Editorial

Perspective — Vascular Tumors of the Retina — Mahesh Shanmugam

Ocular surface, anterior segment and adnexal disorders in Acquired Immunodeficiency syndrome - Analysis of 45 patients — Iyer Geetha Krishnan, Kannan M. Narayana, Jyotirmay Biswas, Amala E George and Rajesh Fogla

Familial band-shaped spheroidal degeneration of the cornea, report of two cases — Geetha K Iyer, Rajesh Fogla & Jyotirmay Biswas

Indocyanine green angiogram in tubercular choroiditis - Case Report — Rupesh V. Agrawal, Dipankar Das, Jyotirmay Biswas, K. Jagannath and H. N. Madhavan

Transpupillary Thermotherapy for Choroidal Melanoma in Asian Indian Population — Mahesh. P. Shanmugam and Rajiv Raman

Degraded stereopsis as a presenting sign of Convergence Insufficiency — S. Jayarajini and Shrikant R Bharadwaj

Last Page — Databases and free softwares on the Net for DNA analyses — Vedam Lakshmi Ramprasad, Pradeep George Paul, Sarangapani Sripriya and Govindasamy Kumaramanickavel
Study of tumors is a fascinating subject. Why do tumors occur? Why some are locally destructive while others are life threatening? What is that little unknown chemical sequence which is lost, leading to the occurrence of multisystem tumors in phakomatosis? These questions may be answered in the future with the mapping of the human genome and further advances in genetics. However, for now we have to be satisfied with rather inefficient methods of cure than prevention in the management of tumors. Vascular tumors of the retina vary from the rather innocuous curiosity, the cavernous hemangioma of the retina to the potentially blinding capillary hemangioma. Of course, the associated systemic features may be life threatening. The “Perspective” of this issue deals with vascular tumors of the retina. In addition, a short case series of Indian patients with uveal melanoma treated with transpupillary thermotherapy is presented as an article.

This issue of Insight also contains articles about the use of ICG in posterior uveitis, short case report on familial climatic droplet keratopathy, anterior segment disease in AIDS patients, databases on the web for DNA analysis and a case report on convergence insufficiency affecting the surgical capabilities of an ophthalmic surgeon.

Dr. Mahesh P Shanmugam
Editor
Perspective:
Vascular Tumors of the Retina

Mahesh Shanmugam

Vascular tumors of the retina include the following:

a. Capillary Hemangioma of the retina
b. Cavernous Hemangioma of the retina
c. Racemose Hemangioma
d. Vasoproliferative tumor of the retina

Capillary Hemangioma of the retina

Capillary hemangioma of the retina may occur as a phakomatosis with central nervous system and multiorgan tumors when it is called von Hippel Lindau syndrome. It may occur without systemic disease as well. It is genetically transmitted as an autosomal dominant mode with incomplete penetrance and variable expressivity. Von Hippel Lindau syndrome is linked to a defect in short arm of chromosome 3 (3p 25-26).

Clinical findings

The ocular lesions are usually diagnosed between 10 – 30 years of age. The early angioma appears as a yellow spot between a feeding arteriole and a draining venule. As the angioma increases in size, the supplying vessels increase in diameter and become tortuous. Visual acuity decreases due to exudation or secondary retinal detachment involving the macula. An appearance of dilated pair of vessels in the posterior pole with macular exudates should prompt one to examine the periphery for a capillary angioma. Multiple or bilateral angiomomas indicate the presence of von Hippel Lindau tumor and screening for central nervous system or systemic disease should be done. The exudation in the macular region may be due to a steal phenomenon or a subretinal migration.

Some authors believe that two forms of disease exist – the exudative form and the vitreoretinal form. In the vitreoretinal form, epimacular membranes form which cause macular traction detachment and decreased vision. Traction on the angiomas can lead to “free floating” angiomas in the vitreous, vitreous hemorrhage and a combined traction rheigmatogenous retinal detachment can also occur.

Angioma of the optic nerve head may occur. This differs from the retinal angioma in that no feeder arteriole or a draining venule is seen. The orange red lesion is ill defined, involves an eccentric part of the optic disc with exudation involving the peripapillary region and simulates papilledema.

