CHANGING TRENDS IN PSEUDORETINOBLASTOMA DIAGNOSES: A 10-YEAR REVIEW FROM THE UNITED KINGDOM

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INTRODUCTION

Retinoblastomas are the most common ocular tumour[1]. However, there are also a group of conditions that simulate retinoblastomas collectively known as Pseudo-retinoblastomas (pseudoRBs). Several studies have shown that children referred for retinoblastomas can have pseudoRBs. It is very important to differentiate these two conditions as the treatment is completely different.

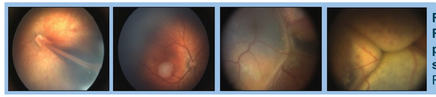


Figure 1: Retinoblastomas and pseudoRBs can appear similar. Left to right: PFV, RB, RB, Coats' disease.

Shields et al. reported in 2013 that 22% of 2171 patients referred for retinoblastoma had a pseudoRB[2]. Furthermore, in 2013 Huang et al. found that out of 369 eyes enucleated for a clinical indication of malignancy, 6% were misdiagnosed with no histopathological evidence found on examination[3]. These studies stress the importance of distinguishing retinoblastomas from pseudoRBs. Currently, there are no reports in the United Kingdom (UK) outlining the occurrence of pseudoRBs based on age at presentation.

Aim: To study the different types and frequency of pseudoRB lesions based on age at presentation.

METHODS

A retrospective, electronic database search was performed for all patients referred for a suspected diagnosis of retinoblastoma at the Retinoblastoma Unit, Royal London Hospital, Barts Health NHS Trust, London, England from the 1st of January 2009 to 31st of December 2018 inclusive. Patients were included only if they were suspected to have a retinoblastoma.

A diagnosis was established based upon examination findings under anaesthesia and included indirect ophthalmoscopy, fundus photography, ultrasonography and fluorescein angiography as necessary.

Patients were then subdivided into groups based on their diagnosis. These groups were then categorised into the following age groups: 0-1 years, 1-2 years, 2-5 years and >5 years.

RESULTS

RESULT 1: PseudoRBs found in this study

Diagnosis, n=121	Number (Percentage)
Coats' disease	41 (34%)
Persistent Foetal Vasculature (PFV)	21 (17%)
Combined Hamartoma of Retina and RPE (CHR-RPE)	16 (13%)
Astrocytic Hamartoma	6 (5.0%)
Toxoplasmosis	5 (4.1%)
Familial Exudative Vitreoretinopathy (FEVR)	5 (4.1%)
Uveitis	4 (3.3%)
Retinal Detachment	3 (2.5%)
Peripheral white tufts	3 (2.5%)
Cataract	2 (1.7%)
Iris Cyst	2 (1.7%)
Coloboma	2 (1.7%)
Racemose Haemangioma	1 (0.83%)
Choroidal Haemangioma	1 (0.83%)
Osteoma	1 (0.83%)
Hypertrophic Scar	1 (0.83%)
Peters Anomaly	1 (0.83%)
Choroidal Xanthogranuloma	1 (0.83%)
HIV Mass	1 (0.83%)
Vasculitis	1 (0.83%)
Vasoproliferative Tumour	1 (0.83%)
Choroidal Neovascular Membrane	1 (0.83%)
Vitelliform Dystrophy	1 (0.83%)

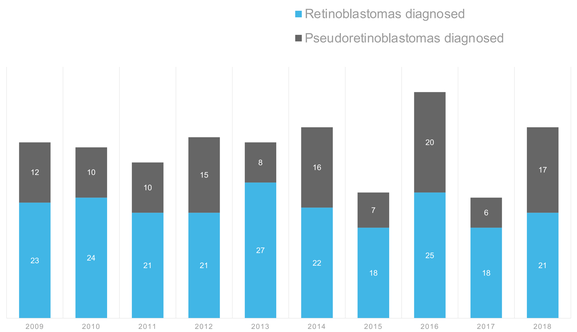
RESULT 2: PseudoRBs and their ages of presentation

