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Case Report

Ocular and brain imaging findings in Peters' anomaly: A case report and literature review ^{☆,☆☆}

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ARTICLE INFO

Article history:

Received 8 March 2020

Revised 23 March 2020

Accepted 7 April 2020

Keywords:

Peters' anomaly

Magnetic resonance imaging

Anterior eye segment

ABSTRACT

Peters' anomaly is a rare congenital eye condition characterized by anterior segment dysgenesis and commonly presents as unilateral or bilateral corneal opacity in the early neonatal period. Peters' anomaly is often associated with congenital brain and skull abnormalities, which are frequently overlooked. In this paper, we present a case of a 5-day-old female neonate with Peters' anomaly, and review the literature for similar reports that describe associated brain imaging findings. In our case, imaging studies show abnormalities involving the anterior segments of both globes with absent intracranial manifestations. Although Peters' anomaly is a condition of interest for ophthalmologists, radiological studies should be performed, and neuroradiologists should be aware of the imaging findings associated with this rare entity.

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Introduction

Peters' anomaly, previously called keratolenticular dysgenesis, is a rare congenital eye condition characterized by abnormal anterior segment development. Peters' anomaly usually presents in the early neonatal period as unilateral or bilateral corneal opacity (leukoma). The annual incidence of Peters' anomaly in the USA is estimated to be 40–60 new cases [1]. Most of these cases have poor vision outcome and would require corneal transplantation.

Peters' anomaly could present as an isolated condition or as a part of a clinical syndrome, eg, Peters-plus syndrome. Besides, Peters' anomaly is associated with multiple ocular abnormalities like cataract, glaucoma, small eye globes (ie, microphthalmia), optic nerve, and optic chiasm hypoplasia, absence of the lens (ie, aphakia), or the iris (ie, aniridia), and retinal anomalies [2,3]. Moreover, Peters' anomaly is also associated with a high prevalence of systemic malformations, like spinal defects, midline facial deformities, skeletal malformations, and, infrequently, developmental brain abnormalities [4–6].

[☆] Funding: The research reported in this paper received no specific funding.

^{☆☆} Disclosure of interest: The authors declare that they have no competing interests.

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<https://doi.org/10.1016/j.radcr.2020.04.011>

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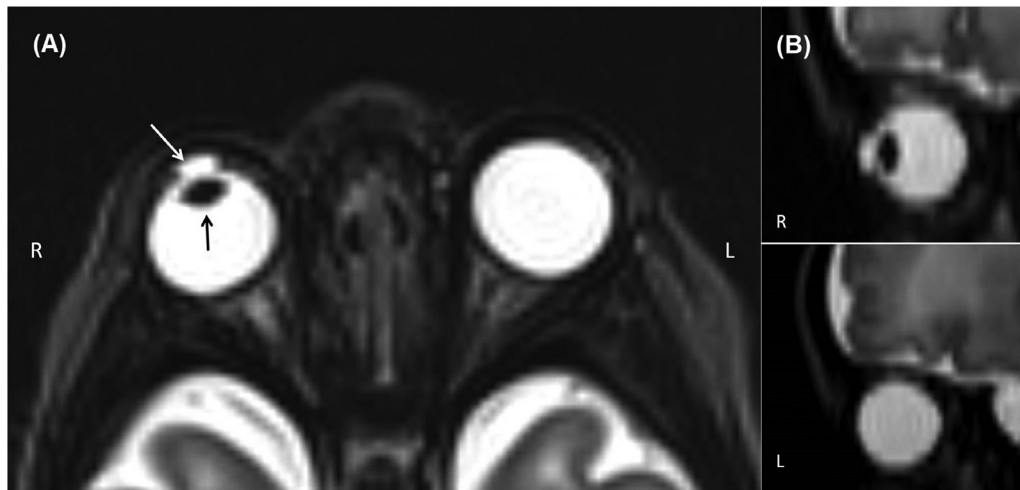


Fig. 1 – (A) Axial and (B) sagittal views T2-weighted images demonstrate abnormality involving the anterior segments of both globes, typical of severe Peters’ anomaly. The right globe shows abnormal development of the anterior segment with anterior corneal staphyloma (bulging; white arrow) but with a normal-appearing lens (black arrow). The left globe demonstrates abnormal development of the anterior segment with an absent lens. R: right; L: left.