Without treatment, most eyes progress to total retinal detachment, neovascular glaucoma and a painful blind eye.

Differential Diagnosis

The retinal angioma may be mistaken for Coat’s disease (no paired dilated vessels in coat’s disease), racemose angioma (no tumor between the arteriole and venule in racemose angioma), intraretinal macroaneurysm (occurs along a arteriole without a draining venule), retinal cavernous hemangioma (no feeder vessels: multiple sac like aneurysmal dilatations), familial exudative vitreoretinopathy, and nematode endophthalmitis.

The disc angioma may simulate papilledema, optic neuritis, peripapillary choroidal neovascular membrane and optic disc granuloma.

Pathology

The lesions are made of a proliferation of capillaries that usually replace full
thickness retina with benign proliferation of endothelial cells and pericytes.

**Diagnosis**

The diagnosis can be made most often on indirect ophthalmoscopy with the classic picture of an orange tumor with a feeding arteriole, draining venule associated with macular exudates. A fundus fluorescein angiogram may however be necessary to delineate early lesions that are not visible on clinical examination. These lesions fill early phases of the angiogram and leak profusely later. The paired vessels are well delineated as well.

**Treatment**

Early treatment of retinal capillary angiomas leads to better visual results. Early stages of the angiomas without retinal detachment are treated with laser photocoagulation. It is preferable to use green, yellow or blue green wavelength to treat these lesions, as red or infrared lasers may not be absorbed well. Lesions < 2 mm are treated with direct photocoagulation. For lesions 3-5 mm, it is preferable to try occlusion of the feeder vessels – the arteriole in the first session and the venule later. The angioma as such can be treated in subsequent sessions. Hemorrhage from the tumor and increase in secondary retinal detachment may occur as complications.

For tumors larger than 5 mm, it is preferable to use triple freeze thaw cryotherapy. A conjunctival incision is usually necessary to treat posteriorly placed tumors, while anterior tumors can be treated without the same. Postoperative increase in the exudative detachment is commonly seen, which settles with time. Hemorrhage from the tumor may also occur.

If the tumors are associated with a bullous retinal detachment, drainage of the fluid, cryotherapy and scleral buckling may be necessary. Advanced vitreoretinal form of the disease may need vitrectomy to relieve tractional or rhegmatogenous retinal detachment. Some authors have tried internal (vitreoretinal route) or external (transscleral route) resection of single large tumors. Eyes with advanced disease that needs surgical intervention usually have a poor visual prognosis.

Transpupillary thermotherapy, plaque Brachytherapy, proton beam irradiation, external beam radiation therapy have been employed in the management of retinal and disc angiomas.

**Systemic features**

In contrast to most phakomatosis, von Hippel Lindau syndrome does not have major cutaneous features. Angiomas, nevi, or café au lair spots may occasionally be seen.

Cerebellar hemangioblastomas is the classic central nervous system lesion of von Hippel Lindau syndrome. It usually causes cerebellar symptoms in the 4th decade of life and can be imaged on a CT scan. Treatment is in the form of surgical resection if possible.

Unilateral or bilateral phaeochromocytomas, cysts of the kidney, pancreas, epididymis and renal cell carcinomas may occur in these patients. It is thus important to follow up patients of von Hippel Lindau syndrome with periodic neurological and systemic evaluation.

**Cavernous Hemangioma of the retina**

Cavernous hemangioma of the retina is also recognized as a phakomatosis with involvement of the retina, skin and the central nervous system. It appears to have an autosomal dominant mode of inheritance.

**Ocular features**

The ocular involvement is usually asymptomatic if situated in the periphery or may cause loss of vision if involving the macula. One patient with a superonasal cavernous angioma has been noted to have associated cone dysfunction. The lesion appears as a cluster of dark red saccules with associated fibroglial proliferation. No feeder arteriole or draining venule is usually seen
though some authors have noted twin vessels to be associated with this tumor. The lesion is non-progressive or may enlarge minimally over time. The tumor may rarely cause vitreous hemorrhage but do not cause exudation. The differential diagnosis of this lesion includes those listed for capillary hemangioma of the retina.

