

# Acute Ocular Complications after Recently Diagnosed Goodpasture's Syndrome – An Unusual Case of Hypertensive Retinopathy

## Akute okuläre Komplikationen nach kürzlich diagnostiziertem Goodpasture-Syndrom – ein ungewöhnlicher Fall von hypertensiver Retinopathie



### Introduction

Ernest Goodpasture first identified Goodpasture's syndrome (GS) in 1919. It is a rare disease with an estimated incidence of about 0.5–1 case per million per year. GS most frequently occurs in two age ranges, 20–30 years and 60–70 years, and typically includes the following triad: acute renal failure, pulmonary hemorrhage, and presence of anti-glomerular basement membrane (anti-GBM) antibodies. Although the overall incidence is relatively low, GS is the cause of approximately one-fifth of all cases of acute renal failure with rapidly progressive glomerulonephritis. If accompanied by pulmonary hemorrhage or secondary malignant hypertension, the disease may be life-threatening [1].

A deeper understanding of GS was gained after the discovery of the anti-GBM antibodies binding reactive epitopes in the basement membranes of the kidneys and lungs, causing activation of the complement cascade, lastly resulting in tissue damage. These antigens are found in other specialized basement membranes, including Bruch's membrane, but clinically only the glomerular and alveolar basement membranes are usually affected. The reason for this seems to be the greater expression and accessibility of epitopes of the NC1 domain of the alpha 3 chain of type IV collagen units in these tissues [2, 3].

The exact cause of GS is still unknown. Genetics with an increased prevalence of HLA-DR15 and HLA-DRB1 and also certain behavioral and environmental factors (e.g., exposure to metallic dust, tobacco smoke, as well as lymphocyte depletion therapy, e.g., alemtuzumab) are thought to increase the risk [4].

GS symptoms can develop gradually, or rapidly in as little as a few days. Sixty to eighty percent of patients have clinical manifestation of both pulmonary and renal disease, 20–40% have renal disease alone, and less than 10% develop only lung disease. Some cases have been reported to develop autoimmune inner ear disease (AIED), presenting with sudden hearing loss [5, 6].

A kidney biopsy delivers a definitive diagnosis. Serologic assays for anti-GBM antibodies are important for initial diagnosis and monitoring of the disease treatment. The therapy involves rapid removal of circulating antibodies, primarily by plasmapheresis, as well as immunosuppression (e.g., corticosteroids and cyclophosphamide) to reduce the new production of antibodies. Currently, a 5-year survival of 80% can be reached with this treatment [4].

While systematic clinical data is missing about GS, numerous case reports and small case series have been published. However, only a few address or include potential ophthalmic manifestations of the syndrome [7–15].

Overall, there are two potential pathophysiological pathways by which GS can lead to ocular symptoms. On the one hand, GS involves anti-basement membrane auto-antibodies, which could lead to primary changes to eye structures due to immunoglobulin deposition in the basement membranes. On the other hand, GS can cause secondary complications, such as severe arterial hypertension, which may lead to vascular and structural changes in the ocular tissue [10].

In the following description, ocular findings in a young patient with GS are carefully described.

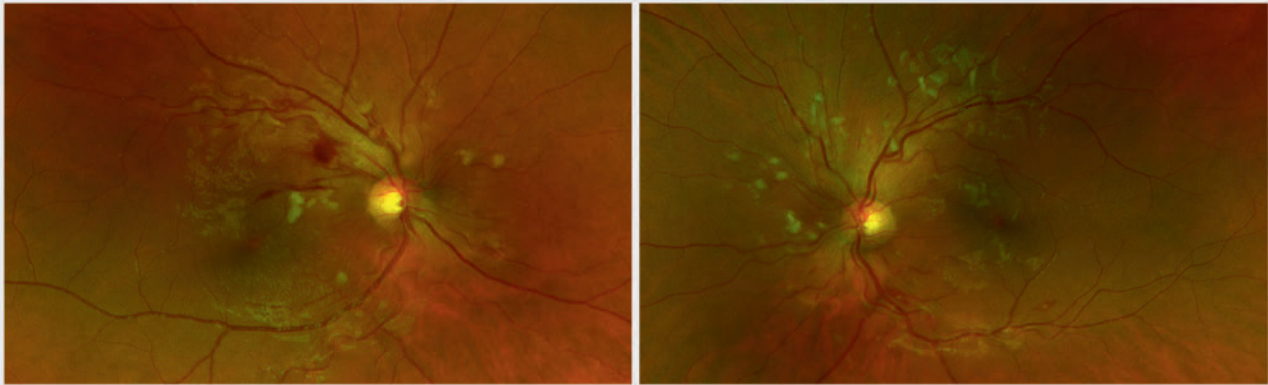
### Case Description

After complaining about bilateral blurred vision and an unusual headache since the previous day, a 17-year-old male patient under immunosuppression was referred to our clinic for suspected acute infectious retinitis. Three months before, Goodpasture's syndrome with glomerulonephritis and pulmonary involvement had been diagnosed. Plasmapheresis and immunosuppressive therapy with cyclophosphamide and corticosteroids had been initiated. Due to rapidly progressive glomerulonephritis and consecutive renal failure, the patient required regular dialysis.

