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CASE REPORT

Intravitreal ranibizumab (Lucentis) for choroidal neovascularization associated with Stargardt's disease

Giuseppe Querques · Maria Cecilia Angulo Bocco · Gisele Soubrane · Eric H Souied

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Abstract
Purpose To describe a young patient with choroidal neovascularization, associated with Stargardt's disease, who underwent treatment with intravitreal ranibizumab.
Methods A 26-year-old man with a diagnosis of Stargard's disease presented at our department for sudden decreased vison in his right eye (20/800). Upon a complete opltha mologic examination, including fluorescein angiography (FA), indocyanine green angiography (ICGA) and optical coherence tomography (OCT), the patient was diagnosed with subfoveal CNV of the right eye. Owing to the subfoveal localization of the CNV, intravitreal ranibizumab injection was performed on this young patient.
Results Three months after the last intravitreal injection of ranibizumab, fundus biomicroscopy, FA, ICGA and OCT revealed the CNV closure and total resolution of the associated cistoid macular edema and serous retinal detachment, with no recurrence and no complication from the intravitreal injection of ranibizumab. Visual acuity improved only to 20/400.
Conclusion Intravitreal ranibizumab injection seems to induce total regression of CNV complicating Stargardt's disease. Further investigations are required to confirm our results.

The authors have no proprietary interest in the materials used in this study.

G. Querques
Department of Ophthalmology, Ospedali Riuniti,
University of Foggia,
Foggia, Italy

G. Querques (✉) · M. C. A. Bocco · G. Soubrane · E. H. Souied
Department of Ophthalmology, University of Paris XII,
Centre Hospitalier Intercommunal de Creteil,
40 Avenue de Verdun,
94000 Creteil, France
e-mail: giuseppe.querques@hotmail.it

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Introduction

Stargardt's disease (STGD), first described by Karl Stargardt in 1909 [1–3], is a hereditary disease that affects the retinal pigment epithelium (RPE) and photoreceptor layer, linked with the ABCA4 gene [4–6]. The disease is characterized by a juvenile onset (first 2 decades), a rapidly progressive course, and a poor visual outcome. However, late onset is commonly observed for STGD, and a continuum with fundus flavimaculatus (FFM) is commonly admitted, based on genetic studies and phenotypic observations [4–6]. The general course of STGD is a progressive central atrophy and thus loss of central visual function. Conversely, choroidal neovascularization (CNV) is a rare complication in Stargardt's disease, associated with a rapid progression and poor prognosis [7].

Ranibizumab (Lucentis, Genentech, Inc., South San Francisco, CA, USA) is a recombinant, humanized, monoclonal antibody antigen-binding fragment (Fab) that neutralizes all biologically active forms of vascular endothelial growth factor (VEGF), effectively used in the treatment of neovascular age-related macular degeneration [8, 9].

We present an interventional case report describing a young patient with CNV, affected with Stargardt's disease who underwent treatment with intravitreal ranibizumab.

Case report

A 26-year-old man diagnosed with STGD 3 years before, on the basis of dark choroid and retinal flecks, presented at

our department for decreased vision in his right eye (RE). The patient signed a comprehensive consent form according to good clinical practice guidelines, before proceeding with any examinations or treatments. His best-corrected visual acuity (BCVA) was 20/800 in the RE and 20/25 in the left eye (LE). On fundus biomicroscopy, the macula of the RE showed a subfoveal greenish-grey lesion, associated with a large subretinal hemorrhage inferior and temporal to the macula, a serous detachment of the neuroepithelium, and cystoid macular edema (CME). The macula of the LE showed a small atrophic lesion. Fluorescein angiography (FA) of the RE showed hyperfluorescence in the macular area due to leakage from CNV into the subretinal and cystoid spaces (Fig. 1a). Indocyanine green angiography (ICGA) frames showed focal hyperfluorescence in the area corresponding to the CNV (Fig. 1b). Optical coherence tomography (OCT-3, Humphrey-Zeiss, San Leandro, CA, USA) confirmed the presence of a subfoveal CNV, characterized by a moderately reflective mass protruding from the retinal pigment epithelium, associated with neurosensory retina elevation and CME in the macular area (Fig. 1c). After discussing treatment options, and being presented with the option of intravitreal ranibizumab, the patient requested that this treatment be given. Three injections of ranibizumab 0.05 ml/0.5 mg were administered monthly without complications. During the follow-up period (6 months), the patient underwent a complete ophthalmologic examination every 4 weeks, including FA, ICGA and OCT. Signs of activity from the CNV (dye leakage on FA/ICGA, and serous retinal detachment/CME on OCT) were considered as major criteria for re-treatment (Fig. 2a,b,c). Three months after the third and last injection, the time of the last follow-up visit, BCVA of the RE was 20/400, fundus biomicroscopy revealed total resolution of the subretinal hemorrhage, FA and ICGA revealed the CNV closure (Fig. 2d,e), and OCT revealed total resolution of the associated serous retinal detachment and CME (Fig. 2f).