The lesion consists of endothelial lined venous aneurysms interconnected by narrow channels. Associated cystic degeneration of the retina may occur.

The diagnosis is evident on fundus examination but the fundus fluorescein angiogram is quite characteristic. These lesions have a slow blood flow which leads to the separation of the plasma from the blood cells, which settle down within the saccule. Fluorescein enters the saccule slowly and fills the supernatant plasma, enhancing the fluid level, creating a "fluorescein cap".

No treatment is required for this lesion. If vitreous hemorrhage occurs, cryotherapy, photocoagulation, low energy plaque may be used to treat these tumors.

Similar lesions involving the central nervous system may lead to seizures and other neurological symptoms. Hepatic cavernous angiomas may also occur. Cutaneous angiomas may involve the back or the neck.

**Racemose Hemangioma**

Racemose hemangioma is more of a vascular malformation than a tumor and if associated with systemic disease, is called the Wyburn Mason syndrome. No definite hereditary pattern has been noted.

Arteriovenous communications in Wyburn Mason syndrome have been classified in to 3 types. In the first type, an abnormal capillary plexus is interposed between the arteriole and the venule. These lesions do not cause symptoms and are not usually associated with cerebral involvement. In type 2 no capillary bed is found and direct arteriovenous communication exists and the patients experience few visual symptoms. Associated cerebral vascular malformation may be found. Group 3 patients have more complex and extensive arteriovenous malformation with visual loss and increased risk of cerebral disease. One or more dilated arterioles emanate from the disc, travel for a variable distance in the retina, form arteriovenous communication and return to the disc. No associated exudation or retinal detachment is found.

The clinical appearance is characteristic and a fluorescein angiogram may show rapid filling of the arteriovenous communication without dye leakage.

Most lesions are stationary and do not need treatment. However, the visual prognosis is poor. Spontaneous intracranial hemorrhages may lead to neurologic symptoms. Bones of the skull, maxilla, and mandible may be involved, causing massive bleeding during dental extraction. Orbital vascular malformations may cause proptosis.

**Vasoproliferative tumor of the retina**

These solitary tumors commonly involve the inferotemporal of inferior quadrants of the retina. They may occur without any antecedent cause, but are may associated with prior uveitis, retinitis pigmentosa, Coat’s disease and familial exudative vitreoretinopathy and toxoplasma scars. They appear as solitary mass lesions with minimally dilated feeder vessels, associated with intra retinal and subretinal exudation and hemorrhage, secondary retinal detachment, premacular fibrosis, tractional retinal detachment, RPE hyperplasia, macular edema and vitreous hemorrhage. Some patients may have multiple or diffuse tumors. The pathogenesis of these lesions is unclear.

Fluorescein angiography shows early filling and late leakage and dilated feeder vessels. If progressive exudation causes loss of vision, cryotherapy, photocoagulation, plaque brachytherapy may be necessary. Epiretinal proliferation may need vitreous surgery.
Reference


Ocular surface, anterior segment and adnexal disorders in Acquired Immunodeficiency syndrome - Analysis of 45 patients

Iyer Geetha Krishnan, Kannan M. Narayana, Jyotirmay Biswas, Amala E George and Rajesh Fogla

Introduction:
AIDS is a potentially lethal, multisystem disorder caused by a retrovirus, the human immunodeficiency virus (HIV). Ocular lesions in AIDS are varied and affect almost all structures of the eye. Patients can have ophthalmic complications during the early phase of AIDS and ophthalmic manifestation of the disease can be the initial manifestation of the underlying systemic HIV infection. An ophthalmologist thereby can be the first clinician to diagnose or suspect HIV infection and its associated opportunistic infections.