0 – 1 year, N = 42	1 - 2 years, N = 21	2-5 years, N = 32	>5 years, N = 26
PFV (36%)	Coats' (52%)	Coats' (44%)	Coats' (35%)
Coats' (17%)	CHR-RPE (19%)	CHR-RPE (13%)	RAH (12%)
CHR-RPE (12%)	PFV (14%)	PFV (6.3%) RAH (6.3%) FEVR (6.3%)	FEVR (7.7%) Uveitis (7.7%) CHR-RPE (7.7%)

RESULT 3: Comparison of the results of the Shields study[2] from 2013 to the current study

Age Group	0-1 years		1-2 years		2-5 years		>5 years	
	Shields et al.	This Study	Shields et al.	This Study	Shields et al.	This Study	Shields et al.	This Study
Top 3 Diagnosis	PFV (49%) Coats (20%) Vitreous Haemorrhage (7%)	PFV (36%) Coats' (17%) CHR-RPE (12%)	Coats (58%) PFV (11%) Vitreous Haemorrhage (5%)	Coats' (52%) CHR-RPE (19%) PFV (14%)	Coats' disease (61%) Toxocariasis (8%) PFV (7%)	Coats' (44%) CHR-RPE (13%) PFV, RAH and FEVR (6.3%)	Coats' disease (57%) Toxocariasis (8%) FEVR (6%)	Coats' (35%) RAH (12%) FEVR, Uveitis, CHR-RPE (7.7%)

RESULT 4: Trends of RB vs PseudoRB referrals over 10 years



DISCUSSION

- **Coats' disease and retinoblastoma continue to be difficult to distinguish from each other prior to tertiary assessment.** The mean age at diagnosis of Coats' disease is 5 years. In our study, the average age of Coats' disease referred for retinoblastoma was significantly lower than average (3.5 years). Atypical age at presentation may have made the diagnosis more difficult.

- **ROP and congenital cataract were rarely suspected as retinoblastomas in our study, while just a few decades ago, they were they leading pseudoRBs[4].** This could be due to the creation of paediatric ophthalmology as a distinct subspeciality in the UK during the last 3 decades

- **CHR-RPE was more common than expected.** This could be due to the unfamiliarity with the condition of referring physicians. Accurate and early diagnosis of CHR-RPE is important as it is associated with neurophakomatoses like neurofibromatosis-2[5].

SUMMARY

- Out of 341 patients that were referred for the suspicion of retinoblastoma, 121 had pseudoRB (35%).
- In total, 23 different types of pseudoRBs identified
- Coats' disease is the most common pseudoRB, followed by PFV and CHR-RPE.
- PFV is the most common pseudoRB in the 1st year of life, but Coats' disease is the most common after the first year.
- Hamartomas (CHR-RPE & RAH) were more prevalent than expected. This might be due to the unfamiliarity of with this lesion among referring physicians.

REFERENCES

1. Dimaras H, Kimani K, Dimba E, Gronsdahl P, White A, Chan H, et al. Retinoblastoma. Lancet (London, England). 2012;379(9824).
2. Shields C, Schoenberg E, Kocher K, Shukla S, Kaliki S, Shields J. Lesions simulating retinoblastoma (pseudoretinoblastoma) in 604 cases: results based on age at presentation. Ophthalmology. 2013;120(2).
3. Huang S, Rutar T, Bloomer M, Crawford J. Analysis of clinical misdiagnoses in children treated with enucleation. Archives of ophthalmology (Chicago, Ill : 1960). 2010;128(8).
4. Howard G, Ellsworth R. Differential diagnosis of retinoblastoma. A statistical survey of 500 children. II. Factors relating to the diagnosis of retinoblastoma. American journal of ophthalmology. 1965;60(4)
5. Grant E.A., Trzupek K.M., Reiss J., Crow K., Messiaen L., Weleber R.G. Combined retinal hamartomas leading to the diagnosis of neurofibromatosis type 2. Ophthalmic Genet. 2008;29(3):133–138.

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