

Case of Sympathetic Ophthalmia

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Case Presentation:

The patient is a 61 year old female whose left eye was lacerated from a motor vehicle accident in 1975, which was r vision. However, 3 months later she developed sympathetic ophthalmia. The left eye was enucleated. Histopathologic granulomatous inflammation. The choriocapillaris were spared. Focal areas of RPE proliferation were found, suggest was treated with oral prednisone for 2 years.

In 1987 the patient developed recurrent uveitis, which was treated with prednisone until 1989. Since April 1993, the granulomatous iritis, with no posterior uveitis. She then developed diabetes mellitus, and complained of muscle ach She was examined by a rheumatologist and a neurologist, but no conclusive diagnosis was made. Her neurologist a peripheral neuropathy. A workup at this time, including rheumatoid factor, ANA, erythrocyte sedimentation rate, ACE X-ray was negative.

The patient was referred in November 1994. On examination, the vision in the remaining right eye was 20/25. The ri of active iritis. The cornea was clear, the iris and lens were unremarkable. Trace cells were noted in the vitreous. Th of the RPE (Fig. 1). Methotrexate was started in January 1995, and prednisone was tapered.



Fig. 1

Discussion:

Sympathetic ophthalmia is a bilateral granulomatous uveitis that occurs after a penetrating injury to one eye. Although conditions, because it is a potentially blinding disease that involves both eyes. The concept of injury to one eye resu traced to the writings of Hippocrates. The earliest clear reference is that by George Bartisch, who wrote that after inj painful, "in this case the other eye is in great danger(1) ."William Mackenzie first gave the complete description of th to describe the histopathology of this entity.

Regarding the incidence of the disease, the literature is filled with dubious data. Often the diagnosis is presumptive Sympathetic ophthalmia occurs more frequently now following nonsurgical trauma. Liddy and Stuart reported an inc reported an incidence of 0.5% of nonsurgical injuries (4). Marak estimated the incidence to be less than 0.01% follo ophthalmia is more common in men, as a result of higher incidence of ocular trauma. An association between HLA-, suggested (6).

There are several ocular entities associated with sympathetic ophthalmia. Phacoanaphylaxis is reported to occur in ophthalmia (7,8). It is thought that the patients with both entities occurring in the same eye have a predisposition for melanoma has also been associated with sympathetic ophthalmia. In a study of 400 cases of sympathetic ophthalm

Pathology, 7 were found to have malignant melanoma (9). In addition, sympathetic ophthalmia was reported to occur after cyclocryotherapy (11) and Nd:Yag cyclotherapy. Nd:YAG cyclotherapy in particular, is associated with a much higher incidence compared with other ocular procedures. A study from University of Illinois showed an incidence of 5.8% after nonconformal cyclotherapy performed at that institution (12).

The onset of sympathetic ophthalmia is usually between 2 weeks and 3 months following an ocular injury, although it can occur and as late as 50 years. About 80% of cases present within the first 3 months. Classically the inflammation is granulomatous and involves the corneal endothelium. The anterior chamber reaction can be relatively mild, and the inflammation can be non-granulomatous; in this case the term "sympathetic irritation" is used. There is usually a moderate to severe vitritis. Dalen-Fuchs nodules can be seen at the periphery. (Fig. 2) Papillitis can be prominent, and may be accompanied by peri-papillary choroidal lesions. Retinal detachment is a complication of the disease. The disease is classically thought of as a choroidal one. Subretinal neovascularization may occur.

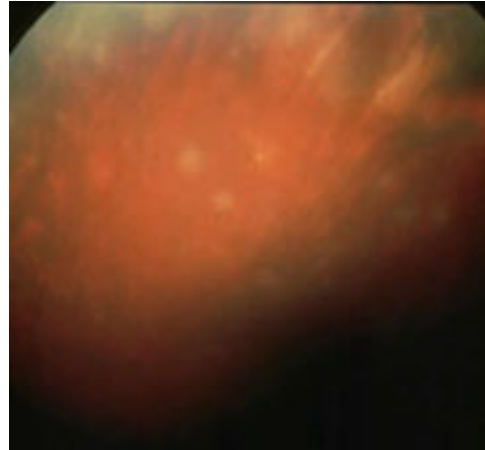


Fig. 2 Dalen-Fuchs Nodules

Extraocular findings such as pleocytosis in the cerebrospinal fluid, hearing disturbances, alopecia, poliosis, and vitiligo can occur in sympathetic ophthalmia, although these findings are rare in sympathetic ophthalmia when compared with VKH.