When the nature and consequence of infection with HIV was first recognised it might have been predicted that the ocular surface would be a likely sight of opportunistic infection. The fact that it is not often the case is of considerable interest. Less attention has been directed towards external disease and anterior segment disorders, yet they too may cause severe morbidity and may provide diagnostic clues in persons at risk for AIDS. Since the original description of ocular involvement in AIDS by Holland and coworkers in 1982,1 a number of clinic based surveys have been reported from different parts of the world.2-5

In India the percentage of AIDS patients is on rise and so are the ophthalmic manifestations of these patients. Since the first description of first two cases by Biswas et al of ocular lesions in AIDS,6 there have been several reports of ocular lesions in AIDS from different parts of India. According to the UNAIDS (United Nations AIDS Control Program) current statistics till June 2000, out of a population of 997 million with a sexually active population of 509 million (15-49yrs) the estimated number of people living with AIDS is 3.7million. Ocular lesions can occur in as high as 70% of the patients with AIDS.1-5

Ocular lesions mainly involve the posterior segment that is the retina and choroid, however, the anterior segment, ocular adnexa and the ocular surface can also be affected and can be one of the initial mode of presentation. We evaluated the ocular lesions in HIV positive patients examined at and referred to our institute our institute and analysed the anterior segment manifestations in these patients.

Materials and Methods:
All HIV infected patients who presented or were referred to our hospital between June 1995 to June 2001 were evaluated. A detailed history with complete ophthalmic examination, which included visual acuity, external eye examination, ocular motility, pupillary reflexes, anterior segment examination by slit lamp biomicroscopy and dilated fundus examination with scleral depression was done with indirect ophthalmoscopy.

Systemic evaluation of these patients was done in an AIDS care and research centre in the city. HIV seropositivity was established by Enzyme Linked Immuno Sorbent Assay (ELISA) for HIV1 and HIV 2 and confirmed by western blot method. External slit lamp and fundus photograph with the abnormal findings was documented. Relevant laboratory and
radiological examination were carried out in all patients and the information was recorded in a precoded proforma. CD4 and CD8 lymphocyte tests were done when indicated.

**Results:**

Out of the 370 HIV positive patients, examined at our institute between June 1995 to June 2001, 150 (40.54%) patients had ophthalmic manifestations. CMV retinitis and cotton wool spots were the most frequently encountered lesions in these patients. Besides that other lesions in the posterior segment were HIV retinopathy, focal chorioretinitis, endophthalmitis, optic atrophy, frosted branch angiitis and vitreous haemorrhage. Thirty percent (45) of these patients were noted to have anterior segment manifestations. These were in the form of blepharitis and meibomitis (13.33%), herpes zoster ophthalmicus (6.66%) (Fig.1), molluscum contagiosum (4.44%) (Fig.2), conjunctival microvasculopathy (2.22%), conjunctival squamous cell carcinoma (2.22%) (Fig.3), nodular scleritis (2.22%), keratoconjunctivitis sicca with Stevens Johnson syndrome (2.22%), corneal opacity (2.22%), healed viral keratitis (2.22%), corneal abscess (2.22%), anterior uveitis (57.78%) and secondary cataract (2.22%).

Out of the five patients with blepharitis three were treated with the regular line of treatment comprising of lid hygiene and antibiotic ointment on the lid margin. One patient presented with an ulcerative lesion over the medial one third of the eyelid which revealed staphylococcus aureus on culture of lid scraping material and was given a course of oral doxycycline 100 mg daily for two weeks with topical eye ointment besides lid hygiene. Scarring at the lid margin occurred after six weeks followed four months later by cytomegalovirus retinitis in the same eye, which regressed with intravenous ganciclovir. However the patient died of multiple systemic infections after a year. The fifth patient revealed extensive blepharitis with multiple pus points on the upper eyelids in both eyes and was treated with the same therapy as mentioned above. One patient had severe meibomitis and was advised regarding lid hygiene besides regular follow up.

Both the patients with molluscum contagiosum had extensive lesions on the skin over the eyelids and over the periorbital skin around and were referred to a dermatologist for further evaluation and management.

Three patients with herpes zoster ophthalmicus had skin lesions at different stages and two of the patients had associated anterior uveitis as well. The other patient had acute retinal necrosis as well and had undergone cataract surgery in the same eye one year back. Two of the patients were treated with oral acyclovir and the patient with acute retinal necrosis was treated with intravenous acyclovir.
One patient had a corneal abscess involving the whole of the cornea with evidence of early panophthalmitis and therefore evisceration was done on an emergency basis in this patient. Subsequent laboratory investigation revealed it to be of fungal origin and the organism was detected to be penicillium.

