

An Eye into the Heart - Retinal vascular changes in Kawasaki Syndrome as a marker of coronary artery disease

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Introduction

Kawasaki Syndrome(KS), a multisystem vasculitis, is the most common cause of acquired childhood heart disease in developed countries. The systemic vasculitic effects of KS leave a physiological footprint on the vascular endothelium with resulting impairment in vasodilatory capacity^{1,2}. The retinal circulation offers a unique non-invasive window to study these changes to systemic vasculature caused by KS.

Objectives

We hypothesize that Kawasaki Syndrome causes longstanding changes in the retinal vasculature as a result of its attendant inflammatory effects. We aim to describe the changes in retinal arteriolar and venular diameters with KS. This knowledge may help to predict the risk of adverse coronary events in patients with a history of Kawasaki Syndrome.

Methodology

We recruited subjects above the age of six with no history of eye disease at least 6 months after acute KS. High-resolution digital retinal photographs centered on the disc and macula were taken using standardized settings. Central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE), were calculated for each retinal photograph by a masked grader according to a standardized protocol⁵.

The control group was made up of children who participated in the Singapore Cohort Study of Risk Factors for Myopia (SCORM). The controls selected were matched for known confounders of age, gender, ethnicity and Body Mass Index. In addition, our analysis adjusted for 'fellow calibre' where venular dimensions were included as an independent variable in the model for arteriolar dimensions and vice versa⁶.

Table 1. Comparison of retinal vascular caliber between cases and controls

	Cases (n=18)		Matched Controls (n=54)	
	Mean	SD	Mean	SD
Age (yr)	10.5	2.55	11.63	1.22
Body Mass Index (kg/m ²)	18.90	3.05	19.06	3.36
CRAE (um)	147.71	16.99	148.71	14.24
CRVE (um)	211.31	18.56	226.67	17.91
Time from Acute KD (yrs)	8.11	3.79		N.A
Current Coronary Complications (Y/N)	2/16		N.A	
Gender (M/F)	9/9		27/27	

Results

Eighteen patients with previous Kawasaki disease (KD) were recruited in this study. These results were compared to a matched control population of 54 from the SCORM database .

In the KS patients studied, the mean time from acute KS was 8.11 years. 2/18 subjects had unresolved coronary complications, namely persistent mild dilatation.

After controlling for age, gender, ethnicity, body mass index and fellow caliber(Table 1), KS subjects had a statistically significant wider CRAE (157.1 μm vs. 149.3 μm, p=0.046) and narrower CRVE of(209.7 μm vs.221.7 μm p= 0. 007) than the controls

Table 2. Comparison of retinal vascular caliber between cases and controls

	Cases (n=18)		Matched Controls (n=54)		P
	Mean	95 % CI	Mean	95% CI	
CRAE(μm)	157.1	147.6 to 166.7	149.3	141.5 to 157.1	0.044
CRVE (μm)	209.7	198.8 to 220.6	221.7	212.7 to 230.8	0.007

Controlling for Age, Gender , Race , BMI and Fellow Caliber

Discussion

Our study shows that KS results in long-standing changes to retinal vasculature .The dilatory effect of KS on retinal arterioles correlates well with the dilatory effects of KS on coronary arteries, suggesting that the increased retinal arteriolar caliber may be a microscopic reflection of the disease processes predisposing KS subjects to coronary aneurysms.

The vast majority of the subjects studied had normal coronary dimensions on echocardiography with only 2 having mild dilatation. This together with the long interval times since the acute illness reinforces the evidence that micro-vascular changes in KS are longstanding and systemic.

The limitations of this study were the small sample size and the wide spread of interval timeframes between acute resolution of disease and retinal analysis. However we believe the results to be noteworthy as the controls were well matched and all known confounding factors have been well controlled in the analysis.

Our study suggests that, retinal vascular changes in KS patients may be used as a surrogate marker for attendant coronary artery changes. Larger scale studies integrating retinal vascular assessment with coronary imaging, should allow us to better understand the utility of retinal photography in therapeutic planning for these patients as they grow into adulthood.

Conclusion

KS results in substantial changes to retinal vasculature leading to a significantly wider retinal arteriolar caliber and narrower retinal venular caliber. Retrospective study may correlate with severity of initial inflammation and longitudinal follow up may allow for coronary risk stratification.

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