A multimodal approach to the treatment of bilateral choroidal metastases from thyroid carcinoma

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Abstract

A 58-year old man, affected by metastatic thyroid carcinoma, experienced a progressive bilateral visual impairment. Ophthalmic examination revealed the presence of a choroidal mass with an associated exudative retinal detachment in both eyes. Twelve years before, a diagnosis of metastatic thyroid carcinoma had been established and the patient had been subject to several therapeutic procedures.

In May 2007, he received a radiotherapy treatment to the left eye with an episcleral plaque and bilateral bulbar injection of bevacizumab. The patient had a rapid and stable visual acuity recovery. Twenty months after treatment, the lesion treated with radiotherapy was still stable whereas the contra-lateral lesion had evolved and determined a vitreal hemorrhage.

Introduction

Choroidal metastases from thyroid cancer are uncommon findings.[1] They often occur in advanced stages, and generally several years after the initial diagnosis. Main related symptoms can include pain and impairment of visual ability. Eye metastases may cause blindness with a rapid degradation of the patient's quality of life.[2,3]

This paper reports a case of bilateral choroidal metastases in a patient in satisfactory general condition, with a long history of metastatic thyroid carcinoma initially responding to radio-metabolic therapy.

A multimodal approach was adopted to treat the ocular lesions, in order to restore his visual acuity. After a follow-up of 18 months, the patient's visual ability was still good, although multiple metastases developed in other sites. A vitreal hemorrhage occurred 20 months after treatment in the right eye, while the lesion treated with brachytherapy remained unaltered.

Case Report

In October 1996, a 58-year old male patient in satisfactory general condition and under medical therapy for arterial hypertension, was treated with total thyroidectomy, parathyroidectomy, bilateral cervical lymphadenectomy and also with resection of a single ischiopubic recurrence. Histo-pathological examination of the thyroid gland and of the bone metastasis revealed a thyroid carcinoma (G3), confirmed by positive thyroglobulin immunostaining, with solid and papillary areas of oxyfil cell-type. No diffusion to neck lymph nodes was found. Disease was scored as T3N0M1, IVC stage following the American Joint Cancer Committee grouping.

After surgery, the patient received a radiometabolic treatment with 131-I. During the follow-up, the thyroglobulin hematic levels were periodically checked.

From 1997 to 2007, a diffusion of multiple metastases was observed; the largest recurrences were treated by surgical resections. In order to limit the development of recurrences, other systemic 131-I radio-metabolic therapies were administered (Figure 1).

In May 2007, the patient presented a progressive visual loss in both eyes; he had a past history of retinal venous thrombosis in his left eye, with a residual best corrected visual acuity of 20/40.

Ophthalmologic examination, performed in May 2007, showed that ocular adnexa, extra-ocular movements and pupillary reactions were normal in both eyes and no exophthalmus was found. No pupillary defects were evidenced and the Best Corrected Visual Acuity was 20/70 in the left eye (LE) and 20/25 in the right eye (RE).

Slit lamp examination of the anterior segment revealed only a light nuclear sclerosis. Intra-ocular pressure was 15 mm of Hg in both eyes.

Ophthalmoscopic examination detected a solid lesion localized in the posterior pole closely to the macula in the RE and a similar lesion in the posterior pole of the LE, where hypertrophic areas of the retinal pigment epithelium related to the previous venous branch occlusion were also evident (Figure 2).

B-scan ultrasound examination confirmed the presence of a slightly elevated, solid choroidal mass in both eyes: in RE it was 1.25 mm in thickness, with an associated serous retinal detachment, in LE it measured 3.3 mm in height and 4.8 mm in maximum base diameter, with an associated serous retinal detachment.

Standardized A-scan echography showed in both lesions an irregular structure with a sharp initial spike and moderate-high internal reflectivity.

Fundus fluorescein angiography evidenced an area of irregular fluorescence with a mild leakage in correspondence of the supero-temporal arcade in the RE. A block of the fluorescence due to the retinal pigment epithelium was noted in the posterior pole of the LE, in correspondence of the choroidal mass. The ischemic maculopathy, secondary to the previous venous thrombosis, appeared as an hypofluorescent lesion with late staining.

Indocyanine angiography showed the hyperfluorescence of the lesion in the RE, especially in the intermediate phases, with wash out of the dye in the late phases. In the LE, indocyanine angiography revealed an atrophic area of retinal pigment epithelium and of choriocapillaris in correspondence of the fovea, while the mass-lesion showed an irregular staining of the dye in the intermediate and late phases (Figure 2).

