravitreal TA when used to treat AMD with PED, would seem to induce a RPE tear in the absence of previous or concurrent adjuvant therapy. Further investigations are required to confirm the mechanism by which the RPE tear occurs. *(Chang Gung Med J 2011;34:320-5)*

Key words: neovascularization, triamcinolone acetonide, age-related macular degeneration, retinal pigment epithelial tear, intravitreous injection

Retinal pigment epithelial (RPE) tears are a known complication of neovascular age-related macular degeneration (AMD). They may occur during the natural course of neovascular AMD, or as a complication after various treatments, such as laser photocoagulation and photodynamic therapy (PDT), especially in eyes with pigment epithelial detachment (PED).[1] Recently, cases where a RPE tear has developed after intravitreal anti-vascular endothelial growth factor (VEGF) injections have been reported.[2-4] Intravitreal injections of triamcinolone acetonide (TA) has been used to treat exudative AMD and have provided favorable results over a short duration.[5] We report a case wherein the patient developed acute RPE tear following intravitreal injection of triamcinolone acetonide for the first time. The injection was being used as a treatment for occult choroidal neovascularization (CNV) with PED due to age-related macular degeneration.

CASE REPORT

A 78-year-old woman complained of blurred vision in her eyes. Best corrected visual acuity was 20/33 in the right eye and 20/200 in the left eye. Ophthalmoloscopy revealed large drusenoid lesions in the macula of both eyes. Fluorescein angiography (FAG) and optical coherence tomography (OCT)

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revealed fibrovascular PED due to the progression of age-related macular degeneration (Fig. 1). Three months later, intraretinal hemorrhage and persistent PED were observed (Fig. 2A and B), and her left visual acuity had decreased to 20/2000. After obtaining informed consent in January 2006, the patient received 4 mg of TA via intravitreal injection into her left eye with no immediate observed post-injection complications. However, one week later, she presented with a RPE tear temporal-inferior to the fovea in the left eye, which was confirmed by fundus photography (FP), OCT and FAG (Fig. 2 C-E). Based on the unfavorable outcome in her left eye after the TA injection, she asked to be switched to bevacizumab therapy. However, her visual acuity did not improve despite two intravitreous injections of bevacizumab at a later time. Based on the fact that a RPE tear had been observed in her left eye after intravitreous TA injection, she was not treated by intravitreal TA injection into the right eye. Her right eye vision, however, then deteriorated to 20/300 over the subsequent follow up period. She then received four intravitreous bevacizumab injections into the right eye, and her visual acuity responded well to the treatment. No RPE tear was observed in her right eye after these injections. The final visual acuity measured in November 2007 was 20/100 in the right eye and 20/2000 in the left eye.

DISCUSSION

Patients with occult choroidal neovascularization and a primary PED are assumed to have a higher risk of RPE tears. RPE tears are a serious complication of exudative AMD. The incidence of spontaneous RPE tear in AMD with fibrovascular PED is about 10% over a 1-year follow up; although the authors of this study have suggested that this figure may underestimate of the true incidence.[6] Other than being a part of the natural course of the disease, RPE tears may also occur as a complication to thermal laser treatment, PDT and intravitreous injection ther-

