Epibulbar Seeding at the Site of a Transvitreal Fine-Needle Aspiration Biopsy

Transocular fine-needle aspiration biopsy (FNAB) with analysis of the aspirate is a diagnostic technique that can be helpful in selected cases of suspected intraocular tumors.\(^1\) In most cases, the improvement in clinical diagnostic imaging permits an accurate diagnosis,\(^2\) but in selected cases, histological confirmation is necessary to rule out other malignancies. The FNAB was introduced into ophthalmology by Schyberg in 1975 for the diagnosis of orbital neoplasm.\(^3\) In 1979, Jakobiec et al\(^4\) proposed the use of FNAB in the evaluation of intraocular tumors. Since then, this technique has been used in a large number of patients without any evidence of local or systemic spread. In this article, we report the first described case of a local epibulbar seeding at the scleral pars plana puncture site after a transvitreal FNAB.

Report of a Case. A 61-year-old man complained of foreign body sensation and progressive visual loss in his left eye for the last 4 months. His medical history was remarkable for a bladder carcinoma that had been treated 6 years previously with transurethral resection and intravesical bacillus Calmette-Guérin therapy. At the time of admission, his visual acuity was 20/20 OD and 1/20 OS. Dilated fundus examination disclosed a temporal inferior amelanotic mass with an associated serous detachment (Figure 1). Ultrasonography revealed a dome-shaped postequatorial choroidal mass. A B-scan demonstrated a moderate to high acoustic solidity without appreciable choroidal excavation or orbital shadowing (Figure 2A). An A-scan showed a high initial spike and median to high internal reflectivity (Figure 2B). The tumoral base was 16 × 18 mm and the maximal elevation was 6.2 mm. The distance to the optic disc was 1 mm. Although clinical appearance was compatible with an uveal melanoma, a metastatic carcinoma could not be completely ruled out. Systemic evaluation did not reveal more clinical findings or distant dissemination. An FNAB of the tumor was performed to confirm the diagnosis.

Under retrobulbar anesthesia, we placed an infusion with fiber optic light at the inferior temporal pars plana. A scleral puncture was then performed at the superior nasal pars plana using a 25-gauge needle attached to a flexible plastic tube, which was connected to a 10-ml syringe. The needle was guided using the operating microscope and a retinal wide field view system. The needle was passed into the lesion and gentle aspiration was performed. Finally, the suction was released before the needle was removed without any complication except a local hemorrhage.

![Figure 1. Fundus examination of the left eye disclosed a temporal inferior choroidal mass.](image)

![Figure 2. A B-scan demonstrated a mass with median to moderate internal reflectivity (A). An A-scan revealed a moderate to high reflectivity (B).](image)

![Figure 3. Cytologic analysis. A, The aspirate showed highly pleomorphic cells with round nuclei, prominent nucleoli, and a different nuclei-cytoplasm ratio (Papanicolaou stain, original magnification ×63). B, Immunohistochemical stain revealed an intense positivity for HMB-45 (original magnification ×63).](image)
The cytological diagnosis confirmed the presence of atypical melanotic cells. The Papanicolaou stain of the aspirate showed highly pleomorphic cells with round nuclei, prominent nucleoli, and a different nuclei-cytoplasm ratio (Figure 3A). Immunohistochemical stain revealed an intense positivity for S100 and HMB-45 (Figure 3B) consistent with melanoma.

A 22-COMS (Collaborative Ocular Melanoma Study) iodine 125 plaque was used for treatment. The total activity of the plaque was 69.60 µCi. The total dose was 85.29 Gy with a dose rate of 92.71 Gy per hour at the tumoral apex. The duration of treatment was 92 hours. Eight months later, the patient consulted for a small and painless orange subconjunctival mass on the superior nasal quadrant at the location of the pars plana puncture (Figure 4). A complete excision was made with triple freeze-thaw cryotherapy and a subconjunctival mass (Figure 5A) with closely packed cells with numerous mitoses, prominent nucleoli, and melanic pigment (Figure 5B) compatible with a local melanoma growth in the puncture area. The histological margins were free.

Comment. Transvitreal FNAB is an invasive procedure useful in the diagnosis of intraocular lesions. Although in most cases clinical findings permit an accurate diagnosis, a definite histological confirmation is required. Important limitations of this technique are the difficulty in obtaining sufficient material for cytological examination, theoretical local complications, and spread of the tumor. On the other hand, few complications have been described. A local hemorrhage in the site of biopsy, in almost all cases, is controlled by increasing the intraocular pressure. Vitreous and subretinal hemorrhage occurred in 9% to 13% of cases with transient visual loss. Other theoretical problems, such as retinal detachment, local recurrences, or systemic dissemination from tumor seeding, have not been previously described.

In nonocular tumors, iatrogenic dissemination of tumoral cells along the needle track has been found immediately after an FNAB, but only a few cases of local seeding with metastasis have been reported. Ryd et al demonstrated local seeding risk in an experimental evaluation with solid and ascitic-growing tumors in mice, where almost 10^2 to 10^4 cells contaminated the needle track in FNAB. The high rate of seeding demonstrated in this study contrasts with the low percentage of local clinical recurrences described in the literature. In experimental studies, the transplanted inoculum probably has a higher proportion of viable malignant tumoral cells and is more aggressive than human tumors.

