



SDI Review Form 1.6

Journal Name:	Ophthalmology Research: An International Journal
Manuscript Number:	Ms_OR_25632
Title of the Manuscript:	Ocular ischemic syndrome associated with primary hyperparathyroidism
Type of the Article	Case study

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	This is an interesting report but in order to more firmly support the hypothesis on causation the authors should consider the following potential criteria: 1) Biologically plausible mechanism. This is weakly described and supported by the literature review provided 2) Coherence with the pharmacokinetics or biochemical effects of purported cause and effect and class effect for purported effect and cause (hypercalcemia from PTH) 3) Analogy from prior animal (experimental) or other human cases 4) Specificity of effect 5) Dose response gradient 6) Exclusion of chance alone 7) Dechallenge/rechallenge	1. The Discussion section of the revised Manuscript includes a description of the possible biological mechanism which is based on current knowledge, as well as the possible role of hypercalcemia in the formation of atherosclerotic plaques. The same has been supported by references, including the proposed criteria by the Reviewers in relation to pharmacokinetics and analogy. <i>"In clinical studies, associations between PTH and vascular stiffness or abnormal endothelial function demonstrate that PH is associated with clinical structural changes in the carotid vasculature and functional changes that reflect increased vascular stiffness. Increased carotid intima-media thickness is an early, clinical predictor of systemic atherosclerosis as well as clinical coronary and cerebrovascular events. Intima media thickness was recently found to be markedly increased in patients with PH and higher calcium levels. Carotid plaque thickness, however, was found to be positively associated with serum calcium levels within the normal range, in subclinical forms of PH. PTH increases production and reorganization of collagen by vascular smooth muscle cells in vitro. Besides the bones and the kidneys, PTH affects other organs, and PTH-receptor mRNA has been found in such different locations as the brain, adrenal gland,</i>



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		<i>bladder, ileum, liver, lung, vascular smooth muscle cells, and skeletal muscle cells . PTH stimulates the vascular smooth muscle cell by binding to the PTH/PTH related Peptide receptor and, thus, increases the intracellular cAMP-levels and reduces the influx of calcium . This is believed to explain the vasodilating properties of PTH, found in vitro as well as in vivo."</i>
<u>Minor</u> REVISION comments		
<u>Optional/General</u> comments		