

Guest editorial

SHAPU: Forty years on Mystery Persists

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In 1975, our team encountered several cases of severe inflammatory eye disease presenting as a white pupil in a red eye with rapid loss of vision. The eyes became soft within a few days with shallow anterior chamber which we called “Malignant Hypotension” in view of the latter’s sinister significance. Unilaterally, little or no pain, predominantly affecting children and difficulty in dilating the pupil and keeping it dilated were some of the other important features. Posterior segment was not visible due to massive exudation in vitreous. Microbiological investigations of aqueous humor did not retrieve any bacterial or fungal organisms. All eyes became pthisical in few weeks despite treatment with topical and subconjunctival antibiotics and steroids. Similar cases appeared again after two years in 1977 with identical presentation and outcome. Both outbreaks began during September and lasted until about January- the next year.

Dr. OK Malla presented at the National seminar for prevention of Blindness held in Pokhara in 1978, few cases of non- infective severe ocular inflammation that he had seen in the same place, the previous year which he called Seasonal Endophthalmitis (SE). These cases shared with cases in Kathmandu with similar clinical features and absence of bacterial organisms on culture. Some of his cases gave history of coming in contact with white moths (Malla, 1978).

On the evening of August 31, 1979, a thought came to my (The main author) mind that tomorrow being September the first, could some cases come this season too. As I woke up next morning I heard the sound of my doorbell ring. At the door there was a gentleman, with his three years old daughter with eye complaints. The child’s right eye had features identical to cases we had seen during previous epidemics. This convinced us of the seasonality of the disease, non –infective nature having been reported in both Kathmandu and Pokhara cases and the devastatingly rapid progress of the disease led our group (Upadhyay, Rai, Ogg, Shrestha) to name it Seasonal Hyperacute Panuveitis (SHAPU).

During 1979 to 1990 updated reports were periodically presented at several international conferences by our group 1982, (ISGO: International Society of Geographic Ophthalmology); 1984 (IUSG: International Uveitis Study Group);

1985 (APAO: Asia Pacific Academy of Ophthalmology); and published in scientific journals (Upadhyay MP, Rai, NC et al. 1979; Upadhyay MP 1983, 1984; Rai NC, Upadhyay MP et al, 1986) with a view to raise awareness about this most rapidly



destructive intraocular inflammation among ophthalmic community and pediatric fraternity. After several years of work, details of clinical features as gathered from examination of hundreds of cases, serological and microbiological tests carried out and histological features of an enucleated eye on light and electron microscopy was reported in a peer reviewed journal for the first time (Upadhyay MP, Rai NC et al 1984; serological tests and histology courtesy Drs Karl Kupfer and Robert Nussenblatt of National Eye Institute).

Prompted by reported observations of contact with a white moth, we exposed guinea pigs and rabbits to live Megalopygidae, Arctiidae, and Noctuidae moths in a closed room in four sets of experimental designs described elsewhere (Upadhyay MP, Rai NC et al, 1984). We concluded that, if moth was indeed either an inducing or transmitting agent, possibly the moths used by us were not the type to produce the disease or that the rabbits and guinea pigs were not susceptible hosts.

Uncertain of the cause of the disease, we treated the eyes with sub-conjunctival antibiotics and steroids in initial years and in later years with intra-vitreous antibiotic and antiviral (acyclovir) without much success. First vitrectomy was performed in a SHAPU case by Dr Shashank Koirala on the day of opening of First SAARC ophthalmology congress held in Kathmandu on 13 September 1991—a historical coincidence. Most delegates who saw the cases admitted to not having seen anything similar earlier. This child made good recovery with vitreous clearing sufficiently to allow a view of the retina in a few days, which revealed a clinical appearance consistent with acute retinal necrosis (Personal communication). The child subsequently developed retinal detachment and was lost for follow up. This led us to think in line of a viral etiology.