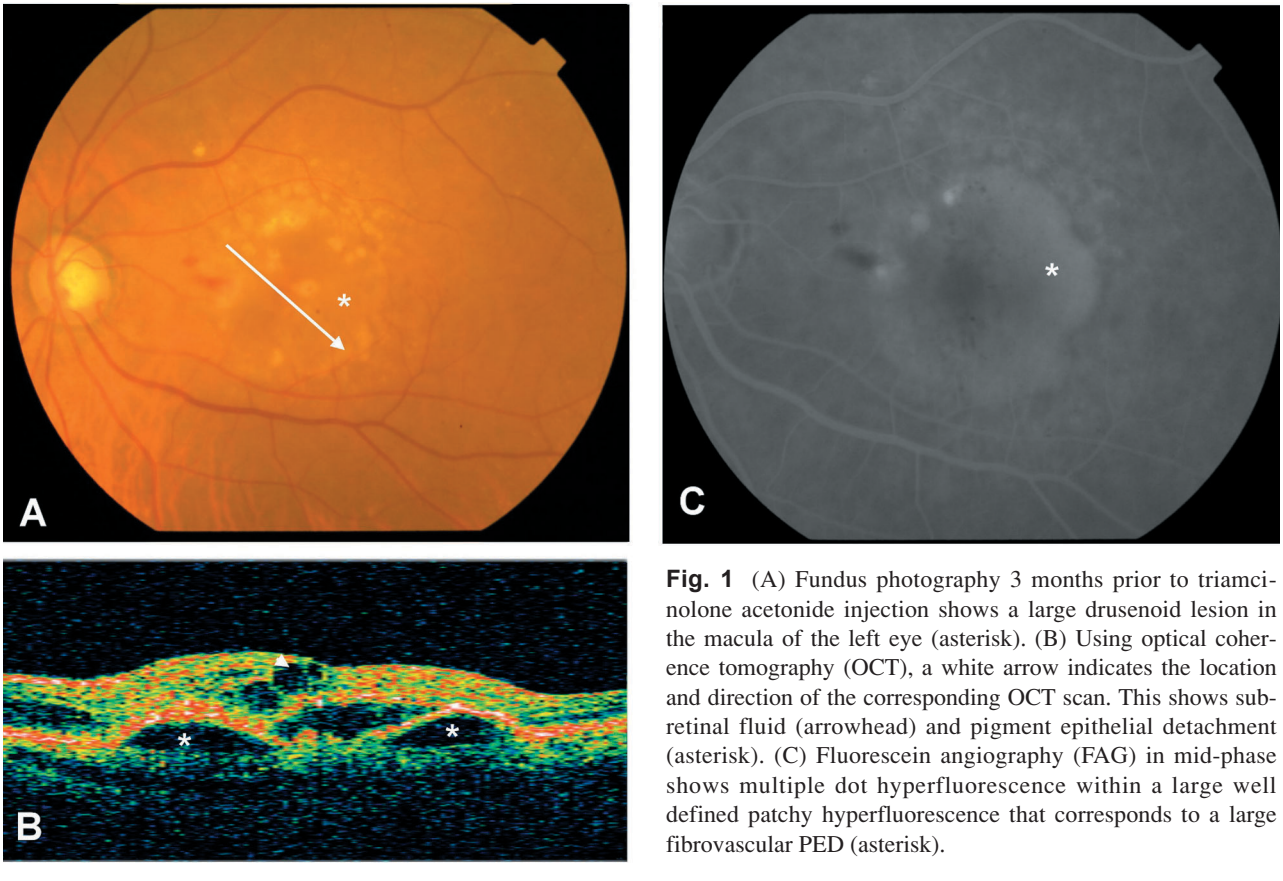

Fig. 1 (A) Fundus photography 3 months prior to triamcinolone acetonide injection shows a large drusenoid lesion in the macula of the left eye (asterisk). (B) Using optical coherence tomography (OCT), a white arrow indicates the location and direction of the corresponding OCT scan. This shows subretinal fluid (arrowhead) and pigment epithelial detachment (asterisk). (C) Fluorescein angiography (FAG) in mid-phase shows multiple dot hyperfluorescence within a large well defined patchy hyperfluorescence that corresponds to a large fibrovascular PED (asterisk).