Although Peters’ anomaly is a condition of interest for ophthalmologists, radiological studies can also play an essential role in the diagnosis and management. Such studies can provide further information on associated anomalies to determine the extent and severity of involvement. To highlight the importance of imaging studies, we present a case of bilateral Peters’ anomaly in a 5-day-old neonate with abnormal eye examination at birth. Additionally, we review the ophthalmology literature for similar reports that describe the associated brain imaging findings. To our knowledge, this report is the first to focus on the orbit and brain imaging findings associated with Peters’ anomaly. We present imaging examples of the globe abnormalities and discuss the brain imaging findings reported in the literature, which could provide helpful insights to radiologists and neuroradiologists handling such cases.

Case presentation

A full-term female baby presented with abnormal eye examination at birth. The prenatal course was uncomplicated except for pelviectasis diagnosed at 29 weeks of gestation but resolved at 33 weeks, and mild ventriculomegaly on prenatal ultrasound (US). Vaginal delivery was uncomplicated, and APGAR scores were 8 at 1 and 5 minutes, respectively. Birth weight and length were within the normal range at 3130 gram (25th–50th percentile) and 48 cm (50th percentile), respectively. Newborn physical exam demonstrated clouding of both eyes. Additional multiple mild midline craniofacial and skeletal anomalies were noted, including abnormal ears, hypertelorism, webbed neck, and foot deformity. Pediatric ophthalmology was consulted and detailed fundoscopic exam at the age of four days demonstrated clouding in both eyes; left eye > right eye. Right eye clouding was more pronounced peripherally but was present both centrally and peripherally.

Similarly, left eye clouding was present both centrally and peripherally, but was more pronounced centrally. Abnormal vascularization was noted in both eyes. The fundoscopic exam was consistent with Peters’ anomaly, and we obtained a brain and orbits magnetic resonance imaging (MRI) the next day to assess for accompanying globe and brain abnormalities. The MRI results show bilateral anterior segment abnormalities (Fig. 1). Importantly, we did not detect any other associated brain anomalies except for mild ventriculomegaly, and the diagnosis was confirmed as Peters’ anomaly. Subsequent genetic testing was significant for the detection of unbalanced translocation, which resulted in 6p25.3p25.2 microdeletion and 16q23.1q24.3 duplication. Additional genetic abnormalities included mutation of the *FOXC1* gene. Further imaging, including MRI and US of the spine and US of the abdomen, demonstrated no other anomalies. The baby subsequently required extensive staged bilateral globe surgeries, including bilateral corneal implants, vitrectomy, left-sided lensectomy, and glaucoma shunt placement with multiple revisions.

Literature review

We searched the ophthalmology literature via the PubMed database using the keyword “Peters’ anomaly.” We identified case reports and case series that reported clinical and radiological features associated with Peters’ anomaly. We restricted our search to articles published in the English language with no publication date specification. Our search results revealed 9 published articles that reported neuro-radiological findings associated with Peters’ anomaly [2,4–11]. The references and results are summarized in Table 1. Noteworthy, the primary focus of the included articles was rarely related to the neuroimaging findings, and the included papers were mostly published in ophthalmology journals. This observation empha-

Table 1 – Neuro-radiological findings associated with syndromic and non-syndromic Peters' anomaly.

Publication	Patient(s)	Neuroradiology findings
Reis et al. [9,10]	Four patients with syndromic and nonsyndromic Peters' anomaly	Agenesis of the corpus callosum, hypoplasia of the inferior cerebellar vermis, absence of the septum pellucidum, thrombosed dural sinus malformation, subependymal gray matter heterotopia, and incomplete rotation of the hippocampal formations.
Almarzouki et al. [2]	Twin boys with non-syndromic Peters' anomaly	Bilateral microphthalmia, globe heterogeneous signal intensity (indicating hemorrhage), hypoplastic optic nerves, and optic chiasm.
Happ et al. [7]	Two patients with syndromic Peters' anomaly	Central white matter volume loss and thin corpus callosum.
Takano et al. [6] and Morimoto et al. [4]	A boy with nonsyndromic Peters' anomaly	Bilateral perisylvian polymicrogyria extended into the frontal, temporal, and occipital lobes.
Neilan et al. [5]	A boy with Peters' anomaly associated with other anomalies	Atretic cranial meningocele and multiple midline craniofacial anomalies
Shanske et al. [11]	A boy with nonsyndromic Peters' anomaly	Microcephaly, and extensive neuronal migration defect
Myles et al. [8]	A twin with bilateral Peters' anomaly associated with other anomalies	A partial or complete absence of the corpus callosum and cerebral calcifications

sizes the importance of our work in providing a new perspective and sheds light on a condition seldom addressed in the radiology literature.

