Interferon-Associated Retinopathy – a Case Report

Interferon-assoziierte Retinopathie – eine Fallvorstellung

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Schlüsselwörter
- Interferon-assoziierte Retinopathie
- chronische Hepatitis C
- okuläre Nebenwirkungen

Key words
- interferon-associated retinopathy
- chronic hepatitis C
- occular side effects

Zusammenfassung

Hintergrund: Interferon alpha wird zur Behandlung von Tumoren und von chronischer Hepatitis C eingesetzt. Interferon-assoziierte Retinopathien sind nicht selten und typischerweise von Cotton-Wool-Exsudaten, Blutungen, teilweise auch Makula- oder Papillen-Ödem, Kapillarverschlüssen und selten retinalen oder choroidalen Gefäßverschlüssen gekennzeichnet. Letztere können irreversibel sein, während die meisten Formen ohne Folgen abheilen. Wir stellen einen Fall einer atypischen Interferon-assoziierten Retinopathie vor, die mit Mikroaneurysmen, Roth-Flecken und Pigmentepithelveränderungen einherging.

Anamnese und Befund: Ein 63-jähriger asymptomatischer Patient wies in beiden Fundi oberflächliche Netzhautblutungen (teils mit weißem Zentrum), einige Cotton Wool Spots und Mikroaneurysmen auf. Zusätzlich wurde um die linke Fovea ein Kranz von chronischen Pigmentepithelveränderungen gefunden, vermutlich als Narbe einer früheren zentralen Netzhautexsudation, kombiniert mit choroidaler Hypoperfusion. Der Patient war seit 6 Monaten unter Interferontherapie wegen chronischer Hepatitis C. Eine arterielle Hypertonie (Risikofaktor), milde mikrozytäre Anämie und milde Glukoseintoleranz waren vermutlich mitverantwortlich für die etwas ungewöhnliche Präsentation der Retinopathie.

Therapie und Verlauf: Unter engmaschiger Kontrolle wurde die Interferon in reduzierter Dosis weitergeführt. Es traten keine visusbedrohlichen Komplikationen auf.

Schlussfolgerungen: Eine Interferon-assoziierte Retinopathie kann auch bei ungewöhnlicher Präsentation vorliegen. Eine frühzeitige Diagnose und engmaschige Kontrollen werden empfohlen, um möglichst visusbedrohliche Komplikationen zu vermeiden. Bei Patienten mit Interferon-asso-

Abstract

Background: Interferon alpha is used for treatment in oncology and for chronic hepatitis C. Interferon-associated retinopathy is not infrequent and typically includes cotton wool spots, haemorrhages, rarely macular or papillary oedema, capillary non-perfusion and sometimes retinal or even choroidal vascular occlusion. The latter may be irreversible, while uncomplicated forms are usually reversible. We report an atypical case of interferon-associated retinopathy, associated with microaneurysms, Roth spots, and retinal pigment changes.

History and Signs: A 63-year-old asymptomatic patient presented with partially white centred, flame-shaped haemorrhages, some cotton wool spots and microaneurysms on both fundi. In addition, the left eye presented chronic pigment epithelium abnormalities surrounding the fovea without signs of exudation, most likely secondary to a previous central retinal exudative detachment combined with choroidal hypoperfusion. Interferon alpha 2a therapy for chronic hepatitis C had been given for 6 months. He was known for arterial hypertension (risk factor), mild microcytic anaemia and mild glucose intolerance, which may be responsible for some unusual features of the retinopathy.

Therapy and Outcome: The patient was closely followed, while the interferon therapy was continued on reduced dosage. No vision-threatening complication was observed.

Conclusions: Interferon-associated retinopathy may show atypical features. Early diagnosis and careful follow-up are recommended in order to avoid progression to irreversible changes. Dose-reduction or even interruption of interferon treatment needs to be considered in cases of interferon-associated retinopathy.

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ziierter Retinopathie sollte eine Dosisreduktion oder ein Therapieunterbruch mit dem zuständigen Internisten besprochen werden.

Background

Interferon alpha is used to treat various systemic disorders, particularly in oncology and for chronic hepatitis C. Interferon-associated retinopathy occurs in 15 – 64% of interferon-treated patients [1, 8, 11]. It can occur even at low dosages. Retinal changes include cotton wool spots, haemorrhages, macular or papillary oedema, capillary non-perfusion and sometimes retinal or even choroidal vascular occlusion [4, 5, 7, 11 – 13]. This drug-induced retinopathy is usually reversible with discontinuation of the treatment, sometimes even under ongoing treatment. However, irreversible and vision-threatening complications may occur, mainly vascular occlusion. Therefore early diagnosis and careful follow-up are recommended in order to avoid progression to irreversible changes. In this article we present a case of atypical interferon-associated retinopathy, associated with microaneurysms, Roth spots, and retinal pigment changes.