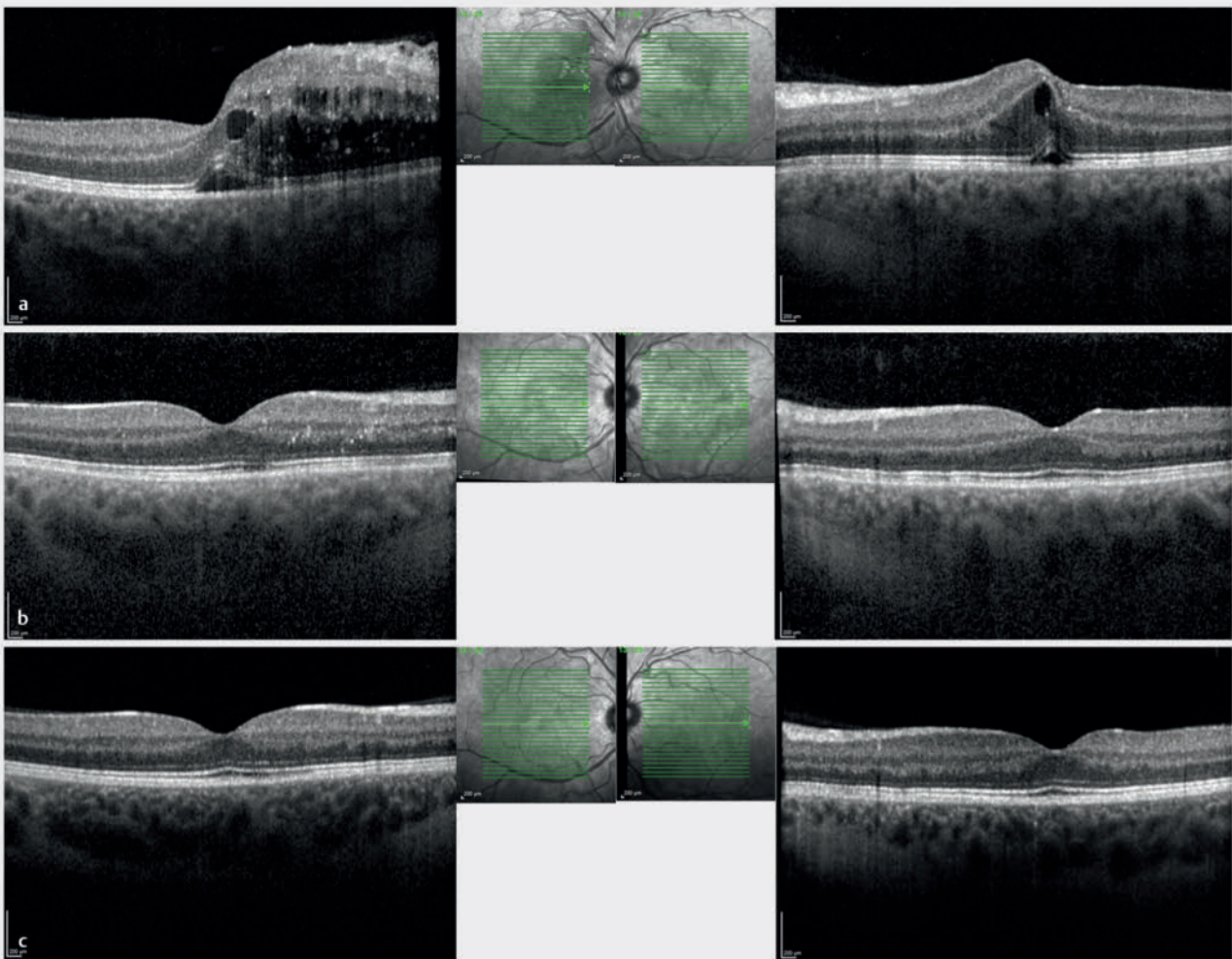
On initial examination, best-corrected visual acuity (BCVA) was 0.64 in both eyes, intraocular pressure was within normal range, and the anterior segment slit lamp findings were unremarkable. Fundus examination revealed bilateral optic disc edema, splinter bleedings along the retinal nerve fibers, multiple cotton wool spots, as well as hard exudates in the macula, suggesting cystoid macular edema (CME; ▶ Fig. 1). Optical coherence tomography (OCT) confirmed the presence of CME in both eyes (▶ Fig. 2a). Fundus changes were consistent with hypertensive retinopathy grade IV, and the patient's arterial blood pressure was 190/112 mmHg.