Based on the search results, the most commonly reported brain imaging findings in association with Peters' anomaly included corpus callosum abnormalities and malformations of cortical development. Less frequently, Peters' anomaly was associated with hypoplasia of the cerebellar vermis, absent septum pellucidum, hippocampus abnormalities, and cerebral calcification. Nevertheless, the exact prevalence of these abnormalities could not be determined and would require further studies. Importantly, the observed brain imaging findings were present in both non-syndromic and syndromic Peters' anomaly making the full characterization of these associations challenging. The primary aim of this report is to bring to the reader's attention the possibility of such abnormalities. More rigorous study designs would be required to draw definite conclusions in this regard and explore the underlying mechanisms linking Peters' anomaly to these associated brain abnormalities.

Discussion

Peters' anomaly is a rare congenital eye condition characterized by anterior segment dysgenesis and usually present as central cornea opacity at birth with variable ocular involvement. At the histological level, Peters' anomaly is thought to result from absence of corneal endothelium related to poor dissolution of the lens vesicle from the surface ectoderm [12]. Although most cases are sporadic, both autosomal dominant and autosomal recessive inheritance have been reported [13]. Although most Peters' anomaly cases are idiopathic, genetic mutations in multiple genes have been implicated, including *FOXC1*, *PAX6*, *PITX2/RIEG1*, and *CYP1B1* [14–18]. These genes are mostly involved in the differentiation of primordial cells

and regulation of neural crest cell migration to the posterior cornea. In our case, the development of Peters' anomaly was likely the result of 6p25.3p25.2 microdeletion and *FOXC1* mutation. Mutations in the transcription factor gene *FOXC1* was previously reported as a cause of anterior segment dysgenesis and Peters' anomaly [18].

Peters' anomaly is commonly associated with other ocular and systemic malformations. The most common systemic abnormalities include craniofacial, spinal, skeletal, cardiac, gastrointestinal, and genitourinary anomalies [19]. Cases of bilateral Peters' anomaly, as observed in our case, are associated with a higher rate of systemic malformations 71.8% vs 36.8% in unilateral Peters' anomaly [20]. In our case, physical examination revealed the presence of multiple craniofacial and skeletal defects. Moreover, Peters' anomaly could present as a part of a clinical syndrome like Peters-plus syndrome. Additional features that accompany Peters-plus include cleft lip or cleft palate, short stature, abnormal ears, mental retardation, and developmental delay [21]. We considered Peters-plus syndrome in the differential diagnosis, but it was later excluded due to the lack of associated features and characteristic genetic mutation pattern. The Peters-plus syndrome is caused by mutations in the *B3GALTL* gene, which encodes for a unique glycosylation protein, and these mutations were not present in nonsyndromic Peters' anomaly like in our case.

The radiological findings in our case were classical for non-syndromic Peters' anomaly, eg, abnormal development of the anterior segment in both eyes, anterior corneal staphyloma (bulging) in the right eye, and absence of the lens in the left eye. Both of these radiological signs have a dramatic appearance on the orbit MRI studies and could be easily spotted by an experienced neuroradiologist. Although a rare condition, Peters' anomaly should be considered when these findings are observed. The differential diagnosis for anterior corneal staphyloma in imaging includes buphthalmos (ie, enlarged eyeball) due to secondary causes like glaucoma, coloboma (congenital iris defect), and axial myopia. The absence of the

lens should be differentiated from ectopia lentis (anterior or posterior displacement of the lens from its normal position), and it could be related to congenital anomalies, traumatic, and surgical removal in cases with previous surgical history.

On the other hand, in our case, we did not detect any associated structural brain anomalies. Although B-scan ocular US can be very beneficial to evaluate the extent and severity of ocular involvement, an orbit and brain MRI scans are also crucial to confirm or exclude the presence of intracranial anomalies and detect additional involvement of optic nerves and optic tracks undetectable by a simple ocular US. Newborn MRI is a safe imaging modality with no added risk of radiation exposure. Based on the literature review, Peters' anomaly could be associated with various intracranial abnormalities like absent or underdevelopment of the corpus callosum and malformations of cortical development. The underlying mechanisms of these brain malformations are not known and would require further studies.

Conclusion

In conclusion, Peters' anomaly is a rare eye condition that should be suspected in any neonate with anterior segment anomalies. Radiologists should also bring into consideration this potential diagnosis in cases of abnormal anterior segment appearance in MRI studies. Additionally, brain imaging studies can provide clinically relevant information and detect associated structural brain anomalies. In our case, we did not notice any associated brain anomalies, and the diagnosis was confirmed as nonsyndromic Peters' anomaly.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s).

Author contribution

RWE: the attending radiologist associated with the case. Contributed to the diagnosis and drafting of the manuscript.

AS: performed the literature review, prepared the images, and drafted the manuscript.

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