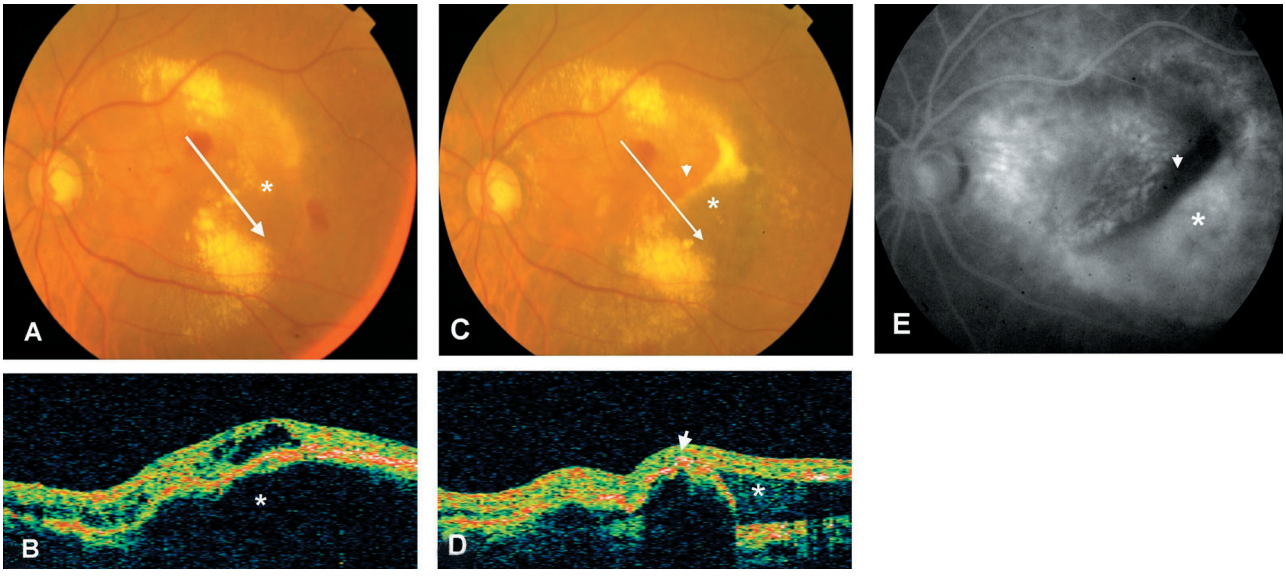

Fig. 2 (A) Left eye fundus photography and (B) OCT 1 week prior to triamcinolone acetonide injection shows a large pigment epithelial detachment (asterisk) due to progression of the age-related macular degeneration. The white arrow indicates the location and direction of the corresponding OCT scan. (C) Fundus photography, (D) OCT and (E) FAG one week after intravitreal triamcinolone acetate injection showing an area with retinal pigment epithelium (RPE) defect inferior-temporal to the fovea (asterisk). An orange band with a well-defined demarcation boundary represents pleated and rolled RPE retraction with a RPE rip (short arrow). The OCT shows an area where RPE is absent with a decreased signal (asterisk) due to the loss of overlying RPE. A hyper-reflective band of retracted RPE with RPE detachment near the centre of fovea (short arrow) is observed with a pleated and tent-like configuration. The rip of the RPE tear is shown as focal disruption between short arrow and asterisk. Mid-phase FAG demonstrates an area of hyperfluoresence corresponding to the area of absent RPE (asterisk) and a hypofluorescent band area representing the area of retracted RPE (short arrow). The rip of the RPE tear is shown as a linear boundary of focal disruption between the short arrow and asterisk.

apy including TA and various anti-VEGF drugs (e.g. bevacizumab, ranibizumab and pegaptanib). The reported incidence rages from 1.8% to 27%.[7]

RPE tears have distinctive features on FAG and OCT. On FAG, RPE tears show as sharply demarcated areas with a hyperfluorescent window defect that corresponds to the area of bare RPE; this is adjacent to an area of blocked hypofluorescence that corresponding to the area of redundant RPE.[8] A dark band of the RPE on FA represents retracted, redundant, folded, or pleated RPE. On OCT, the characteristic feature of a rip is a focal disruption in the RPE layer.[9] The torn and detached RPE often retracts and may have three different appearances, namely a pleated, tent-like, or dome-shaped configuration.[10] The redundant RPE is often irregular in contour and has a thicker hyperreflective reflex.

