

Commentary on the Masquerades of a Childhood Ciliary Body Medulloepithelioma: A Case of Chronic Uveitis, Cataract, and Secondary Glaucoma

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Commentary

"The masquerades of a childhood ciliary body medulloepithelioma: A case of chronic uveitis, cataract and secondary glaucoma" by Chua et al. [1] is a case report of a healthy two year old boy who presented with a unilateral cataract, anterior uveitis and glaucoma after an innocuous history of blunt ocular trauma. The diagnosis of a ciliary body medulloepithelioma was only made over a year later when the child presented with a mass lesion in the ciliary sulcus (Figure 1). Prior to this diagnosis, the child had undergone several intraocular procedures such as lensectomy, anterior vitrectomy, trans-scleral cyclophotocoagulation laser procedure as well as a glaucoma drainage surgery. Enucleation was eventually performed, followed by adjuvant chemotherapy in view of the malignant histological features of the tumor as well as the possible risk of periorbital tumor seeding due to the presence of a Baerveldt tube implant. This case highlights the difficulty of an early diagnosis and prompt treatment of ciliary body medulloepithelioma as a result of its occult anatomical location, insidious growth process and its secondary effects on proximal intraocular tissues in the anterior chamber. Secondary glaucoma is a common presenting feature of this condition and is often refractory to medical therapy. Hence, knowledge of an underlying ciliary body medulloepithelioma is pertinent in the decision making of subsequent intervention in intraocular pressure control.



Figure 1: Ciliary body medulloepithelioma. A clinical photograph showing a flesh-coloured fibrovascular tumor invading the anterior chamber and its angles.

Ciliary body medulloepithelioma is the commonest ciliary body tumor in childhood. The term "medulloepithelioma", coined by Grinker in 1931, best describes the origin of the tumor from the primitive medullary epithelium located along the inner layer of the optic cup. This undifferentiated medullary epithelium forms the non-pigmented ciliary body epithelium in the later years of development. The clinical picture is typical of a nonhereditary slow growing locally invasive tumor in a child of a median age of 2-5 years old [2]. This condition is uncommon in adulthood [3]. Histopathological studies have classified ciliary body medulloepitheliomas as benign or malignant in nature, with or without teratoid features. Three case series in the literature have highlighted that approximately 50-63% were nonteratoid, while 38-50% had teratoid features [2,4,5]. Hyaline cartilage was most frequently seen in the teratoid group [3]. In both groups, there were a higher proportion of malignant cases compared to benign ones. Clinical features such as histological diagnosis, extent of involvement as well as visual prognosis, are important in the consideration of tumor management.

The presentation of a ciliary body mass is usually a late one [4,6]. This tumor remains well hidden in the ciliary body region posterior to the iris till a critical size of about 10×7 mm is reached before it becomes clinically evident [7]. In our case, the tumor only became clinically apparent over a year after presentation and measured 11×8 mm on ultrasound examination (Figure 2). As such, the early clinical picture is often one that masquerades as the pathology of other ocular structures that are in close proximity to the tumor, with up to 88% of misdiagnosed cases in a reported series [3]. The lens is very frequently involved and the child can present with a myriad of lens-related pathology such as a lens opacity [7-9], lens notching (referred to as a "lens coloboma") [4,6,7] and ectopia lentis [7,10,11]. A notched lens in the absence of a uveal coloboma should prompt the ophthalmologist to exclude an underlying ciliary body medulloepithelioma [4]. The tumor may incite an inflammatory response and be misdiagnosed as a chronic granulomatous anterior uveitis [8,9]. Glaucoma is also a common early clinical feature [9] as a result of the tumor's close proximity to the anterior chamber angle as well as its secondary inflammatory and ischemic effects. The frequent association between the presence of cyclitic membranes and ciliary body medulloepithelioma has been described in the literature [3]. It is thought that these features could represent local migration of the tumor tissue into the anterior vitreous space. When present with or without a cataract, cyclitic membranes may be mistaken for a persistent hyperplastic primary vitreous, retinoblastoma or Coat's disease. A delay in clinical diagnosis of more than one year between the child's initial presentation and the histopathological diagnosis of the tumor has been reported [2], with an estimated 20-39% of cases