A conjunctival papillomatous growth with surface keratinization with prominent feeder vessels was noted on the lateral bulbar conjunctiva in one patient and was clinically suspected to be having squamous cell carcinoma of the conjunctiva which was histopathologically proven on excisional biopsy with frozen section.
One patient, a 30 year old male presented with secondary cataract following anterior uveitis.

Though twenty six patients had anterior uveitis, it was most commonly secondary to cytomegalovirus retinitis, or due to herpes zoster ophthalmicus and idiopathic in only two cases.

Discussion:

As 70% of AIDS patients eventually develop ocular complications, the role of the ophthalmologist in the management of a HIV positive patient is becoming increasingly important. The first ophthalmic report about patients with ocular diseases attributed to AIDS in India was published in 1995.

In our study, the majority of patients were men, in the 20-40 years age group. This is also reflected in the national statistics. Heterosexual exposure to commercial sex workers was the most common risk factor for HIV infection.

Ocular manifestations of HIV infection in any geographic area depends on a number of factors including the availability of health care facilities and the prevalence of the disease patterns. The most common ophthalmic opportunistic infection in our study was CMV retinitis.

Among the anterior segment manifestations, the most common one in our study was lid infections(without posterior segment manifestations). Five patients in our study had blepharitis. In countries with warm climates, the prevalence of Staphylococcus aureus is as high as 95% in lid cultures, and subclinical and mild infections are quite common. In our patients due to immunodeficiency the infection was more severe and led to lid ulceration and extensive blepharitis. Such unusual lid infections should arouse the suspicion of immunocompromised state of the patient. These lesions also pose a risk of transmission of HIV during the ophthalmoscopic examination of these patients.

Molluscum contagiosum affects 10-20% of symptomatic HIV infected individuals. Extensive molluscum contagiosum in the eyelid has been reported in patients with AIDS. There has been one case report of a patient with epibulbar molluscum contagiosum.

Herpes zoster ophthalmicus (HZO) is recognised as a marker for HIV infection particularly in sub-Saharan Africa, where 92% of patients with HZO were found to be HIV positive. In our study there were four patients with HZO. Of which only one patient presented as healed keratitis with decreased corneal sensation and healed anterior uveitis, unlike other reports which state a higher incidence of corneal involvement in HIV infected patients (89% versus 65%). A 17% incidence of acute retinal necrosis following HZO in patients who were HIV positive has been reported. One out of the four patients developed subsequent acute retinal necrosis.

Corneal epitheliopathy in the form of phospholipidosis has been described in two patients in which ganciclovir and acyclovir given systemically were implicated. Our study included a patient with a focus of epithelial dysplasia with pigmentation without any evident cause.

Although rare, the HIV positive patient appears to be at a higher risk for anterior segment fungal infection. Keratitis due to Candida albicans infection has been reported in AIDS patient without a history of trauma or use of topical corticosteroids. Cryptococcal keratitis has been described in a 30 year old AIDS patient who also had Cryptococcal meningitis and disseminated cutaneous lesions. In our patient the causative organism was Penicillium, detected following evisceration.

Squamous cell carcinoma is the third most common neoplasm associated with HIV infection, following Kaposi’s sarcoma and lymphoma. One patient in our study underwent successful excisional biopsy of conjunctival squamous cell carcinoma without any recurrence over a 6 month period of follow up. Unlike the US studies we did not observe Kaposi’s sarcoma of the eye.
Stevens-Johnson syndrome (SJS) has been reported following treatment with dapsone and trimethoprim sulphamethoxazole as well as others in HIV infected patients. In our study one patient developed SJS following trimethoprim sulphamethoxazole prophylaxis. Despite profound immunosuppression and alteration in cell mediated immunity, AIDS may paradoxically show the development of particularly severe SJS and toxic epidermal necrolysis including ocular features.24

 Conjunctival microvasculopathy may be present in 75% of patients with AIDS and are similar to those seen in sickle cell disease. The exact cause for this abnormality is not yet known, though a number of theories have been speculated.

