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SHORT COMMUNICATION

Phthisis bulbi and buphthalmos as presenting signs of retinoblastoma: A report of two cases and literature review

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PURPOSE. *To report two cases of bilateral retinoblastoma (RB) with unusual presentations.*
METHODS. *The medical records of 321 patients from the Retinoblastoma Referral Center in Siena were reviewed. A total of 111 patients had bilateral RB, 2 of them presenting with phthisis bulbi and buphthalmos. Both patients underwent bilateral enucleation. Clinical features, imaging studies, and histopathology were reviewed.*
RESULTS. *These 2 cases represent 0.62% (2/321) in our series. Histopathology did not reveal viable tumor cells in the phthisical eyes; in both buphthalmic eyes the tumor was active, infiltrating the choroid and optic nerve.*
CONCLUSIONS. *Phthisis bulbi and buphthalmos are unusual presenting signs of RB. This very rare combination of these two signs in different eyes of the same patient is probably due to a delay in diagnosis. (Eur J Ophthalmol 2006; 16: 465-9)*

KEY WORDS. *Retinoblastoma, Phthisis, Buphthalmos, Pathology, Radiology*

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INTRODUCTION

Leukocoria and strabismus are the most frequent presenting signs of retinoblastoma (RB) (1).

Rare and atypical signs of RB include hypopyon, hyphema, retinal detachment, heterochromia, pain, buphthalmos, orbital cellulitis, proptosis, endophthalmitis, and phthisis bulbi (1-3).

Unusual clinical signs of RB, which are commonly observed in older children (4), cause delay in diagnosis, resulting in poor prognosis.

In unilateral phthisis, the diagnosis of RB is difficult, while the very rare combination of one phthisical eye and one buphthalmic eye has been reported as a presenting feature in bilateral RB (5). We report two girls with RB presenting with phthisis bulbi and contralateral buphthalmos and review the literature on the topic.

PATIENTS AND METHODS

The medical records of 321 RB were reviewed. A total of 111 patients had bilateral RB, 2 of them presenting with simultaneous phthisis bulbi and buphthalmos. Both patients underwent bilateral enucleation. Clinical reports, imaging studies, and histopathology were reviewed in each case and the data are critically analyzed.

Case 1

A 30-month-old girl was referred to our center in 1987 for buphthalmos of the left eye and phthisis bulbi of the right eye. The left preauricular lymph node was enlarged. Examination under anesthesia (EUA) showed a phthisical right eye with a completely distorted anterior chamber and a thickened, opaque cornea measuring 6 mm in diameter. The left eye showed buphthalmos, with a hazy

