# Case Report

# Ocular Malformations with Presumable Intraocular Calcification

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*This is a case of ocular malformations with presumable intraocular calcification based on computed tomography (CT) imaging, magnetic resonance imaging (MRI) and ocular ultrasound (US) findings. The authors presented the clinical, imaging and pathological findings of this case. Intraocular calcification is the most important finding in retinoblastoma, which requires aggressive management. It is important to distinguish it from other intraocular lesions, especially intraocular calcified hematoma.*

**Keywords:** *Intraocular calcification, Retinoblastoma, Ocular dysgenesis*

***J Med Assoc Thai 2015; 98 (7): 719-23***
***Full text. e-Journal:*** *http://www.jmatonline.com*

A neonate presented with ocular dysgenesis, which was characterized by central corneal opacity and megalocornea. Over a period of four months, the eye globes experienced enlargement. Retinoblastoma was suspected because of bilateral progressive intraocular calcified masses. Therefore, enucleation was performed and the histopathological study revealed poor development of ocular structures.

The most likely diagnosis of intraocular calcification in early childhood is retinoblastoma. Nevertheless, other diseases such as retinal astrocytic hamartoma (giant drusens), retinopathy of prematurity, chronic retinal detachment, Kawasaki disease, choroidal osteoma, or retinal gliosis should be considered. We present an unusual case of a progressively enlarged, presumed, intraocular calcification mass.

## Case Report

A Thai female newborn presented with bilateral cloudy cornea since birth. She was the child of non-consanguineous parents. Her antenatal care history was unremarkable. Her mother had an atrial septal defect (ASD), which was repaired when she was young. She was delivered full term, with normal birth weight. On the eye examination, the visual fixation in both eyes was questionable. She had bilateral buphthalmos, severely thin and cloudy corneas with total iridocorneal adhesions (Fig. 1). The corneal diameters were 15 mm. The intraocular pressures (IOP) were 24 to 25 mmHg and 35 to 38 mmHg in the right and left eye, respectively. During the dilated fundoscopic examination, the view was obscured due to corneal opacity, but the red reflex was still presented. She also had systolic murmur; yet, the electrocardiography showed right bundle branch block, and the echocardiogram showed atrial septal defect without evidence of congestive heart failure. Furthermore, prominent bilateral renal pelvis was detected on renal sonography.

The presumptive diagnosis was severe bilateral irido-corneo-trabecular dysgenesis, compatible with the spectrum of Peter's anomaly in both eyes.

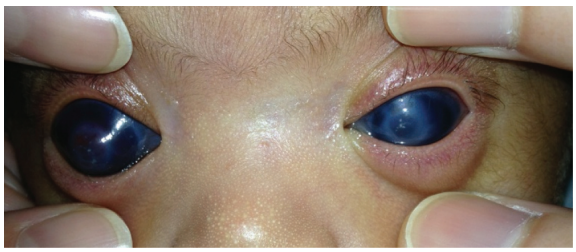

**Fig. 1** Anterior segment examination revealed buphthalmos, central corneal opacity, severe thinning of the cornea, a diameter of 15 mm in both eyes with total iridocorneal adhesions.

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Subsequently, an eye examination under general anesthesia (EUA) was performed. The intraoperative findings showed a flat anterior chamber and under-development of the iris, which attached anteriorly to the thin opaque corneas. There was straw-color intraocular fluid without evidence of lens or vitreous. At that time, no definite mass was detected. A planned glaucoma surgery was unsuccessful owing to the severely thin sclera and cornea, and unidentifiable anatomical landmarks.

A month later, the IOPs in the right and left eye were 9 and 27 mmHg, respectively. Her left eye also had epiphora and progressive buphthalmos. The patient was referred for a second opinion by means of an endoscopic examination and the possibility of ciliary body ablative treatment.

Two months post-surgery, computed tomography (CT) imaging of the brain and orbits revealed bilateral calcified intraocular lesions with retinal detachment, without evidence of optic nerve involvement (Fig. 2A-C). The ocular ultrasound (US) confirmed these findings (Fig. 2D). The differential diagnoses were postsurgical treatment and/or inflammation with calcified hematoma. Moreover, a small possibility of retinoblastoma could not be excluded, and Coat's disease was less likely. At the 1- and 2-month intervals of serial CT imaging, the suspected calcific masses showed an increase in size bilaterally. The diagnosis remained uncertain between retinoblastoma and calcified chronic hematoma. As a result, magnetic resonance imaging (MRI) was performed, which revealed expanding calcific masses (Fig. 3A-C) and an adjacent retinal detachment (Fig. 3C) associated with subretinal hemorrhage (Fig. 3C). The following ocular US also confirmed the growing calcific masses (Fig. 3D). After discussing all the treatment options with the family, the left eye underwent enucleation because retinoblastoma was suspected.