With publication of our detailed report of clinical features and other investigations, SHAPU was included in a uveitis monograph “Uveitis: Fundamental and clinical practice” as a new uveitis entity (Nussenblatt et al 1989) and subsequently updated.

Although cases continued to occur in the following years, very few reports appeared in the literature between 1990 and 2004. Dr Anu Mananadhar, with several publications cited in the reference, has been a constant crusader against the disease (several publications cited in the references) has been constantly reporting this condition. Reports of favorable visual outcomes of SHAPU-affected eyes after vitrectomy was reported (Bhanju RN et al, 2003) and outcome of medical treatment of SHAPU in 2010 (Shrestha E, 2010). Manadhar’s work has revealed additional clinical features

The Mystery

1. Is SHAPU an infective condition due either to bacteria, viruses, fungi or protozoa? Bacteria, such as *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Acinetobacter* have been reported at different times, so have been viruses albeit in small number of cases, while in large number of cases organisms were not recoverable at all. If the cause is infection, available evidence remains controversial and uncertain. Further investigations with newer molecular techniques to confirm or rule out microbes as a cause would be the direction for future investigation. Alternatively, is it an immune reaction to some unknown uveitogenic antigens?

2. Role of moth: There is increasing evidence of possible role of moths in SHAPU. Earlier circumstantial evidence of exposure/contact with moths has been subsequently reinforced by clinical observation of intra-stromal follicles in the cornea in some cases. It has now moved from the realm of possibility to that of probability. How does moth cause this disease? As a vector of microbial agents? injecting toxins or as uveitogenic agents? The debate about which moth, if it is a moth, Gazelina or Tussock or some others may be of lesser importance from public health perspectives of prevention of disease at this time as long as we can educate people to be away from the suspects, albeit without causing excessive alarm.
3. Why should it preferentially affect children? Is it that these children share a common genotype/phenotype which make them vulnerable?
4. Why is it seen only in Nepal when the moths are found all over the world (Beccaloni, G., M. Scoble, et.al. (eds.). 2003)
5. While we pursue efforts to establish the cause, it will be necessary to have a consensus on a common diagnostic protocol harnessing the opportunities offered by newer molecular technologies.
6. Can uveal biopsy provide some answer to resolve the diagnostic dilemma? How safe it is in acutely inflamed eyes? If obtainable, biopsy subjected to molecular diagnostic techniques may provide clues to possible infective nature or immune process
7. Since it will take a while to establish the cause, what should be the optimal treatment modality in the interim? When is the ideal time for a vitrectomy, immediately or later? Delaying vitrectomy may result in loss of valuable time and likelihood of diagnosis, or a too early an intervention may jeopardize the chances of successful outcome with non-surgical interventions. Systemic as well as ocular injections of steroids have been used, high antibiotics are being given, in some with adverse effects.
8. These are issues, which we ophthalmologists (and microbiologists, entomologists, epidemiologists,) in Nepal need to solve ourselves as the disease is confined to Nepal. Of course, advice of colleagues from abroad would also be of great help.
9. The reason we need to act in cohesion is the continued threat that SHAPU presents to the sight and eyes of our children. The other reason for this is because, SHAPU remains the commonest reported cause of Panuveitis (15.2%) among all ages and for (27.7%) of all forms of uveitis in children among 1221 cases in the largest series of uveits from Nepal. (Manandhar A, 2016).

Conclusion

It is still a very confusing state of affairs as to the cause, as bacteria have been reported, viruses detected, immune reaction hypothesized, moths are suspected.

Which of these it is? Is it all of these at different times with changing patterns conditioned by climate change? We are living in an ever changing and labile ecosystem. We therefore need to keep all options open and not be bogged down by dogma. Some of the measures outlined may help us to get to the truth or provide some clues to take us close to the truth. A collaborative work between ophthalmologists, microbiologists,

virologists, entomologists, epidemiologists, immunologists is desperately needed and recommended in future to solve the mystery.

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Source of support: nil. Conflict of interest: none