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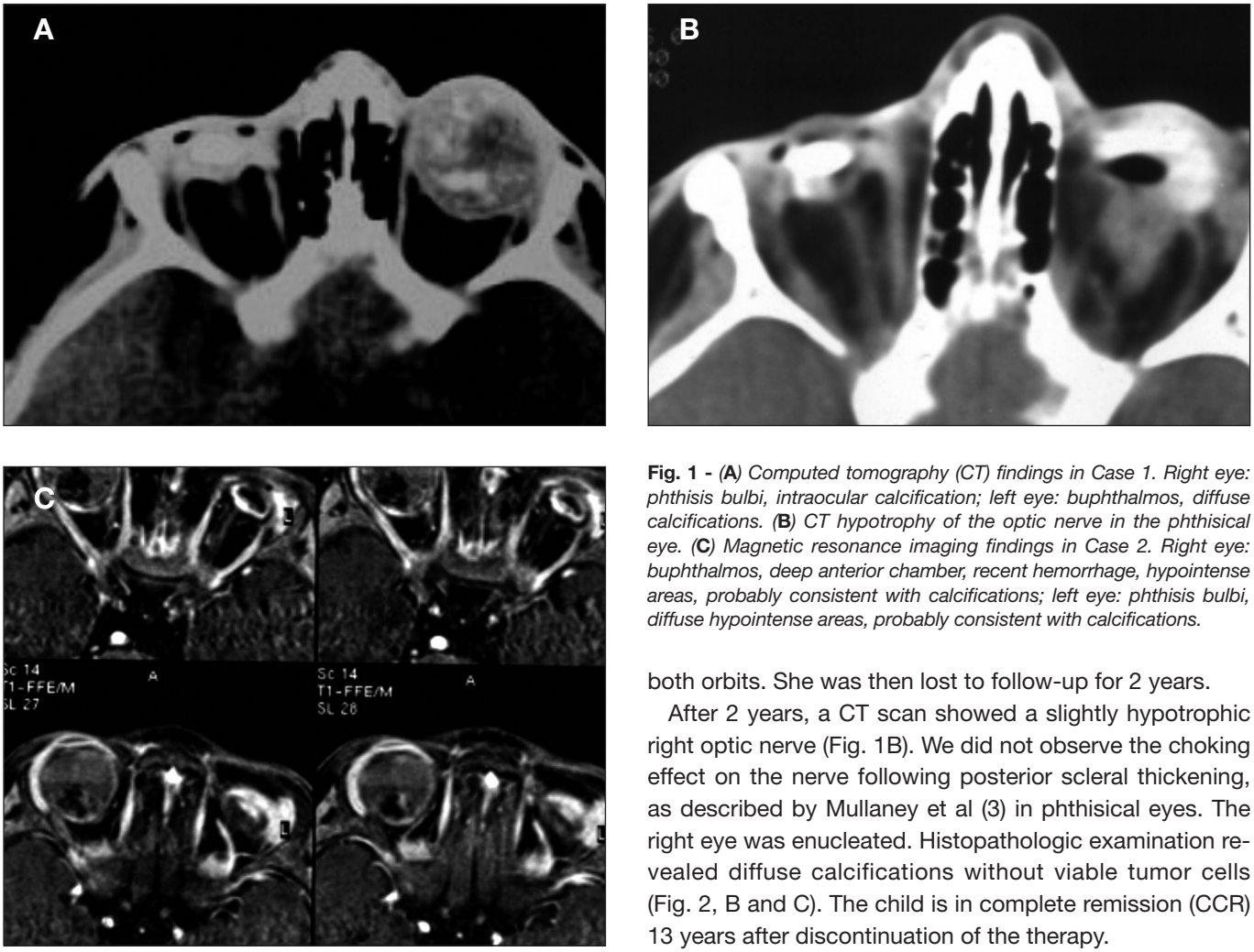


Fig. 1 - *(**A**) Computed tomography (CT) findings in Case 1. Right eye: phthisis bulbi, intraocular calcification; left eye: buphthalmos, diffuse calcifications. (**B**) CT hypotrophy of the optic nerve in the phthisical eye. (**C**) Magnetic resonance imaging findings in Case 2. Right eye: buphthalmos, deep anterior chamber, recent hemorrhage, hypointense areas, probably consistent with calcifications; left eye: phthisis bulbi, diffuse hypointense areas, probably consistent with calcifications.*

cornea measuring 14.5 mm in diameter; tumor cell seeding was present in the anterior chamber. Intraocular pressure (IOP) was 40 mmHg. The combination of phthisis bulbi and contralateral buphthalmos was highly suggestive of bilateral advanced retinoblastoma.

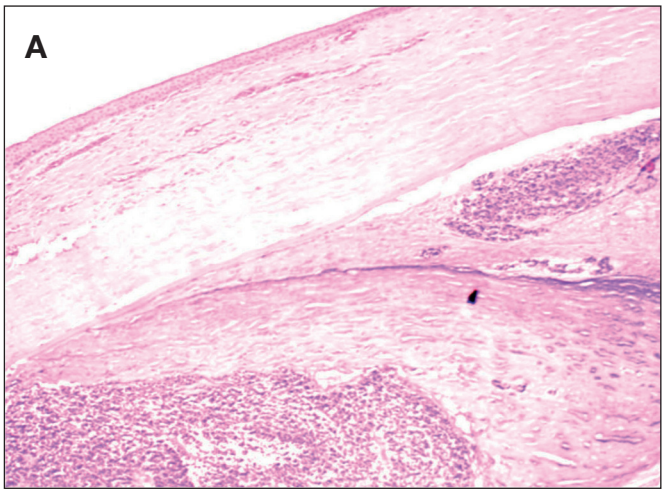
Computed tomography (CT) scan showed an almost totally calcified phthisical right eye. A mildly hyper-attenuating mass with calcification areas was present in the buphthalmic left eye. The optic nerve of both eyes had the same thickness (Fig. 1A). The left buphthalmic eye was promptly enucleated. Family history was negative.