 Anterior uveitis in AIDS patients occurs secondary to CMV retinitis, or due to herpes zoster, could be drug induced or idiopathic.

 The prevalence of AIDS in India is at its iceberg only and the focus has shifted from the developed countries to the underdeveloped areas. The epidemic will pose a challenge to all practitioners of medicine including ophthalmologists. Recognising these manifestations at an early stage, performing appropriate laboratory investigations and early treatment can help in reducing the morbidity and mortality of AIDS.

 References:


Familial band-shaped spheroidal degeneration of the cornea, report of two cases

Geetha K Iyer, Rajesh Fogla & Jyotirmay Biswas

Bietti et al in 1955, described an unusual degenerative corneal condition characterized by deposition of yellowish globules in the superficial layers of the cornea. This condition was noted predominantly in men who spent long periods of the time working outdoors. Initially termed as “Bietti’s corneal degeneration”, this condition has been assigned many names including “climatic droplet keratopathy”, “Labrador keratopathy”, “chronic actinic keratopathy”, “elastotic degeneration” and “spheroidal degeneration”.

This condition usually begins at an older age, seen more frequently with increasing age and does not seem to have a familial propensity. However there are a few case reports in literature that describe the rare occurrence of this condition in families.

We describe the familial occurrence of bilaterally symmetrical primary band-shaped spheroidal degeneration of the cornea in two siblings.

Case reports:

Case 1

A 37-year-old male presented to our clinic in June 2001 with the history of progressive visual loss in both eyes associated with photophobia, irritation, and watering since the age of 15 years. The patient had undergone corneal scraping in both eyes 7 years back followed by a significant improvement in both his symptoms and visual acuity. The general health of the patient was within normal limits with no relevant occupational or environmental history.

On examination his best-corrected visual acuity (BCVA) was counting fingers at ½ meter in both eyes. Slit lamp examination revealed presence of sub epithelial and anterior stromal golden yellow refractile globular deposits in the interpalpebral area, extending on either sides of the horizontal limbus onto the conjunctiva in both eyes. A small area of central clearing was noted in the right eye. Superficial corneal vascularisation associated with minimal stromal scarring was also noted in the interpalpebral region. The epithelium was intact though irregularly elevated by the underlying deposits. Corneal sensations were normal. There were no other associated ocular abnormalities. Rest of the ocular examination was found to be normal.

A deep lamellar keratoplasty was performed in the left eye along with amniotic membrane transplantation. Postoperatively he was treated with topical corticosteroids and tear substitutes. At last follow up two months later, his BCVA in the left eye had improved to 6/12.

Case 2:

The elder sister, 38 years old presented with a similar history. On examination her BCVA in the right eye was 6/24; and hand movements close to face in the left eye. Slit lamp biomicroscopy of the eyes revealed similar clinical picture of a central band of golden yellowish spheroidal deposits in the anterior stroma involving the interpalpebral area and extending on either side on to the conjunctiva in both eyes. (Fig 1) The central cornea was spared above the visual axis in the right eye. Large nodules with irregular elevation of overlying epithelium were noted in the left eye. Corneal sensations and rest of the ocular examination was within normal limits.
A deep lamellar keratoplasty was performed in the left eye. At last follow up six weeks later, her BCVA had improved to 6/24 in the left eye and slit lamp biomicroscopy revealed a clear lamellar graft. (Fig 2)

Histopathological findings of the corneal tissue obtained during surgery in both the cases, revealed basophilic globular deposits in the anterior stroma, thinning of the epithelium and destruction of the Bowman’s layer at places. The corneal globules had a characteristic autofluorescence and staining properties with stains for elastin, which were consistent with diagnosis of spheroidal degeneration.