During the acute phase of the disease, fluorescein angiogram shows multiple subretinal hyperfluorescent spots, which correspond to the observed Dalen-Fuchs nodules. Less commonly, hypofluorescent spots are seen with late staining, similar to angiographic findings in posterior multifocal placoid pigment epitheliopathy. During the late cicatricial phase of the disease, the areas corresponding to the nodules become atrophic, and appear on the angiogram as window defects. (Fig. 3)

The sequelae of the inflammation include secondary glaucoma and cataract, retinal and optic nerve atrophy, retinal and choroidal atrophy. (Fig 4)

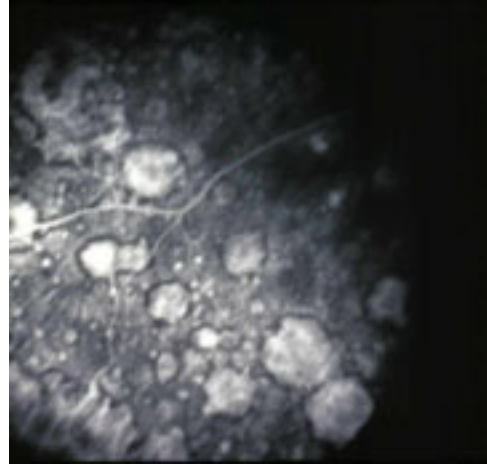


Fig. 3 FA: Dalen Fuchs Nodules

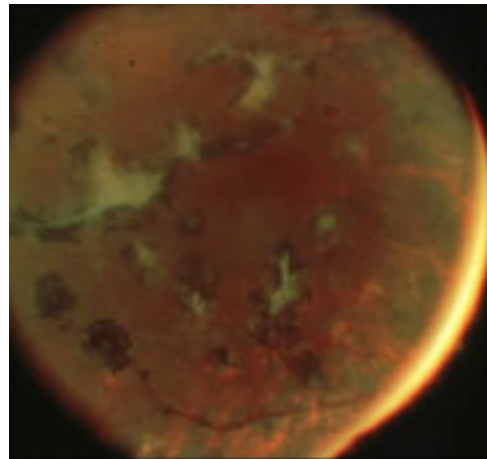


Fig.4 Subretinal fibrosis

Histopathologically, a diffuse granulomatous, non-necrotizing inflammation is seen throughout the uveal tract. The infiltrates consist of a mixture of lymphocytes, eosinophils, and sometimes plasma cells. (Fig. 5) The infiltrates can also have large numbers of eosinophils, and sometimes plasma cells. They are thought by Fuchs to represent migrated and transformed retinal pigment epithelial cells. It has been demonstrated, by using monoclonal antibodies, that Dalen-Fuchs nodules are composed of Ia⁺, OKM1⁺ cells, which are depigmented RPE cells (13,14). (Fig. 6)

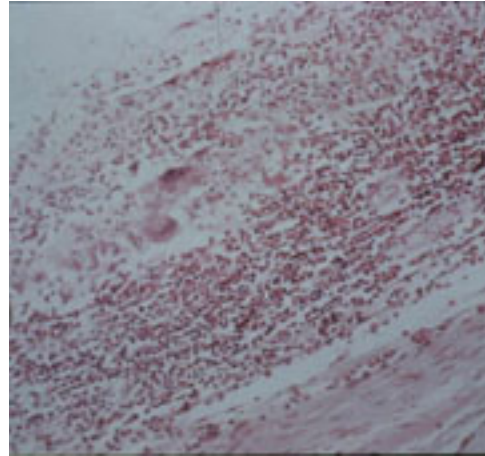


Fig. 5 Choroidal thickening

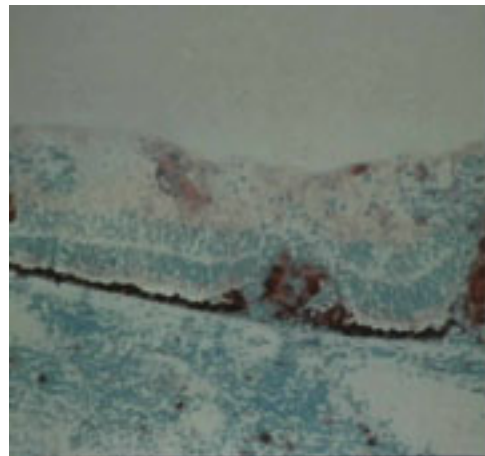


Fig.6 Dalen Fuchs nodules

Jakobiec and colleagues also noted that the predominant infiltrating T cells were the CD8 subset (13). Chan and colleagues found several months after the initial trauma and found the predominant T cells were the CD4 subset. However, when late infiltrating T cells changed to the CD8 subset (14). Therefore it appears that as the disease progresses, there is a change in the infiltrating T cell subset. Although sympathetic ophthalmia is thought to be a T cell mediated disease, there was a study that reported 4 of 29 eyes had a predominant B cell infiltrate (15).

Histologically, compared to VKH, classic sympathetic ophthalmia is characterized by sparing of the choriocapillaris and this may be the result of the eyes being enucleated early in the course of sympathetic ophthalmia; in contrast, eyes with VKH show a more extensive course of inflammation.