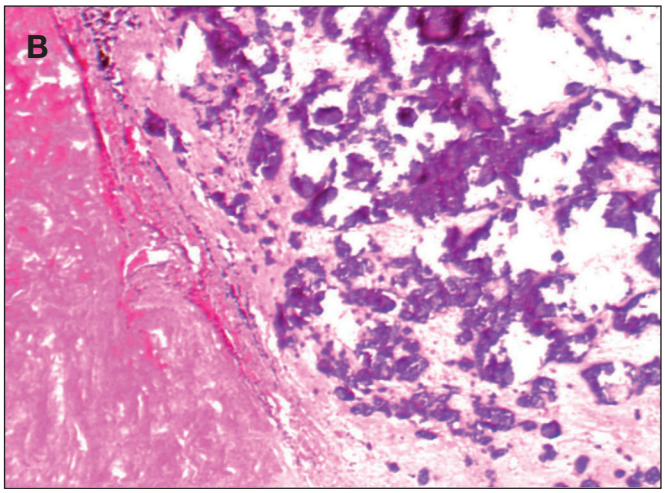
Histopathologic examination revealed active endophytic RB infiltrating the anterior chamber, the ciliary body, the iris, and the sclera (Fig. 2A). The biopsy of the preauricular lymph node revealed metastatic spread. The child received chemotherapy (CHT) (6 cycles of vincristine and cyclophosphamide) and radiotherapy (RT) (4000 cGy) on both orbits. She was then lost to follow-up for 2 years.

After 2 years, a CT scan showed a slightly hypotrophic right optic nerve (Fig. 1B). We did not observe the choking effect on the nerve following posterior scleral thickening, as described by Mullaney et al (3) in phthisical eyes. The right eye was enucleated. Histopathologic examination revealed diffuse calcifications without viable tumor cells (Fig. 2, B and C). The child is in complete remission (CCR) 13 years after discontinuation of the therapy.

Case 2

A 17-month-old Kossovar girl was examined at our center in 2001. Bilateral RB was diagnosed at the age of 11 months in the presence of an orbital cellulitis in the left eye; a normal-sized right eye was reported without further details. At our first EUA the right eye was buphthalmic and had a hazy cornea, lens opacities, and deep anterior chamber; the corneal diameter was 15 mm and the IOP was 50 mmHg (Fig. 3A). The left eye was phthisical, containing a yellowish calcified mass in the anterior chamber (Fig. 3B). Both corneal and lens opacifications precluded posterior segment examination. Magnetic resonance imaging (MRI) confirmed buphthalmos of the right eye, which contained a heterogenous mass with signs of recent bleeding, very low signal areas possibly consistent with calcifications, and poor enhancement after contrast medium administration. On the left side a smaller than