Optical Coherence Tomography showed a massive detachement of the neuro-epithelium in the RE (Figure 3); a hypertrophic hyperreflective area of the retinal pigment epitheli-

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Key words: choroidal metastases, thyroid carcinoma, radiotherapy, anti-VEGF factors.

Acknowledgments: the authors are grateful to the Pisa section of the "Lega Italiana per la Lotta Contro i Tumori" for supporting the present publication.

Contributions: radiotherapy treatment and follow-up: MGF, MDL; ophthalmologic follow-up: FGE; radiotherapy treatment planning, data analysis and dose evaluation: FP; brachytherapy: MGF, SR, FGE; endocrinological follow-up: CG, FB, EM; text editing: CG, MDL, MGF, FGE, FB, FP; text reviewing: EM, LC.

Conflict of interest: the authors reported no potential conflict of interests.

Received for publication: 20 May 2009.
Revision received: 28 May 2009.
Accepted for publication: 2 June 2009.

Rare Tumors 2009; 1:e4
doi:10.4081/rt.2009.e4

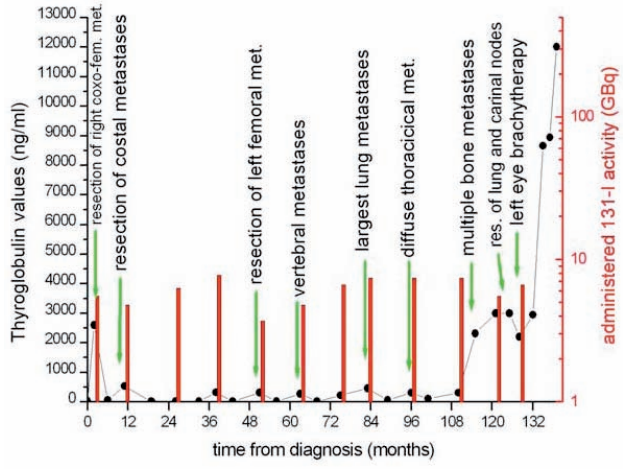

Figure 1. The figure shows hematic thiroglobulin concentrations (in ng/mL), starting from initial thyroidectomy, as a function of the follow-up time in months (140 months from October 1996 to June 2008); black dots report thyroglobulin hematic levels in ng/mL (left black scale); red bars show the 131-I activities in GBq (right red scale), administered during the follow-up.

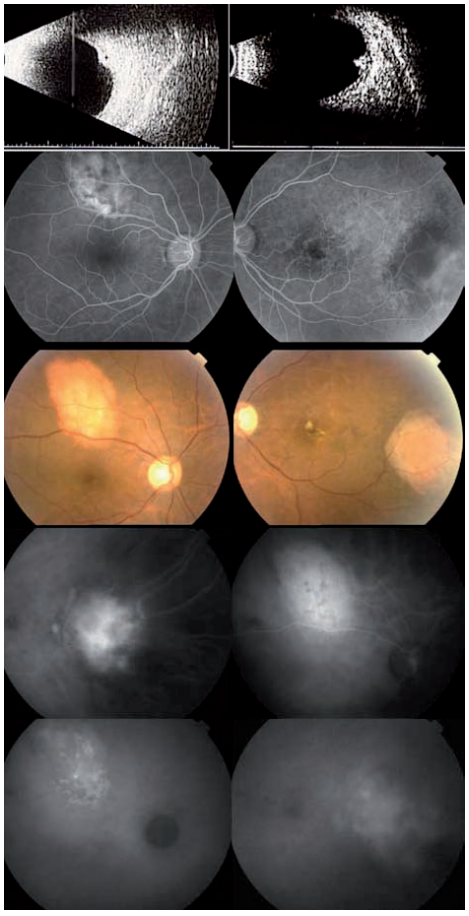

Figure 2. The figure shows, from top to bottom, basal B-scan ultrasound, fluorescein angiography, fundus view, intermediate phase indocyanine angiography and late phase indocyanine angiography of both eyes before brachytherapy. The images on the right side refer to the left eye.

