

Pseudoretinoblastoma in enucleated eyes of Asian patients

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ABSTRACT

Introduction: Retinoblastomas of the eye are a cause of childhood blindness and have a high rate of mortality, as well as a hereditary mode of transmission. Other conditions that mimic retinoblastomas are known as pseudoretinoblastomas, and are managed differently. Although pseudoretinoblastoma and the accuracy of retinoblastoma diagnosis have been reviewed in Caucasian patients, published studies in Asian patients are lacking. The purpose of this article is to report our experience with pseudoretinoblastomas in two major ophthalmological centres in Asia.

Methods: A case series of 28 enucleations carried out for suspected retinoblastoma at the Singapore National Eye Centre and KK Women's and Children's Hospital, Singapore, between January 1991 and December 2002, is reported. All cases were subjected to a detailed history from parents, followed by external ocular examination, slit-lamp biomicroscopy and binocular indirect ophthalmoscopy. Ancillary studies, such as B-scan ultrasonography and computed tomography, were employed as necessary to confirm the diagnosis. Histology was obtained on all cases.

Results: Of the 28 cases, 25 (89 percent) were found on histological analysis to be retinoblastomas. Three (11 percent) were pseudoretinoblastomas. There were two cases of Coat's disease and a case of presumed ocular toxocariasis. These three cases were described in detail.

Conclusion: Although our sample size is small, the percentage of confirmed retinoblastomas was found to be only slightly higher than that found in western countries. Our findings are consistent with their findings that Coat's disease and presumed ocular toxocariasis are the more common causes of pseudoretinoblastoma.

Keywords: Coat's disease, eye enucleation, retinoblastoma, toxocariasis

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INTRODUCTION

A child presenting with leukocoria presents diagnostic conundrums. Possible diagnoses are many and include persistent hyperplastic primary vitreous, Coat's disease, ocular toxocariasis, congenital cataract, retinopathy of prematurity, retinoblastoma, von Hippel's disease, inflammatory pseudoglioma, Norrie's disease and organised intraocular haemorrhage⁽¹⁾. The management of these pseudoretinoblastomas is quite different to that of retinoblastoma, so it is important for physicians to recognise them and distinguish them from retinoblastoma. Excluding retinoblastoma is of primary importance because of the high incidence of mortality with this condition, and also because it has a hereditary mode of transmission.

Although pseudoretinoblastoma and the accuracy of retinoblastoma diagnosis have been reviewed in Caucasian patients, published studies in Asian patients are lacking. We report the frequency of pseudoretinoblastoma in a case series of 28 eyes enucleated for presumed retinoblastoma at the Singapore National Eye Centre and the KK Women's and Children's Hospital, Singapore, between 1991 and 2002.

METHODS

We reviewed the case records of 28 eyes that were enucleated for suspected retinoblastoma between January 1991 and December 2002 in two public eye institutions in Singapore. All cases were subjected to a detailed history from the parents, followed by external ocular examination, slit-lamp biomicroscopy and binocular indirect ophthalmoscopy. Ancillary studies such as B-scan ultrasonography and computed tomography (CT) were employed as necessary to confirm the diagnosis. Histology was performed on all cases.

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Fig. 1 Photomicrograph shows a detached retina with subretinal exudates (Haematoxylin & eosin, $\times 100$).

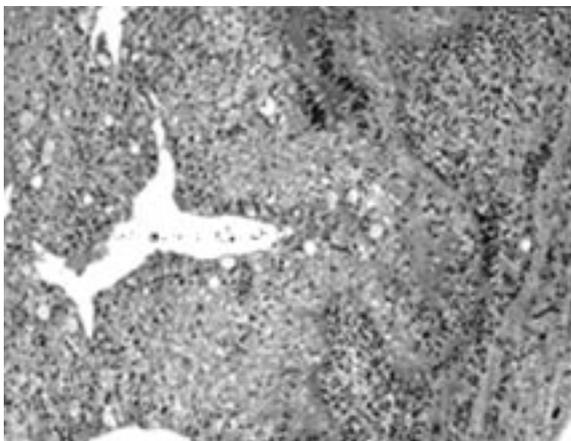


Fig. 2 Photomicrograph shows a detached retina with subretinal exudate comprising foamy histiocytes. Telangiectatic vessels within the retina (far right of picture) (Haematoxylin & eosin, $\times 200$).

RESULTS

25 (89%) out of the 28 enucleated eyes proved to be retinoblastomas on histology while three (11%) were found to have pseudoretinoblastoma. Two patients had Coat's disease and the third, presumed ocular toxocariasis.

Case 1

A 22-month-old boy presented with leukocoria which was noted by his mother three months previously. The affected eye did not fix or follow objects and he objected to occlusion of the other eye. On examination, there was leukocoria of the affected eye, with an afferent pupillary defect and a total retinal detachment with "multinodular exophytic tumours" noted. CT of the head was normal while CT of the orbits revealed higher attenuation soft tissue masses in the posterior two-thirds of the orbit. Enucleation was carried out three weeks later with implantation of a glass ball implant wrapped in donor sclera. Histology of the eye showed retinal detachment with a subretinal exudate (Fig. 1) comprising foamy macrophages, some of them with ingested pigmented

rod-like structures in a proteinaceous background (Fig. 2). A few cholesterol clefts were present, with most of them being surrounded by proteinaceous material. A focus of telangiectatic vessels was seen. The features were noted to be compatible with Coat's disease.