History and Signs

A 63-year-old asymptomatic patient was referred by his private ophthalmologist with bilateral retinal lesions resembling hypertensive retinopathy. His best corrected visual acuity was 0.8 in both eyes. Anterior segment examination was entirely normal, intraocular pressure was measured at 12 mmHg in both eyes. Fundoscopy revealed in both eyes flame-shaped haemorrhages, partially with a white centre (Roth spots), some cotton wool spots and microaneurysms. They were mainly found along the vascular arcades and in the mid-periphery. In addition, the left eye presented some pigment epithelium abnormalities surrounding the fovea. The discs were found to be normal. There was no macular oedema and no hard exudation.

Fluorescein angiography was performed. Vascular perfusion was not delayed and no sign of vascular occlusion was found. The pigmentary changes surrounding the left fovea became well visible, without signs of exudation (**Figs. 1, 2**).

The patient presented a medical history of interferon alpha 2a therapy since 6 months for chronic hepatitis C, and a nephrotic syndrome due to extramembranous glomerulonephritis as well as arterial hypertension, mild microcytic anaemia and mild glucose intolerance. In this context, we diagnosed a bilateral interferon-associated retinapathy with atypical presentation under the influence of the comorbidities.

Therapy and Outcome

The patient was closely followed, while the interferon therapy was continued on reduced dosage. In this patient only mild peripheral vascular occlusion occurred after another 3 months. No vision-threatening complication was observed.

Discussion

Interferon-associated retinopathy is not infrequent and has been described repeatedly in the literature. In case of its occurrence, recommendations vary from close observation to interruption of interferon treatment [2, 4, 8 – 11, 13]. There is a general consent that vision-threatening complications can occur; however, they are rare. Therefore, it is often difficult to weigh the risk of continued treatment against its undoubted benefits. Reducing the dosage of interferon may be a reasonable compromise. On the other hand, it is not known whether there is a dose-effect relationship.

Recently the development of interferon-associated retinopathy has been found associated with elevated VEGF serum levels. It was speculated that VEGF might play a pathogenic role in the disorder [1]. Other reports found an association with arterial hypertension [2, 8, 13] and with diabetes mellitus [13]. These patients may need to be followed particularly carefully and, in case of retinopathy, interferon therapy should probably be interrupted if possible.

In our patient we observed a couple of unusual retinal changes. This raises the question as to whether the clinical presentation is a direct effect of interferon or secondary to associated comorbidities. In this case, it strongly resembles hypertensive retinopathy. However, the signs persisted over months despite medically well controlled blood pressure. We conclude that the pathology

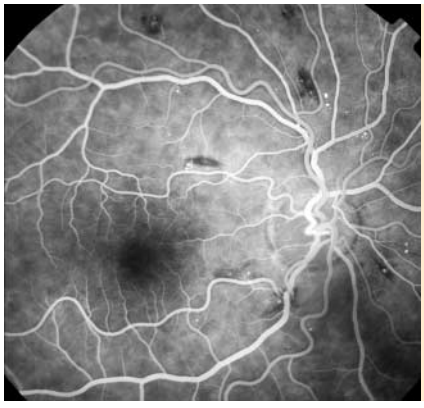

Fig. 1 The right fundus presented with cotton wool spots and flame-shaped haemorrhages, partially with a white centre. Fluorescein angiography – here shown only for the posterior pole – revealed the presence of microaneurysms.

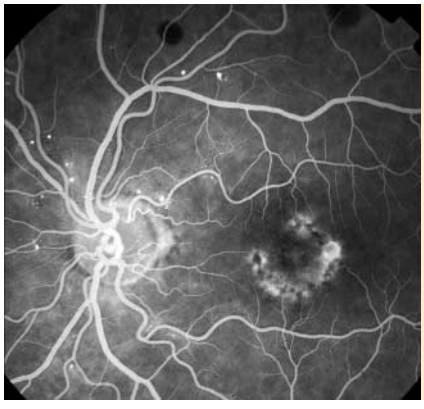

Fig. 2 The left fundus presented, in addition to the changes described for the right eye, some perifoveal changes particularly well visible on angiography. No exudation was observed.

is mainly due to interferon, but that its unusual features were influenced by the comorbidities.

Firstly, microaneurysms are not usually reported in association with interferon. They might be signs of capillary occlusion, hypertensive, diabetic or drug induced. Secondly, the white centre of the haemorrhages may be due to the anaemic component. Thirdly, the chronic perifoveal pigment epithelium changes in the left eye resemble a chain of chronic Elschnig spots, because of their dark pigmented centre and surrounding hypopigmentation [6]. Their curious circular distribution, however, suggests an association with a retinal rather than a choroidal pathology. A higher concentration of Elschnig spots has been described in areas of serous retinal detachment [3]. In our patient, the pigmentary changes may actually be secondary to a transient period of choroidal hypoperfusion, associated with central serous retinal detachment. Interestingly, interferon-associated perimacular exudative changes have been reported in one report [9], and macular choroidal ischaemia in another [5].

Conclusion

Interferon-associated retinopathy may show atypical features, influenced by coexisting pathologies. Early diagnosis and careful follow-up are recommended in order to avoid progression to irreversible changes. Special care needs to be taken with coexisting risk factors like arterial hypertension or diabetes. Dose-reduction or even interruption of interferon treatment needs to be considered in cases of interferon-associated retinopathy.

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