Discussion

Choroidal neovascularization is a rare complication of STGD. We report the case of a 26-year-old man in which, owing to the subfoveal localization of the CNV of the RE, we performed intravitreal ranibizumab injection. In this patient, intravitreal ranibizumab stopped the leakage and progression of the CNV, but BCVA did not improve significantly at the end of the follow-up; thus, anatomical and functional post-treatment improvement did not progress in the same fashion. Based on the results from the use of ranibizumab in the treatment of neovascular age-related

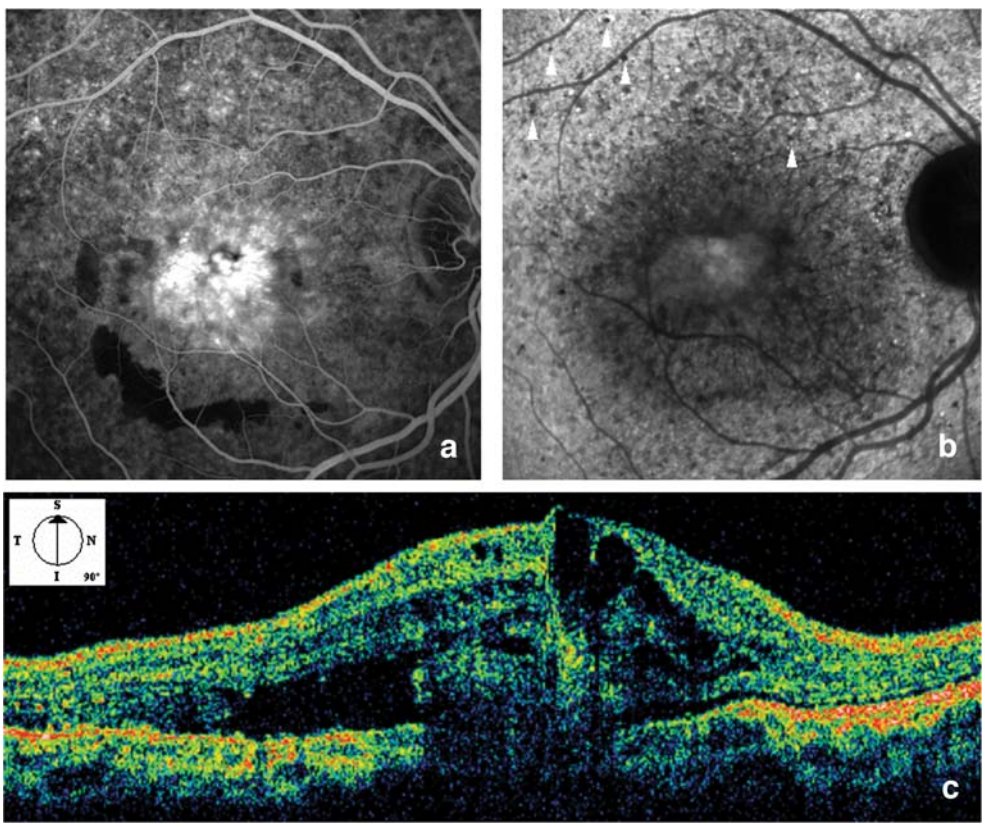

Fig. 1 Fluorescein angiography late frame of the right eye shows hyperfluorescence in the macular area due to leakage from the choroidal neovascularization (CNV) into the subretinal and cystoid spaces, and blocking hypofluorescence due to subretinal hemorrhages inferior and temporal to the macula (*top left panel*, **a**). Indocyanine green angiography (ICGA) late frame shows focal hyperfluorescence corresponding to the CNV (*top right panel*, **b**). *Arrowheads* show some hypofluorescent retinal flecks associated with hyperfluorescent pinpoints on ICGA (*top right panel*, **b**). Optical coherence tomography scan shows moderately reflective mass protruding from the retinal pigment epithelium, corresponding to the CNV, associated with cystoid spaces and neurosensory retina elevation in the macular area (*bottom panel*, **c**)