The ensuing gross examination revealed a left eyeball measuring 2.3 cm in diameter. The optic nerve was 0.4 cm long and 0.3 cm in diameter, and looked unremarkable. The cut-surface examination showed a small lens, measuring 0.2 cm in diameter, and separation of the posterior part of the retina with subretinal blood clotting, about 1 cm in diameter. The histopathological study revealed an unremarkable conjunctiva. The cornea had 2 to 4 squamous cell layers of epithelium, and there were no Bowman's layer, Descemet's membrane or endothelium (Fig. 4A). Additionally, fibroblast hypercellularity and

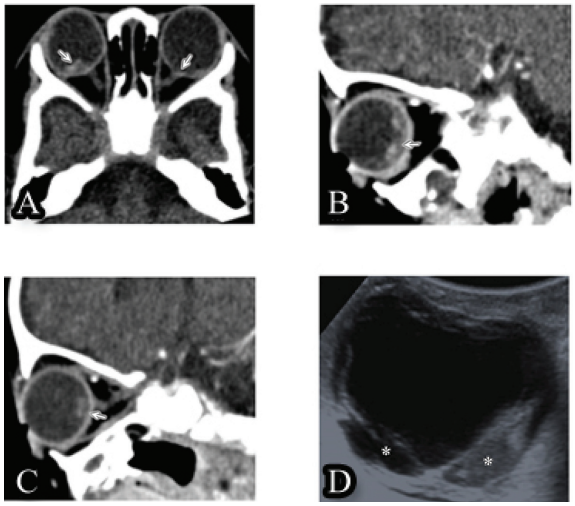


**Fig. 2** Plain axial CT scan of orbits shows enlargement of both globes with intraocular calcified soft tissue lesions (A, arrows). Enhanced sagittal reformatted CT scan of the right (B) and left (C) orbit reveals enhancement of the intraocular lesion (arrow). Additional ultrasound (US) found bilateral retinal detachment (D, * shown in right globe).

microcalcification was detected in the collagenous corneal stroma (Fig. 4A, see black arrow). There was a thin and elongated iris that adhered to the posterior surface of the cornea (Fig. 4B), resulting in the obliteration of the anterior chamber angle. The ciliary bodies (Fig. 4C), the trabecular meshwork, and the canal of Schlemm (Fig. 4D) were well-formed. There was also hypoplasia of the lens (2 mm in diameter) that was located eccentrically. Furthermore, the presence of the anterior capsule, an incomplete posterior capsule, and the absence of lens epithelium were detected (Fig. 4E). The retina showed maldeveloped retinal layers and retinal separation, with an increased vascular proliferation in the separated area. There was also some serum collection under the retina with numerous hemosiderin-laden macrophages (Fig. 4F, see small picture), but without evidence of calcification. Finally, the optic nerve was unremarkable (Fig. 4G).

## Discussion

Intraocular calcification in children is the most important feature of retinoblastoma to distinguish it from other intraocular lesions[1]. Intraocular calcification is rarely found in retinal astrocytic hamartomas (giant drusens), retinopathy of prematurity, chronic retinal detachment, Kawasaki disease[2], choroidal osteoma[3],

