Cat Scratch Disease Associated with Retinal Vein Occlusion

Avi Rubinov MD1, Eytan Z. Blumenthal MD1 and Itzchak Beiran MD1,2

1Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel
2Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

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Catscratch disease is a zoonotic infection caused by the gram-negative rod Bartonella henselae. It is typically a benign, self-limiting, acute febrile illness that is accompanied by regional lymphadenopathy. Ocular manifestations of this disease usually do not involve severe visual loss. Classically, a papule or pustule initially develops at the site of a cat scratch followed by regional lymphadenopathy with or without fever. The affected nodes may become suppurative [1]. In about 5–10% of cases CSD may present with ocular symptoms, ranging from primary oculoglandular syndrome to neuroretinitis and, rarely, vascular occlusions due to localized vasculitis [2]. Neuroretinitis manifests as optic nerve head swelling and the partial or complete formation of a macular star, usually within 2–4 weeks [2]. Systemic antibiotic treatment with doxycycline 100 mg twice a day, rifampin 300 mg twice a day, ciprofloxacin 750 mg four times a day, or azithromycin 500 mg four times a day is the treatment of choice [2]. The role of systemic corticosteroids in the treatment of CSD is controversial [3].

A 34 year old Caucasian male presented with acute painless loss of vision in his right eye 4 days earlier. Upon examination the best corrected visual acuity was counting fingers 1.5 m in the right eye and 20/20 in the left eye. He had a +2 right relative afferent pupillary defect and the intraocular pressure was 16 mmHg in the right eye and 12 mmHg in the left. Anterior segments were normal in both eyes. Dilated fundus examination showed a central vein occlusion with macular edema and blurred disk margins in the right eye [Figure 1A]. The left eye fundus was normal.

The patient reported a febrile illness of 6 days duration 4 weeks prior to his initial ocular examination and recalled being scratched by a cat several weeks earlier. Laboratory workup was normal except for elevated liver enzymes (alanine and aspartate aminotransferase, gamma-glutamyl transpeptidase, alkaline phosphatase), elevated erythrocyte sedimentation rate, C-reactive protein, complement C3, as well as positive serology for B. henselae (immunoglobulin M and G). Herpes simplex type 1, cytomegalovirus and varicella zoster virus were all IgG positive but negative for IgM, suggestive of past infection. An extended coagulation panel was normal. Fluorescein angiography of the right eye demonstrated peripapillary leakage and signs of retinal vasculitis in the inferior half of the retina [Figure 2]. Macular spectral domain optical coherence tomography of the right eye demonstrated severe macular edema [Figure 3].

Antibiotic treatment was started with doxycycline 100 mg and rifampin 300 mg twice daily for 1 month. Two intravitreal bevacizumab injections were given to the right eye 1 month apart, resulting in amelioration of the macular edema. Best corrected visual acuity at last follow-up was 20/60. Repeat blood workup showed

CSD = cat scratch disease
normalization of erythrocyte sedimentation rate and C-reactive protein. Rarely, vasculitis caused by *B. henselae* leads to a decrease in vision [1]. One reported case of retinal vein occlusion due to *B. henselae* was treated with laser photocoagulation and bevacizumab [1]. The present case supports the use of intravitreal bevacizumab injection for the treatment of macular edema caused by venous occlusion secondary to *B. henselae* neuroretinitis. In young patients with arterial or venous retinal occlusive disease, cat scratch disease should be included in the differential diagnosis.

**Correspondence**
Dr. A. Rubinov  
Dept. of Ophthalmology, Rambam Health Care Campus, Haifa 31096, Israel  
Phone: (972-4) 854-2668  
email: avi@rubinov.com

**References**

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**Capsule**

**Two signals for maximal T cell activation**

T cell activation requires increased intracellular calcium and the activity of various enzymes, such as the kinase Itk. Wang et al. report that two signals, calcium and lipids, converged on Itk for maximal activation of T cells. The same region of the Itk protein bound to the signaling lipid PI(3,4,5)P3 and to the calcium-binding protein calmodulin. PI(3,4,5)P3 and calmodulin enhanced the binding of each other to Itk. The binding of both PI(3,4,5)P3 and calmodulin was necessary so that T cells produced maximal levels of an inflammatory cytokine, interleukin-17A.

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Eitan Israeli

**Capsule**

**Putative cis-regulatory drivers in colorectal cancer**

The cis-regulatory effects responsible for cancer development have not been as extensively studied as the perturbations of the protein coding genome in tumorigenesis. To better characterize colorectal cancer (CRC) development Ongen et al. conducted an RNA-sequencing experiment of 103 matched tumor and normal colon mucosa samples from Danish CRC patients, 90 of which were germline-genotyped. By investigating allele-specific expression (ASE) the authors show that the germline genotypes remain important determinants of allelic gene expression in tumors. Using the changes in ASE in matched pairs of samples they discovered 71 genes with excess of somatic cis-regulatory effects in CRC, suggesting a cancer driver role. The authors correlated genotypes and gene expression to identify expression quantitative trait loci (eQTLs) and found 1693 and 948 eQTLs in normal samples and tumors, respectively. They estimate that 36% of the tumor eQTLs are exclusive to CRC and show that this specificity is partially driven by increased expression of specific transcription factors and changes in methylation patterns. They also show that tumor-specific eQTLs are more enriched for low CRC genome-wide association study (GWAS) P values than shared eQTLs, which suggests that some of the GWAS variants are tumor-specific regulatory variants. Importantly, tumor-specific eQTL genes also accumulate more somatic mutations when compared to the shared eQTL genes, raising the possibility that they constitute germline-derived cancer regulatory drivers. Collectively the integration of genome and the transcriptome reveals a substantial number of putative somatic and germline cis-regulatory cancer changes that may have a role in tumorigenesis.

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Eitan Israeli