The exact pathogenesis of RPE tears remains unknown and several potential mechanisms have been proposed including the following. Firstly, that various therapeutic modalities induce tangential shearing forces that affect the contracting CNV, which overlies a weakened RPE layer.[11] Secondly, that there is increased liquid transport into the sub-RPE space due to the presence of the hydrophobic Bruch's membrane associated with AMD.[12] Thirdly, that vitreoretinal traction related to globe deformation and vitreous syneresis and incarceration is elicited by the injecting needle.[13] Fourthly, that there is an extreme fluctuation in intraocular pressure. Finally, that there is an interruption in maintenance of the RPE tight junctions that is mediated by VEGF.[14,15] Recently, some variables associated with the risk of RPE tears have been proposed, including a large PED basal diameter and vertical height.[16,17] In our case, a large PED, an increased vertical height and acute onset of RPE tear after intravitreous injection TA seems to provide further evidence about the pos-

sible mechanisms.

TA treatment has shown anti-edematous and anti-angiogenic effects in various experimental investigations and clinical studies,[5,18,19] Intravitreal TA has been used in previous pilot studies to treat exudative AMD and some patients have shown a vision improvement post treatment. In addition, a greater gain in VA has been reported for eyes with PED than in eyes with minimal classic subfoveal neovascularisation. In our patient, the cause of the RPE tear after intravitreal TA injection may have been associated with the rapid action of the intravitreal TA in decreasing the intraretinal and subretinal fluid over a short time, namely one week. Recently there has been a report showing resolution of subretinal fluid after the use of bevacizumab in a spontaneous RPE tear associated with AMD.[20] The two additional injections of bevacizumab were effective at decreasing intraretinal edema, but there was no change in the RPE tear and no significant improvement in vision.

Our case presented with bilateral AMD with a large PED. It has been reported that AMD with a large PED basal diameter and vertical height has a high risk of RPE tears after intravitreous injection of anti-VEGF agents.[16,17] TA has the disadvantage of being associated with late ocular complications and cataract formation when compared to various anti-VEGF agents. Anti-VEGF should be made the treatment of choice if it is available and cost should not be a consideration. However, the cases available are too few to establish an association between TA injection and RPE tear induction and to allow comparison with the incidence when various other anti-VEGF agents are used. Nevertheless, it is important that high risk patients are told of this possible complication.

To our knowledge this is the first case to be reported of an acute RPE tear during the first week after intravitreal TA when this is used to treat AMD with PED without previous or concurrent adjuvant therapy. Additional studies are needed to determine the lesion's characteristics, to understand the mechanism involved, and to reduce the risk that this serious problem will occur.

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纖維血管性色素上皮細胞剝離病患之玻璃體內注射丙酮特安皮質醇發生視網膜色素上皮細胞撕裂

吳佩昌 陳勇仁 郭錫恭

一位 78 歲之女性雙眼被診斷出纖維血管性視網膜色素上皮細胞剝離之老年性黃斑病變，因爲左眼視力惡化下降至 0.01，病患接受左眼玻璃體內注射 4 毫克的類固醇 (triamcinolone acetonide) 治療，注射後並沒有任何立即的併發症；但是一週後，在視網膜黃斑中心小凹外下方卻出現視網膜色素上皮細胞撕裂，此病變在眼底照相、眼底螢光攝影及光學同軸斷層檢查得到證實；相對的，右眼玻璃體內注射癌思停 (Bevacizumab) 卻沒有造成類似的病變。不僅眼內注射抗血管內皮生長因子會造成視網膜色素上皮細胞撕裂，此病例顯示在沒有治療過的纖維血管性視網膜色素上皮細胞剝離之老年性黃斑病變病患，玻璃體內注射類固醇治療也可能會造成急性視網膜色素上皮細胞撕裂，更進一步的研究並證實視網膜色素上皮細胞撕裂的機轉是必須的。(長庚醫誌 2011;34:320-5)

關鍵詞：新生血管，丙酮特安皮質醇，老年性黃斑病變，視網膜色素上皮細胞，玻璃體內注射

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