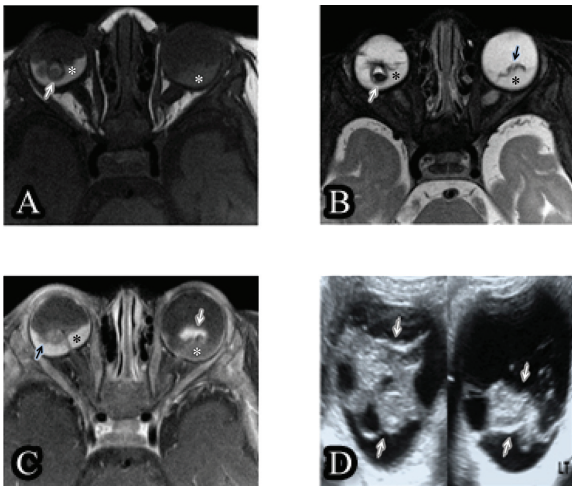


**Fig. 3** MRI, axial T1-weighted image shows an increased size of bilateral intraocularcalcified masses (arrow) associate with subretinal hemorrhage and retinal detachment (*) of both globes (A). Axial T2-weighted image shows an increased size of bilateral intraocular calcified masses (arrows). Associate with subretinal hemorrhage and retinal detachment (*) of both globes (B). Axial, T1-weighted, Gadolinium-enhanced imaging shows enhanced intraocular soft tissue masses (arrows) associate with subretinal hemorrhage and retinal detachment (*) of both globes (C). Additional US confirmed the increased size of the bilateral intraocular hyperechoic masses (D, arrows).

and retinal gliosis[4]. Our patient presented with severe bilateral eye malformation, and suspected intraocular calcification masses from CT and MRI imaging, whereas the pathological study showed intraocular hemorrhage without calcification. This should serve as a reminder that progressively enlarged intraocular calcification masses may be found in intraocular hemorrhage as well.

The patient displayed ocular developmental anomalies of the anterior and posterior segment, which include developmental disorders involving the cornea, iris, angle, lens, and retina. This is especially true for the neural crest component of the secondary mesenchyme that develops into the corneal stroma, corneal endothelium, anterior chamber angle, and iris stroma. The retina develops from the neural ectoderm, with the retinal pigment epithelium (RPE) developing from the outer layer of the optic cup and the neurosensory retina from the inner layer of the optic cup.

The patient displayed bilateral multiple malformations, which are related to abnormalities

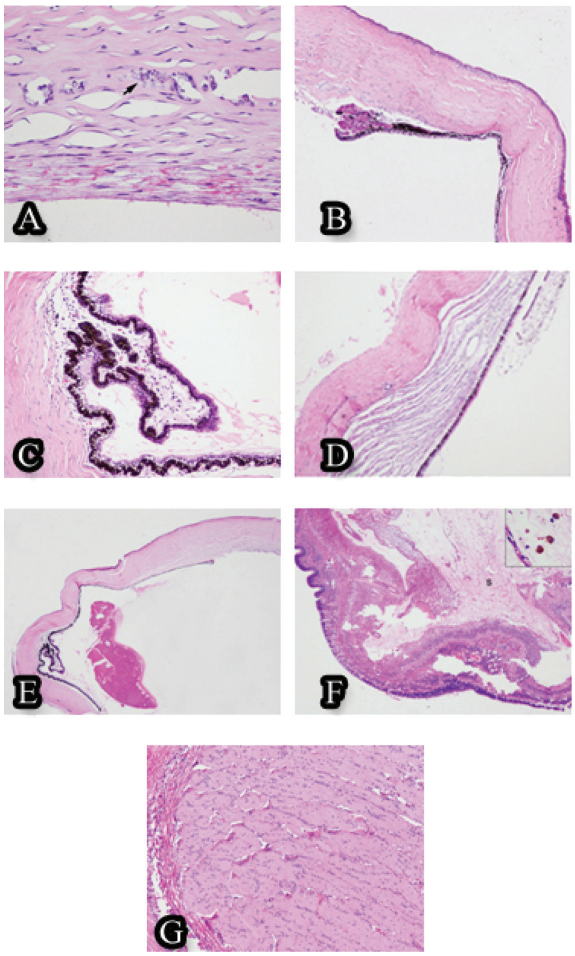


**Fig. 4** Histopathological study, cornea showed absence of Bowman's layer, Descemet's membrane and endothelium. Collagenous stroma showed hypercellularity of fibroblasts and microcalcification (A, arrow). There was an adhesion of the iris to the posterior surface of the cornea, with a thin and elongated iris (B). Ciliary body was well-developed (C). Trabecular meshwork and Schlemm's canal were well-formed (D). The lens showed hypoplasia (2 mm in diameter), an eccentric position, presence of the anterior capsule, an incomplete posterior capsule and absence of epithelium (E). Depicted are retinal separation and serum collection(s) under the retina with numerous hemosiderin-laden macrophages, maldeveloped retinal layers, and increased vascular proliferation in the separated area (F, small picture). Optic nerve was unremarkable (G).