The concept that an autoimmune reaction against retinal antigens, triggered by exposure of intraocular antigens, as has long been entertained. Lymphocytes from patients with sympathetic ophthalmia were demonstrated to respond to retinal antigens. Although no circulating antiretinal S-antigen antibodies were found, the serum from patients with sympathetic ophthalmia shows a positive reaction to the outer segments of the photoreceptors and the Muller cells, when placed over normal human retinal tissue (16). These antigens, detectable in normal human retina, are found on the retinal Muller cells of eyes with sympathetic ophthalmia (17). This evidence that retinal Muller cells may have an immunoreactive role.

The closest animal model for sympathetic ophthalmia is the uveitis induced by immunization with the ocular antigens in mice. The induced uveitis has many features of sympathetic ophthalmia, including Dalen-Fuchs nodules, and like sympathetic ophthalmia is a T cell mediated disease. However, although the disease induced in animals can involve the choroid, it is essentially retinal in origin. Sympathetic ophthalmia primarily involves the choroid.

A hypothesis of the pathogenesis of the disease is that the perforating wound leads to the drainage of ocular antigens occur under normal circumstances. The injury may also allow adjuvants such as bacterial endotoxin to enter the eye inflammatory response to the degree to bypass certain suppressor mechanisms.

Kuppner et al studied samples from iris, ciliary body, choroid and retina from normal eyes and from eyes with acute and found the expressions of VLA-4, VLA-5, VCAM-1, ICAM-1 and CD44 were significantly increased in acute sympathetic normal eyes; VLA-6 was moderately increased in both acute and fibrotic cases of sympathetic ophthalmia (18). Further molecules in the pathogenesis of the disease may lead to immunotherapies with adhesion molecules as the specific. Enucleation of the injured eye before the onset of inflammation in the sympathizing eye is the only way to prevent sympathetic ophthalmia. It is indicated that enucleation within 2 weeks of the onset of the inflammation may lead to a more benign course and better vision (19,20). However, when the exciting eye still has useful vision, early enucleation can not be recommended, because it is associated with more superior vision.

Medical treatment should begin with corticosteroids. Prednisone 1-1.5 mg /kg is given for 3 months, followed by a slow taper on 15-20 mg of prednisone for up to a year. In a study of patients treated with steroids, 65% of eyes were 20/60 or better (21).

Other immunosuppressive drugs used in the treatment of this disease include methotrexate, cyclosporine, chlorambucil. Nussenblatt and colleagues reported good results in 5 patients treated with cyclosporine (22). Tessler and colleagues reported good results in 5 patients treated with short-term high dose chlorambucil (23). Ishioka and colleagues treated one patient with FK506. Finally of interest, sympathetic response in other organs such as the testis, has been observed. The disease occurs in the testis (25). It has been shown that the ischemic testis releases a factor into the blood stream that is cytotoxic to normal testis. This factor can be prevented by the administration of steroids. It has also been suggested that auto-antigens release an immunologic response which involves the contralateral testis, accounting for the pathologic changes.

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Review Questions for Sympathetic Ophthalmia

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1. Which of the following statements is false:
 - a. the incidence of sympathetic ophthalmia is higher following ocular trauma than ocular surgery.
 - b. the incidence of sympathetic ophthalmia is higher in men.
 - c. sympathetic ophthalmia develops only after penetrating ocular injury or surgery.
 - d. HLA-A11 is associated with sympathetic ophthalmia.

2. All of the following are associated with sympathetic ophthalmia except:
 - a. phacoanaphylaxis
 - b. malignant uveal melanoma
 - c. intraocular lymphoma
 - d. cyclocryotherapy

3. Which of the following is false regarding sympathetic ophthalmia:
 - a. Mutton fat KP's can be present.
 - b. If the inflammatory response is nongranulomatous, the diagnosis of sympathetic ophthalmia should be doubted.
 - c. Extraocular findings such as hearing disturbances, hair and skin changes can occur.
 - d. Retinal involvement can be found, although classically sympathetic ophthalmia is a choroidal disease.

4. Which of the following statements regarding Dalen-Fuchs nodules is false:
 - a. They are typical, but not pathognomonic of sympathetic ophthalmia.
 - b. On fluorescein angiogram, they may block early and stain late.
 - c. On fluorescein angiogram, they may appear as window defects.
 - d. They are shown to be composed of depigmented RPE cells and lymphocytes.

5. All of the following statements are correct except:

- a. Sympathetic ophthalmia may represent an autoimmune inflammatory response.
- b. Circulating antiretinal S-antigen antibodies are present in patients with sympathetic ophthalmia.
- c. Lymphocytes from patients with sympathetic ophthalmia were shown to respond to several autoantigens.
- d. The expression of certain adhesion molecules is significantly increased in eyes with sympathetic ophthalmia.

6. (True / False) Once sympathetic ophthalmia develops, enucleation of the injured eye does not alter the course of the disease.

7. (True / False) Medical treatment of sympathetic ophthalmia with corticosteroids is often effective, with more than half eyes retaining useful vision.

ANSWERS:

- 1. c (references 10, 11, 12)
- 2. c (references 7, 8, 9, 11)
- 3. b (reference 5)
- 4. d (references 13, 14)
- 5. b (references 16, 18)
- 6. False (references 19, 20)
- 7. True (references 21)