Case 2

A 4-year, 9-month-old boy was noticed at a routine eye screening at school to have reduced vision in his left eye. There was no pain or redness, and on examination, visual acuity was no perception of light (NPL) in that eye. There was leukocoria, exotropia, a semi-dilated pupil and rubeosis iridis. A large mass was seen in the fundus with "cottage cheese" appearance and vessels on the mass. His parents did not give consent for CT evaluation of the lesion. The eye was enucleated two weeks after presentation and he had an acrylic implant with no wrapping. Histology revealed retinal detachment with retinal gliosis and presence of telangiectatic vessels. Areas of haemorrhage and fibrin deposition were seen, as well as PAS-positive material. Aggregates of cholesterol clefts were surrounded by multinucleated giant cells in the subretinal and intraretinal areas. Fluid from the retroretinal exudate was examined cytologically and stained with fat stain. This revealed the presence of many lipoidal macrophages. There was no malignancy seen and the findings were consistent with Coat's disease.

Case 3

A 5-year-old boy, who was living in Seychelles, was noted by his mother to have leukocoria. There was no medical history or family history of retinoblastoma. On examination, visual acuity was hand movements in the affected eye and 6/6 in the other eye. There was posterior synechiae of the iris and the lens was clear. A retrolental mass was responsible for the leukocoria. CT of the orbits revealed a patchy increase in the density of the right vitreal cavity and a fluid level suggestive of vitreous haemorrhage and tumour growth. There was no calcification. Magnetic resonance (MR) imaging of the orbits showed evidence of retinal detachment, fluid level and possibly a tumour mass in the right eye. Review and investigations initiated by a paediatric oncologist, including lumbar puncture and bone marrow aspiration, were normal.

Enucleation was performed one month after presentation and a hydroxyapatite implant was implanted. Biopsy of the eye showed total retinal detachment with subretinal exudate and collagenised retrolental fibrosis (Fig.3). A subretinal scar extended

TABLE 1. Summary of case series of pseudoretinoblastoma.

Authors	Cases of presumed retinoblastoma	Cases of pseudoretinoblastoma	Percentage
Chuah et al [*]	28	3	11
Robertson and Campbell ⁽²⁾	49	8	16
Margo and Zimmerman ⁽³⁾	56	15	27

* This series

to the ciliary body and showed an aggregate of multinucleated giant cells and an epithelioid granuloma (Fig. 4). No malignancy was detected. The diagnosis was granulomatous chorioretinitis with total retinal detachment and scar formation of unknown aetiology, probably secondary to ocular toxocariasis. He returned to Seychelles soon after. Subsequent attempts made to contact him were unsuccessful.

DISCUSSION

To the best of our knowledge, there are no published case series of pseudoretinoblastoma patients in Asia. In this series of enucleated eyes in Singapore, three out of 28 (11%) proved to be pseudoretinoblastomas. This percentage is quite close to that found by Robertson and Campbell, who found that in 49 enucleated eyes in which retinoblastoma was in the differential diagnosis, between 1954 and 1974 at the Mayo Clinic, eight (16%) were pseudoretinoblastomas⁽²⁾. Although our series was small, our percentage is lower to that found by Margo and Zimmerman, where in a series of 56 eyes which were enucleated for suspected retinoblastoma, 27% turned out not to have retinoblastoma⁽³⁾.

The difficulty in the diagnosis of leukocoria is well known because retinoblastoma may mimic diseases such as Coat's disease⁽⁴⁾, and enucleation has been advocated in such cases when in doubt⁽⁵⁾. Conversely, atypical Coat's disease with intraocular calcification may also mimic retinoblastoma⁽⁶⁾. Two-thirds of our cases of pseudoretinoblastomas turned out to be Coat's disease. Shields et al⁽⁷⁾ found that of 500 patients referred for possible retinoblastoma, 212 (42%) were diagnosed as pseudoretinoblastomas, of which the most common were persistent hyperplastic primary vitreous (28%), Coat's disease (16%) and presumed ocular toxocariasis (16%). Although our series was small, our cases are consistent with their findings of Coat's disease and presumed ocular toxocariasis being the more common causes of pseudoretinoblastoma.