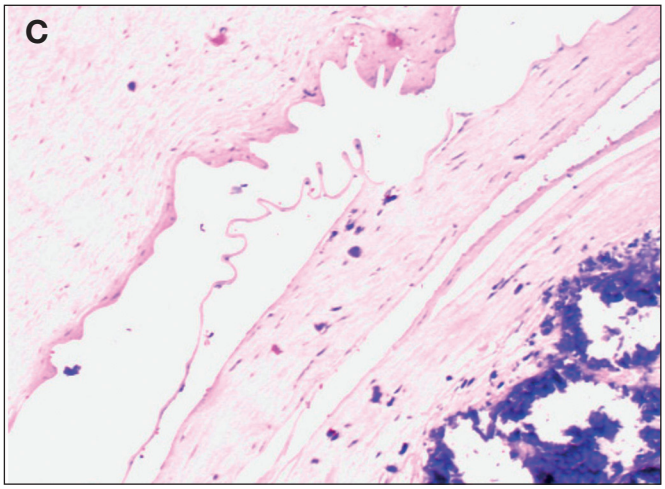


Fig. 2 - (**A**) *Histopathologic findings: the anterior chamber is diffusely infiltrated by neoplastic cells, which also infiltrate the ciliary body and the iris in the buphthalmic eye.* (**B, C**) *Phthisis bulbi with atrophy of the retina and uvea. The vitreous cavity is filled with sclerotic tissue with diffuse calcification; viable neoplastic cells are not seen.*

normal orbit contained a phthisical eye, which was mainly hypointense (probably due to calcium content) (Fig. 1C). Bilateral enucleation was performed. Histopathologic evaluation of the right eye revealed RB with necrosis and calcifications diffusely infiltrating the choroid and the lens. The optic nerve was involved and the surgical cut edge was infiltrated. In the left eye, sclerosis, calcifications and retinal atrophy without tumor cells were noted. The child received 6 cycles of carboplatin and etoposide and EBRT (4000 cGy on the right orbit). No recurrent or metastatic disease was observed 2 years after treatment.

DISCUSSION

Buphthalmos is reported with an incidence of 0.7% (1) and 1.5% (2) in various series of RB cases. The combination of phthisis and simultaneous buphthalmos is extremely rare, but highly suggestive of bilateral RB (3). Only six similar cases have been reported until now (5-9). In a series of 14 patients with phthisical eyes reviewed by Boniuk and Zimmerman, two had both phthisis bulbi and buphthalmos at diagnosis (5). Hiatt et al reported a 16-month-old girl with a phthisical eye and contralateral buphthalmos with an orbital mass (6). Khodadoust et al examined three brothers with familial RB, all of them with a phthisical eye; one of them developed contralateral buphthalmos (7). In a series of 15 RB cases, Schuster and Ferguson described an 18-month-old patient with phthisis in one eye and secondary glaucoma with megalocornea in the other (8). Harrison et al reported a 14-month-old girl with bilateral RB presenting with simultaneous phthisis bulbi and buphthalmos (9).

The two cases reported herein represent 0.62% (2/321) in our series. It is most likely that the changes developed due to delayed diagnosis. Lack of knowledge of atypical presentations of RB mimicking orbital cellulitis and anterior and posterior segment inflammation may explain such a delay. It has been documented in a very large series that most of the clinically confusing cases are represented by intraocular inflammation associated with retinoblastoma (10). In Case 2, orbital cellulitis preceded phthisis bulbi, as reported also by others (3, 11). Endophthalmitis and orbital cellulitis seem in fact to be caused by tumor necrosis and to represent prephthisical events.