during the eye organogenesis period (4$^{th}$ to 8$^{th}$ week of gestation); yet, she did not have any significant systemic abnormality. During the fourth week of gestation, the optic pits deepen and form the optic

vesicles. Disruptions during this stage will induce the presence of severe eye abnormalities such as coloboma, enophthalmos, and microphthalmos[5]. Hence, the abnormalities of our patient probably developed beyond this stage. During the fifth week of gestation, the lens vesicle is formed[5]. It might be the inception of abnormal development in this case because the lens was small and distorted. In the sixth gestational week, the development of the retina and the differentiation of the neural retina happen[5], our patient displayed maldeveloped retinal layers. In the seventh week of gestation, the mesenchymal cells migrate forward and contribute to the formation of corneal stroma, endothelium, trabecular meshwork, and Schlemm's canal[5]. The patient showed 2 to 4 squamous cell layers of corneal epithelium, an absence of the Bowman layer, hypercellularity of fibroblasts in the collagenous stroma, microcalcification in the collagenous stroma, and an absence of Descemet's membrane and endothelium. Therefore, a period of abnormal development earlier than the eighth week of gestation, which involves corneal well-differentiation, had happened.

Peter's anomaly is characterized by central corneal opacities, associated with abnormalities of corneal endothelium, Descemet's membrane and posterior corneal stroma. It is also associated with anomalies of the anterior segment structures. The cause may be a defect of the neural crest or ectoderm, resulting in failure or delay in the separation of the lens vesicle from the surface epithelium. The causative event may occur in the migratory neural crest cells between the fourth and seventh weeks of gestation. Associated systemic abnormalities include congenital heart disease.

In conclusion, the cases of ocular malformation with suspected progressive intraocular calcification mass and intraocular hemorrhage should be differentiated from retinoblastoma.

**What is already known on this topic?**

Intraocular calcification is the most important finding in retinoblastoma, which requires aggressive management. It is important to distinguish it from other intraocular lesions.

**What this study adds?**

The presented case showed that progressive intraocular calcification found in intraocular hematoma is not a malignancy case. It is important to distinguish it from retinoblastoma especially in case of ocular malformation.

**Potential conflicts of interest**

None.

**References**


1. Chung EM, Specht CS, Schroeder JW. From the archives of the AFIP: Pediatric orbit tumors and tumorlike lesions: neuroepithelial lesions of the ocular globe and optic nerve. Radiographics 2007; 27: 1159-86.
2. Che Mahiran CD, Alagaratnam J, Liza-Sharmini AT. Leucocoria in a boy with Kawasaki disease: a diagnostic challenge. Singapore Med J 2009; 50: e232-4.
3. Morris RJ, Prabhu VV, Shah PK, Narendran V. Combination therapy of low-fluence photodynamic therapy and intravitreal ranibizumab for choroidal neovascular membrane in choroidal osteoma. Indian J Ophthalmol 2011; 59: 394-6.
4. Deshmukh SD, Ashturkar AV, Babanagare SV, Gokhale SK, Deshpande AA. Massive retinal gliosis: an unusual case with immunohistochemical study. Indian J Ophthalmol 2011; 59: 246-8.
5. Jamieson RV, Grigg JRB. Clinical embryology and development of the eye. In: Hoyt CS, Taylor D, editors. Pediatric ophthalmology and strabismus. 4th ed. Edinburgh: Saunders Elsevier; 2013: 9-15.

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*คณะผู้นิพนธ์นำเสนอการตรวจพบทางคลินิก ภาพเงา และพยาธิวิทยาของผู้ป่วย ที่มีโครงสร้างตาผิดปกติร่วมกับการพบหินปูนในลูกตาจากการตรวจด้วยเอกซเรย์คอมพิวเตอร์ คลื่นแม่เหล็กไฟฟ้า และการตรวจคลื่นเสียง หินปูนในลูกตาเป็นสิ่งตรวจพบที่สำคัญที่สุดในโรคมะเร็งจอตา ซึ่งต้องการการดูแลรักษาอย่างเต็มที่และก้าวร้าว จึงมีความสำคัญมากที่ต้องแยกจากความผิดปกติอื่นในลูกตาโดยเฉพาะอย่างยิ่งหินปูนจากก้อนเลือด*