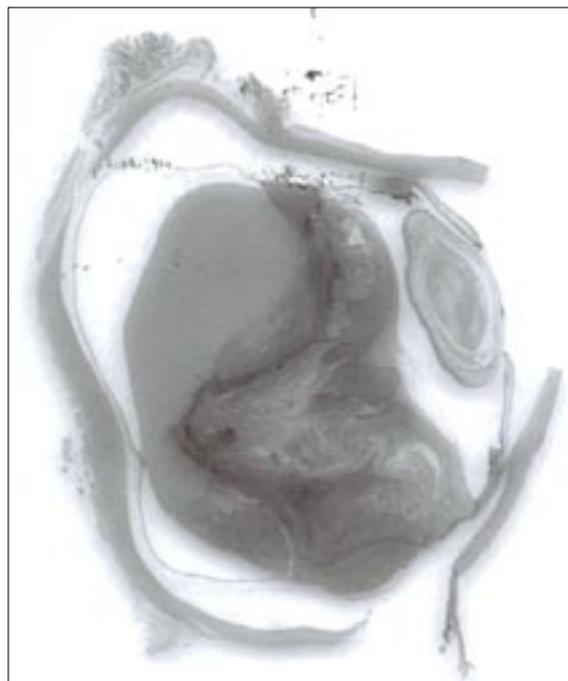


Fig. 3 Photomicrograph of the eyeball shows retinal detachment with subretinal exudate (Haematoxylin & eosin, $\times 20$).

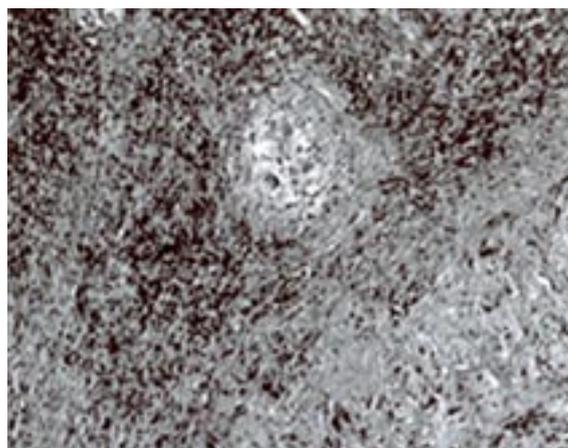


Fig. 4 Photomicrograph shows epithelioid granuloma with multinucleated giant cells (Haematoxylin & eosin, $\times 200$).

At another tertiary referral centre, Howard and Ellsworth⁽⁸⁾ found between 1959 and 1964 that of 500 patients referred for possible retinoblastoma, 265 (53%) were diagnosed as pseudoretinoblastomas. In their series, persistent primary hyperplastic vitreous (19%) was also the most common cause, but Coat's disease was only the eighth most common (4%) and "larval granulomatosis" was the sixth most common cause, comprising 6.5% of the cases. Thus Coat's disease and presumed ocular toxocariasis pose differential diagnostic problems with retinoblastoma. It is important for the clinician to make the correct diagnosis in such cases to avoid mismanagement of cases. Several features may help in distinguishing between the two.

Coat's disease, which usually becomes clinically evident in the first decade of life with mean age of presentation at five years of age, is unilateral (95%), and affects males more commonly (76%)⁽⁹⁾, without any family history of the disease. The vitreous is clear and there is irregular telangiectasia of the retinal blood vessels with accumulation of yellow subretinal exudation and glistening subretinal cholesterol, but no distinct mass is present. On ultrasonography, subretinal echoes are minimal and calcification is rare at the level of the retinal pigment epithelium. In contrast, retinoblastoma presents younger, with a mean age of 1.5 years and has a 50:50 sex predilection. 40% are bilateral and there is a 10% chance of family history. There may be white fluffy seeds in the vitreous, no retinal exudation but a retinal mass on examination. There may be subretinal echoes from seeds on ultrasonography and calcification seen within the retinal tumour in 90% of cases. This calcification may also be detected on CT.

Ocular toxocariasis occurs in slightly older children with a history of contact with puppies or a prior history of visceral larva migrans. It can produce a solitary fundal mass of a diffuse endophthalmitis that simulates an endophytic retinoblastoma. However, it is characterised by organising vitreoretinal traction and signs of inflammation such as posterior synechiae and a secondary posterior subcapsular cataract. Vitreoretinal traction and inflammatory signs are very unusual in retinoblastoma.

Our third case, a five-year-old boy, presented with posterior synechiae and no calcification. These factors are in favour of ocular toxocariasis. However there was a suggestion of a mass both on examination and CT scan. Case 1 was a 22 month-old boy who ultimately proved to have Coat's disease, although this is a younger presentation of Coat's disease than usual. His CT did not show calcification. Case 2 was nearly five years old. Ultrasonography and/or CT might have picked up any absence of calcification and prevented an enucleation, but the eye was NPL anyway.

Although our series was small, they nevertheless represent the first reported cases of pseudoretinoblastomas in Asian eyes in the English literature. The three cases seem to suggest that Asian eyes present similarly for pseudoretinoblastoma as in Caucasian eyes, in that Coat's disease and toxocariasis have to be taken into consideration based on the history and examination findings. In conclusion, certain conditions may mimic retinoblastoma and it is often difficult to make a correct diagnosis. However, features exist which make it easier to make the correct diagnosis and should always be taken into consideration before performing an enucleation for suspected retinoblastoma, especially if the eye still has some useful vision.

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