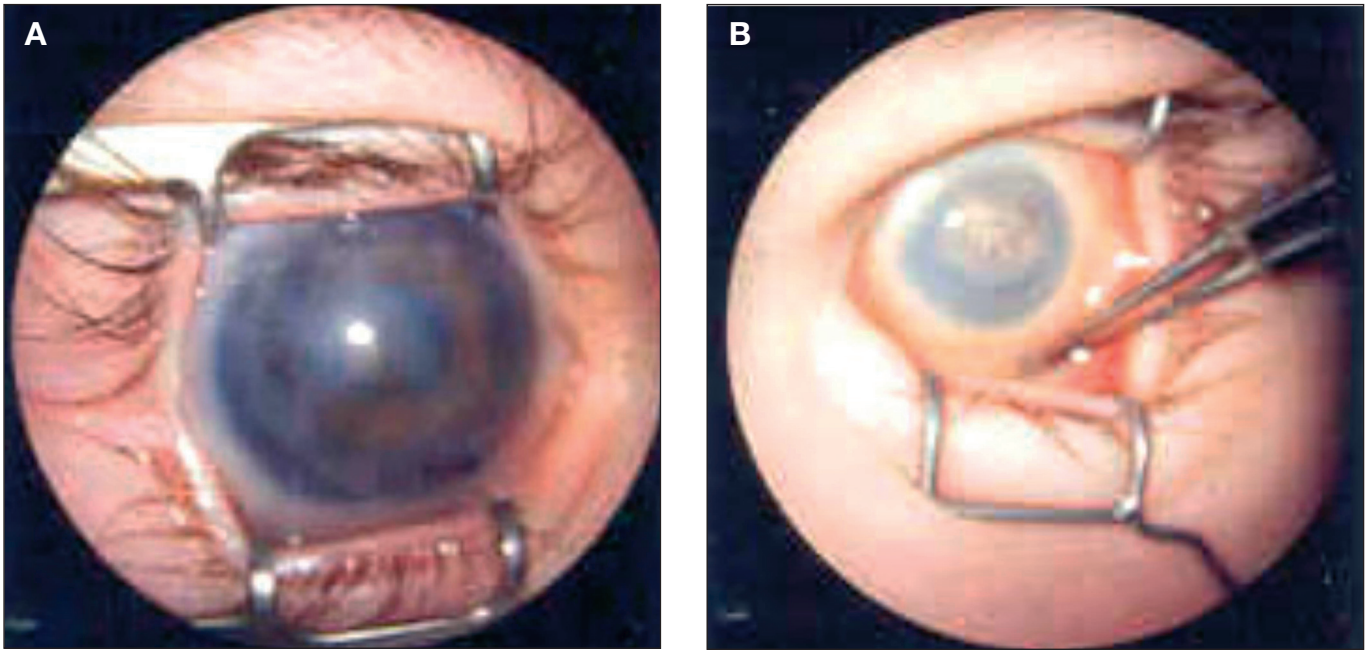


Fig. 3 - *(**A**) Buphthalmic eye with a corneal diameter of 15 mm, hazy cornea; lens opacities and deep anterior chamber are also seen. (**B**) Phthisical eye with a corneal diameter of 7 mm; anterior chamber is occupied with a yellowish, calcified mass.*

There are conflicting reports in the literature about whether viable tumor cells are present in phthisical eyes in patients with retinoblastoma. In our patients, both buphthalmic eyes contained active tumor, while in phthisical eyes no viable tumor cells were identified. Only 1 out of 14 phthisical eyes contained viable tumor cells in the series of cases reported by Boniuk and Zimmerman (5). Khodadoust et al reported the presence of fossilized or hidden tumor cells in phthisical eyes (7). In contrast, Mullaney et al found viable tumor cells in all phthisical eyes and/or optic nerves of their series encompassing 10 cases (3). Furthermore, Hiatt et al (6) and Schuster and Ferguson (8) found viable cells in both phthisical and buphthalmic eyes. Finally, a patient described by Harrison et al developed a fungating mass in a phthisical eye (9). These reports highlight the importance of enucleation of both phthisical and buphthalmic eyes.

The possibility of RB must always be kept in mind in childhood eye pathology. Unusual clinical presentations of RB are the cause of both misdiagnosis and delayed therapy. The knowledge of atypical RB presentations is essential to suspect retinoblastoma and hence to ensure prompt diagnosis.

The presence of buphthalmos and phthisis bulbi in the same patient is coincidental and may reflect the progression of a bilateral untreated retinoblastoma; in fact a phthisical eye is an evolution of a buphthalmic eye harboring retinoblastoma. We emphasize that any child presenting with phthisis bulbi of unknown origin should be suspected of harboring retinoblastoma and should undergo ultrasound examination, CT, and MRI with gadolinium.

Both buphthalmic and phthisical eyes in the same child can carry viable tumor cells; therefore bilateral enucleation should be always performed in these cases and the histopathologic findings (e.g., diffuse invasion of the choroid, sclera, or optic nerve) should indicate the most appropriate therapeutic strategy, following enucleation.

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