A sudden rise in blood pressure values above 180/120 mmHg by definition is an urgent hypertensive crisis, and in conjunction with severe organ damage, as suggested by the fundus findings, is considered an emergency hypertensive crisis [16]. Immediate emergency department admission for antihypertensive treatment was organized.

Under tight blood pressure control, follow-up visits at 1 week and 1, 3, and



► **Fig. 1** Optos fundus photography at first clinical presentation.



► **Fig. 2** Optical coherence tomography (OCT) at first clinical presentation (a), at 3 months (b), and at the 12-month (c) follow-up.

6 months revealed a significant improvement of BCVA and reduction of CME. At the 3-month visit, BCVA was restored to 1.25 in both eyes. Biomicroscopy of the fundus revealed almost complete resolution of hemorrhages and cotton wool spots. While central retinal thickness was again normal in the OCT examination, intraretinal hyperreflective foci and irregularities of the external limiting membrane (ELM) and ellipsoid zone (EZ) were still detectable (► Fig. 2b).

Final examination was conducted 1 year after the onset of the ocular symptoms: BCVA was 1.6 in the RE and 1.25 in the LE. Fundoscopic examination revealed normal optical discs and physiological macular reflexes. A discrete retinal vessel tortuosity was still observable. The OCT showed a slight remaining irregularity of the outer plexiform and nuclear layers in both eyes (► Fig. 2c).

One month after the final ophthalmological examination, the patient received a renal transplantation. At the time of obtaining the patient's consent for this case report, the patient stated that he had returned to work full time as a gardener and had no ocular complaints.

## Discussion

Ocular involvement in the presented case is likely due to secondary complication of GS and may indicate an emergency.

The few reported cases of GS with ocular fundus changes involve patients between 19 and 44 years of age [7–12, 14, 15]. At 17 years, the presented patient is the youngest GS case with ocular manifestation with full clinical and morphological workup over a time span of 12 months.

In a literature review from 1964 by Benoit et al., in only 2 cases (4%) of 52 patients described with GS were ocular fundus changes (asymptomatic hemorrhages and exudates) described [15]. A later review reported fundus abnormalities in 6 out of 56 patients with GS (11%) [14]. In 1988, Köhler published a case report of a 19-year-old patient with GS and unilateral macular edema. Similar to our case, there was also an association with severe hyper-

tension [9]. Thirty years later, Lommatzsch et al. described hypertensive retinopathy with cotton wool spots, hard exudates, and hemorrhages related to GS in a 22-year-old man [7]. Other ocular findings, such as serous retinal detachment and choroidal neovascular membranes, are also described in the literature [10, 12, 13]. In 1975, Jampol et al. described two cases of central retinal detachment in association with malignant hypertension due to GS.

In these cases, the eye is an observation window that can provide information about potentially fatal end-organ damage. Especially in an adolescent patient, as presented here, acute hypertension, with blood pressure values well above the threshold, often presents only with mild systemic symptoms [17]. Furthermore, the ocular examination can aid in the detection of circumstances, where the definition of severe hypertension with respect to the numeric blood pressure values is not met but still end-organ damage is likely. In the presented case, the sum of the ocular findings and the elevated blood pressure indicated a hypertensive emergency requiring blood pressure control within 24 hours [18–21].

At the time of the onset of ocular symptoms, immunosuppressive therapy was still in place to control GS. Therefore, the deposition of anti-GBM antibodies, causing an occlusive vasculitis in the deep capillary plexus and leading to the presented ocular findings, seems less likely. Also, to date, no specific anti-GMB antibodies in human ocular tissue have been demonstrated [10, 12]. Rather, the observed ocular findings were most likely due to the GS-related renal insufficiency with secondary development of acute arterial hypertension and subsequent retinal perfusion disturbances, clinically presenting as hypertensive retinopathy grade IV. Furthermore, once blood pressure control was achieved, the retinal findings showed improvement.

Nevertheless, even 1 year after acute hypertensive retinopathy, subtle OCT findings can be detectable. As this case shows, residual changes with irregularities and blurriness of the outer plexiform and outer nuclear retinal layers could still be observed. Hypertensive foci and changes to

the EZ nearly completely resolved after 1 year.

In conclusion, if signs of hypertensive retinopathy are present, blood pressure should be measured routinely. As this rare case displays, signs of hypertensive retinopathy in a young patient may indicate a rare life-threatening state.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

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