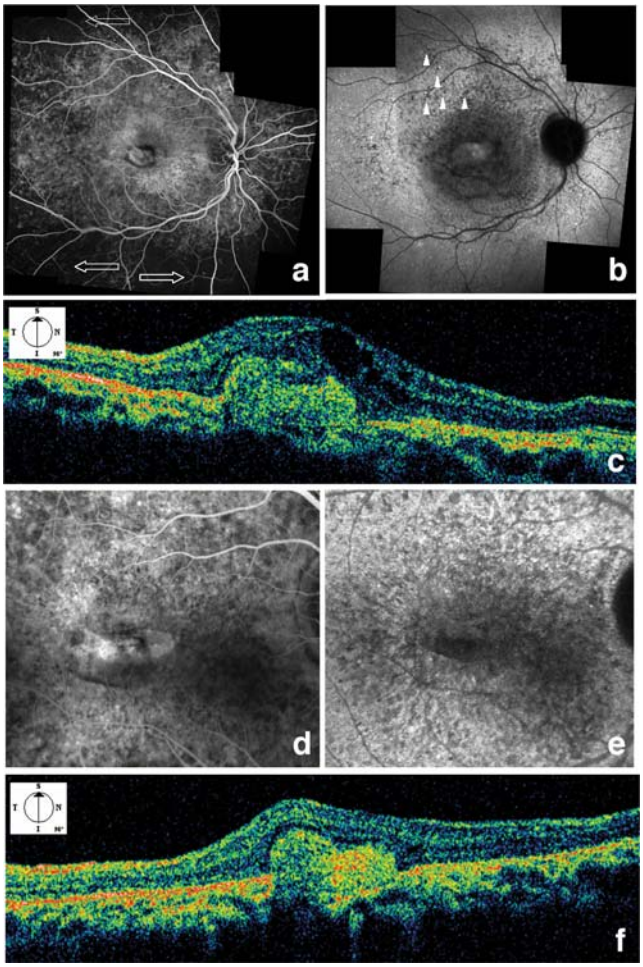

Fig. 2 Fluorescein angiography (FA) late frame of the right eye, 1 month after the first intravitreal Ranibizumab injection, shows hyperfluorescence in the macular area due to leakage from the choroidal neovascularization (CNV) (*top left panel*, **a**). *Open arrows* show dark choroid on FA (*top left panel*, **a**). Indocyanine green angiography (ICGA) late frame shows focal hyperfluorescence corresponding to the CNV (*top right panel*, **b**). *Arrowheads* show some hypofluorescent retinal flecks associated with hyperfluorescent pinpoints on ICGA (*top right panel*, **b**). Optical coherence tomography scan shows moderately reflective mass protruding from the retinal pigment epithelium, corresponding to the CNV, associated with cystoid spaces and shallow neurosensory retina elevation in the macular area (*middle upper panel*, **c**). FA late frame of the right eye, 3 months after the last (third) intravitreal ranibizumab injection, shows moderate hyperfluorescence in the macular area and absence of leakage due to the choroidal neovascularization (CNV) closure (*middle lower left panel*, **d**). Indocyanine green angiography late frame shows dishomogeneous hyperfluorescence, corresponding to the fibrotic CNV, and absence of leakage (*middle lower right panel*, **e**). Optical coherence tomography scan demonstrates absence of both neurosensory retina elevation and cystoid spaces in the macular area, and reduced size of the CNV, which, due to the post-treatment gliosis, appears increased in reflectivity (*bottom panel*, **f**)

macular degeneration [8, 9], we decided to discuss with our patient the possibility of intravitreal injection of ranibizumab, because of the large size of the lesion. Conversely, as previously reported by us in a short case series of patients affected with late-onset fundus flavimaculatus complicated with CNV [10], PDT seems to be effective in inducing total regression of CNV and in improving significantly visual acuity, at last in small size CNVs. Unfortunately, it is not possible to perform a direct comparison between this case treated by ranibizumab and those treated by PDT, because of the difference in age between the patients and in onset of the diseases, and because of the different features of the fundal appearance (STGD/FFM) and of the CNVs as well. In addition, it seems hardly realistic to perform a large double-masked study in this disorder, because of the low frequency of CNV associated with this rare macular dystrophy, and the poor prognosis of its natural evolution.

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