having had more than one type of intraocular procedures performed for the management of the masquerading conditions prior to tumor diagnosis [2,3]. Likewise in our case, the patient had undergone an anterior chamber tap, followed by lensectomy, anterior vitrectomy, trans-scleral cyclophotocoagulation laser procedure and Baerveldt tube surgery based on the provisional clinical diagnosis of a traumatic uveitis, cataract and glaucoma over the 1-year period. The history of a blunt ocular trauma was undoubtedly a red herring and hence the differential diagnosis of an underlying neoplastic pathology was not entertained until the presentation of the mass lesion. In hindsight, the presence of cyclitic membranes, alongside with the ultrasound findings of hyperechogenic material temporal to the lens surface during the initial examination of the child, should have led the ophthalmologist to maintain a high index of suspicion and perform frequent detailed exam of the ciliary sulcus region with scleral indentation and ultrasound imaging. Understandably, the tumor might have been difficult to identify when small. However, with frequent examinations of the ciliary sulcus conducted over time, the growing mass lesion could potentially be picked up earlier. The typically described ultrasound features of an echo-reflective ciliary body mass with cystic spaces [2-4,9] were consistent with our ultrasound findings of the mass lesion.



Figure 2: Ultrasound image of the ciliary body medulloepithelioma.

Intraocular tumors can be associated with raised intraocular pressure. This form of secondary glaucoma may be an initial presentation or a late feature of the underlying neoplastic process. A case series of 2704 eyes with intraocular tumors were reviewed and about 5% of these eyes were associated with elevated intraocular pressure [12]. Depending on the histopathology, size and anatomical location of the intraocular tumors, some tumors such as melanomas, medulloepitheliomas and retinoblastomas, are more prone to tumor-induced glaucoma. With ciliary body medulloepitheliomas, secondary glaucoma could be present in up to 50% of cases [2,3,5]. Buphthalmos may be observed in younger children with chronically raised intraocular pressure, like in our patient who had a corneal diameter of 14 mm and an elongated axial length of 25.8 mm. Ciliary body medulloepithelioma-associated glaucoma could be a result of iris neovascularization due to a tumor-induced hypersecretion of angiogenic factors (neovascular) [7], angle closure secondary to tumor mass effect, tumor seeding into angle and/or trabeculitis secondary to tumor-induced uveitis. The interplay of more than one pathogenetic

mechanism likely explains the refractory nature of intraocular pressure control in this group. Maximal medical therapy is often suboptimal and depending on the visual prognosis, some form of surgical intervention will usually be necessary. The main conundrum lies in the prompt diagnosis of an underlying ciliary body medulloepithelioma as the cause of glaucoma. The diagnosis of a tumor-induced secondary glaucoma would influence subsequent decision made regarding surgical management of the intraocular pressure. Filtration surgery is a contraindication as there is a high risk of tumor seeding into the periocular/orbital tissue. Unless enucleation is performed for a painful blind eye with an extensive intraocular tumor involvement, a trans-scleral cyclophotocoagulation laser procedure is often performed as an adjuvant to maximal medical therapy in selected cases of limited tumor involvement where the globe can be potentially salvaged. The decision to perform a Baerveldt tube surgery was reasonable prior to the tumor diagnosis in our case. However, if the diagnosis of a ciliary body medulloepithelioma had been made earlier, a filtration surgery would not have been performed. In which case, the trans-scleral cyclophotocoagulation laser treatment could have been repeated if an enucleation was deemed unnecessary.

The management of ciliary body medulloepithelioma depends on the tumor size, visual prognosis and presence of extraocular extension [13]. Due to the presence of a large mass lesion and poor visual prognosis in our patient, he had undergone an enucleation. This was followed by a course of chemotherapy in view of undifferentiated highly mitotic cells on histology as well as the high risk of orbital tumor seeding. Although enucleation is often performed in these cases, globe-sparing procedures can be considered in cases of small tumors with minimal secondary complications. These procedures include sectoral tumor resection in the form of iridocyclectomy and plaque radiotherapy. In the presence of orbital extension, an aggressive approach in the form of orbital exenteration is necessary to minimize risk of recurrence and/or systemic metastasis.

In view of the lessons learnt from several case series, maintaining a high index of suspicion is paramount in striving towards an early and prompt diagnosis of ciliary body medulloepithelioma. This is especially so in the presence of childhood neovascular glaucoma, notched lens, cataract-glaucoma complex and chronic uveitis that is unresponsive to steroidal treatment. Iris neovascularization is an early manifestation of ciliary body medulloepithelioma and any patient with such manifestation without any apparent reason should be examined carefully [7]. Detailed examination of the ciliary sulcus includes scleral indentation, gonioscopy and ultrasound biomicroscopy and should be repeated over time. Wherever necessary, examination under anesthesia should be performed. Though ciliary body medulloepithelioma is often locally invasive, it is important to exclude systemic metastasis in those cases with delayed diagnoses, malignant transformation on histology as well as extraocular tumor extension [3,13]. Cases with systemic involvement will require adjuvant chemotherapy and may have a poorer survival prognosis.

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