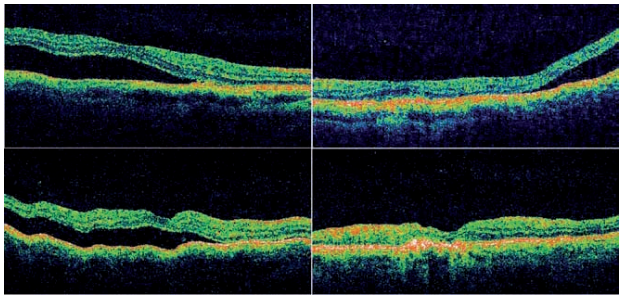

Figure 3. Optical Coherence Tomography before brachytherapy (top) and in October 2008 (bottom) of macular region in the right eye (left side) and the left eye (right side), showing the reduction of fluid (central black area). The red region in the left eye corresponds to the area interested by a previous thrombotic episode.

um (due to the previous macular scar) and a detachment of the neuro-epithelium temporal to the macula were also found in the LE. Although a biopsy was not obtained from the choroidal masses, diagnosis of presumed bilateral choroidal metastases from thyroid carcinoma was based on the patient's medical history and on ophthalmologic findings: the occurrence at the posterior pole, the solid appearance, the yellow-orange color, the presence of serous detachment of the sensory retina, the moderate echographic internal reflectivity of the masses showing an irregular internal reflectivity, the absence of demonstrable vascular pulsations and the hyperfluorescence with late staining were suggestive of a secondary lesion.

At the end of May 2007, the lesion in the LE was treated with an episcleral 106Ru plaque brachytherapy.

The small lesion in the RE was not irradiated because of its small volume, its localization close to the macula and the risk of macular radiation damage. A week after plaque removal, an intra-vitreal injection of bevacizumab (Avastin; Genentech, San Francisco, CA) was performed in both eyes in order to reduce the serous retinal detachment.

In October 2008 an US scan indicated that the lesion in the right eye remained unchanged and the mass in the left eye was reduced to 2.5 mm in height. OCT showed a marked reduction in height of the neuro-epithelium detachement in the right eye and a disappearance of the temporal fluid in the left eye (Figure 3). BCVA was still 20/20 in the right eye and 20/40 in the left eye. The other metastases showed a generalized progression.

At the end of 2008, the patient began a chemotherapy treatment with anthracycline.

A vitreal hemorrhage occurred 20 months after treatment in the right eye, while the lesion treated with brachytherapy remained still unaltered.

Discussion

Eye metastases are an important clinical problem, because they represent the most common cancer of the eye and may occur in 12% of patients with metastatic carcinomas.[4] Nevertheless, ocular metastases from thyroid carcinoma are uncommon and bilateral synchronous metastases have a rare occurrence and represent a clinical challenge.[5-8]

Taking into account all the currently available therapeutic options, a flexible approach should be planned, depending on the clinical situation.

The therapeutic approach should consider the presence of painful symptomatology, patient's life expectancy, clinical ophthalmo-

logic assessment and general conditions.

Enucleation should be considered in presence of painful eye with secondary neovascular glaucoma. In all other situations, an organ sparing approach should be considered.

Brachytherapy is particularly effective in administering a high-dose to a single lesion of small volume. This method involves temporary placement of an episcleral radioactive device, in correspondence to the tumor, until the prescribed dose is administered.

Generally, the treatment can be performed in an outpatient setting and is well tolerated, determining mild to moderate toxicity; moreover, the results are satisfactory in terms of visual function and organ preservation. Photocoagulation by means of xenon or argon ion lasers has been used in the past as an option in selected small choroidal melanomas. Recently, it has been replaced by TTT that has been proven to be effective in treating selected small volume lesions. Currently, TTT is also used as a supplement to plaque radiotherapy.[8]

Bevacizumab is a full-length recombinant humanized monoclonal antibody directed against VEGF, originally indicated for the treatment of metastatic colorectal cancer. The antiangiogenic properties of bevacizumab, administered via intravenous infusion or intravitreal injection, have been studied in patients with age-related macular degeneration, choroidal neovascularization, and other retino-choroidal vascular diseases.[9,10]

Therefore, bevacizumab can reduce retinal ischemia that could lead to radiation retinopathy and exudative retinal detachment in order to improve visual acuity and to reduce development of neovascular glaucoma.

Macular lesions create a clinical challenge for which treatment with intra-vitreal bevacizumab seemed promising. One might theorize that, like laser photocoagulation, bevacizumab may decrease the ocular ischemia resulting from plaque radiation or may induce a decrease of vascular permeability in non-vital tissue. Clearly, testing these theories is beyond the scope of this study. However, clinical series in the literature showed encouraging results in treating ischemic radiation therapy.

In the present case, intra-vitreal bevacizumab administration probably achieved a reduction of serous detachment in the posterior pole, thus restoring a useful visual function.

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