In contrast, no cases of local recurrences after FNAB in ocular tumors have been described before. This fact had been explained by Jakobiec et al because the aspiration is through the vitreous or the aqueous humor. This indirect transocular approach from the opposite side of the lesion would make a mechanical washout of tumoral cells from the needle surface. However, several studies have demonstrated tumoral seeding cells after transscleral and transvitreal FNAB in enucleated tumor eyes. Glasgow et al revealed that a transvitreal approach contained significantly fewer cells than transscleral aspirates. The few malignant cells along the needle track seem to disappear spontaneously and could be insufficient for tumor growth. In addition, experimental animal studies have shown the difficulty in transplanting tumor cells in vitreous, and most of the malignant ocular tumors are treated by irradiation or excision after diagnosis, which probably prevents implantation of metastasis in most cases.

In conclusion, transvitreal FNAB is a useful and safe tool in clinical diagnosis based on previous reports. However, there is a potential risk of vascular dissemination and a real risk of local malignant seeding as described in this report. For this reason, this technique should only be used when there is a reasonable doubt about the diagnosis and the expected results may modify management of the lesion.

Josep M. Caminal, MD, PhD
Silvia Sanz, MD
Marta Carreras, MD, PhD
Isabel Catala, MD, PhD
Jorge Arruga, MD, PhD
Guillermo Roca, MD

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Two Cases of Reis-Bücklers Corneal Dystrophy (Granular Corneal Dystrophy Type III) Caused by Spontaneous Mutations in the TGFBI Gene

Reis-Bücklers corneal dystrophy (RBCD) is an inherited corneal disorder that was first described by Reis1 in 1917 and later by Bücklers2 in 1949. Affected individuals have an onset early in life and have frequently recurring, painful corneal erosions, superficial corneal opacities, and significant visual impairment. The literature on this entity, which has several synonyms (granular corneal dystrophy [GCD] type III, superficial variant of GCD, corneal dystrophy of Bowman layer type I), is bewildering not only because of the nomenclature but also because this genetically determined disorder has been confused with a different condition, Thiel-Behnke corneal dystrophy (TBD). Although RBCD and TBD are now considered distinct clinicopathologic disorders,3 precise diagnosis of these corneal disorders was difficult until recently because it relied only on the clinical and histopathologic features.

Both RBCD and TBD are autosomal dominant disorders of the superficial corneal stroma that manifest as recurrent corneal erosions in early childhood.1-4 Reis-Bücklers corneal dystrophy tends to cause more extensive corneal opacities, more severe visual impairment, and a higher frequency of recurrence compared with TBD.3 Because the clinical phenotypes of RBCD and TBD are similar (especially in young individuals), an accurate distinction between the 2 disorders necessitates either a microscopical examination of corneal tissue or a molecular genetic analysis. Microscopically, RBCD is characterized by confluent opacities in the Bowman layer and the subepithelium that result from extracellular bodies that stain red with Masson trichrome stain and appear as crystalloid, rod-shaped bodies by transmission electron microscopy.1,2,3 On the other hand, TBD exhibits honeycomb-shaped opacities in the Bowman layer and “curly” fibers by transmission electron microscopy.3 Thus, RBCD and TBD may be accurately diagnosed if an excised corneal specimen displays these microscopic characteristics.

In addition to examining tissue samples, the identification of specific mutations in the transforming growth factor β-induced (TGFBI) gene on chromosome 5q31 has led to another diagnostic technique. In 1997, Munier et al5 established that different mutations in this gene cause several distinct inherited corneal disorders. This landmark publication reported an arginine-to-glutamine mutation at codon 555 (R555Q) in a patient diagnosed with RBCD, but Munier and colleagues did not document the clinical, light microscopic, or electron microscopic findings in this individual. Soon thereafter, Okada et al6 documented the R555Q mutation and the slitlamp photographs of a patient with honeycomb opacities diagnosed clinically with the Thiel-Behnke form of GCD. They also identified a novel TGFBI mutation, R124L, in a proband and his mother with the geographic corneal opacities of RBCD.7 The phenotypes associated with these 2 mutations were not documented histopathologically by light or electron microscopy. Subsequent studies8-10 confirmed that RBCD is associated with at least the R124L mutation whereas TBD stems from the R555Q mutation. The discovery that distinct genetic mutations in the TGFBI gene cause RBCD and TBD further defines these disorders as separate clinicopathologic entities. Most importantly, these disorders differ in prognosis,10 and therapy may be inappropriate if the disease is misdiagnosed.

Methods. Patients. Two unrelated children were diagnosed with Reis-Bücklers corneal dystrophy by ophthalmologists at different major medical institutions. Both affected individuals were invited to participate in a molecular genetic evaluation of their corneal disorder at Duke University Medical Center, Durham, NC. The institutional review board at Duke University approved this research project. After written informed consent was obtained from the parents of the 2 affected individuals, all of the available clinical records and photographs were reviewed. Family histories and pedigrees were compiled. The parents and other family members were examined clinically.

Histologic Examination. Tissue from a superficial diagnostic corneal biopsy of proband A was placed in formalin, embedded in paraffin, then sectioned and stained with hematoxylin-eosin and Masson trichrome. Corneal tissue was not obtained from proband B.

DNA Analyses. Blood samples or buccal scrapings from the unaffected parents as well as from affected and unaffected siblings were gathered. Leukocyte DNA was extracted with the Puregene Blood Kit or the Puregene Buccal Cell Kit (Gentra Systems, Minneapolis, Minn). All of the exons of the TGFBI

Correspondence: Dr Caminal, Hospital de Bellvitge, Ophthalmology Department, calle 18, Feixa Llarga s/n, 08907 L’Hospitalet de Llobregat, Barcelona, Spain (jmcaminal@csub.sc.es).

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