Discussion:

Bietti’s original description of corneal degeneration characterised by deposits of yellowish, oily globules, although described by a variety of terms, is most commonly referred to as spheroidal degeneration. Fraunfelder and colleagues divided this condition into 3 basic forms: 1) primary corneal type occurring bilaterally associated with increasing age and without any evidence of prior ocular disease, 2) secondary corneal type associated with preexisting ocular pathology, and 3) conjunctival type wherein conjunctival deposits are prominent with or without corneal involvement.

Patients with primary corneal type have bilateral, golden yellow deposits in the interpalpebral cornea, predominantly in elderly males who spend long periods of time outdoors. Initial corneal involvement begins at the periphery and the central cornea is usually spared. Familial occurrence is extremely rare.

Our cases do not fit into the classification described by Fraunfelder et al. Both the patients were young, were siblings, and had bilateral involvement of the central cornea, without any evidence of associated ocular disease. Based on history, the corneal changes seem to have started between the age of 15 - 20 years. Both the patients underwent deep lamellar keratoplasty with good postoperative visual outcome.

Meisler et al have reported similar findings in three brothers, with early onset in life, two of them in the third decade. Hida et al have also reported familial occurrence of this condition in three cases from two consanguineous families.

Although familial occurrence of primary spheroidal degeneration is extremely rare, both our cases indicate that, there seems to be a variant which has a familial tendency,
occurs early in life, with initial involvement of the central cornea. Lamellar keratoplasty is successful in restoring useful vision in these cases.

References:


Indocyanine green angiogram in tubercular choroiditis - Case Report

Rupesh V. Agrawal, Dipankar Das, Jyotirmay Biswas, K. Jagannath and H. N. Madhavan

Introduction:

Indocyanine green angiography (ICGA) is a newer diagnostic imaging technique which employs the use of a tricarbocyanine dye which has its peak absorption and fluorescence in the near infrared range. It is used mainly in the diagnosis and accurate topographical localisation of occult choroidal neovascular membranes. ICGA has the potential to become very useful in the field of inflammatory disorders of the choroid. The different findings of indocyanine green angiography in chorioretinal inflammatory disorders was documented by Guyer et al. The typical findings of ICGA in acute posterior multiple placoid pigment epitheliopathy, serpiginous choroiditis, birdshot retinochoroidopathy, multiple evanescent white dot syndrome and Vogt Koyanagi Harada syndrome have already been documented. Herbert et al have described a case of presumed tuberculous choroio retinitis which on indocyanine green showed unevenly sized and irregularly distributed hypofluorescent dots & areas in the intermediate phase. In the late phase some of the hypofluorescent areas became isofluorescent & some areas of local hyperfluorescence were also seen. The combination of FA with ICG could help in reaching the most accurate differential diagnosis in cases of chorio-retinal diseases.

We describe the fundus fluorescein angiogram (FFA) & ICGA findings in a case of miliary tuberculosis of the choroid and correlate the angiographic findings with clinical presentation.

Case Report:

A 47 year old female presented to our institute with pain and redness in the right eye of 2-3 months and decreased vision of two weeks. Her chest x-ray showed the presence of military tuberculosis. She was on antituberculous treatment (Rifampicin 450 mg tab once daily, Isoniazide 300 mg once daily, Pyrazinamide 750 mg tab once daily) for the past two weeks and on topical corticosteroid, cycloplegic and antiglaucoma eye drops for diagnosis of choroiditis with secondary glaucoma. She had ductal adenocarcinoma of the breast three years back for which she underwent excision and radiotherapy.

On examination her best corrected visual acuity in the right eye was 20/200 and in the left eye was 20/20. Extraocular movements were full, free and painless. On slit lamp examination there was circumciliary congestion in the right eye, corneal haze and presence of mutton fat keratic precipitates on corneal endothelium. There was mild anterior chamber reaction of 1+. Lens showed very early posterior subcapsular cataract. Gonioscopy revealed open angles with scattered peripheral anterior synechiae and increased pigmentation of the trabecular meshwork in both eyes. The left eye was normal on slit lamp examination. Applanation tension was 16 and 14 mm of mercury in right and left eye respectively. On dilated fundus examination media haze due to significant vitritis was noted in the right eye (Fig.1A). The disc and macula were not visualised clearly. Active choroiditis patch half disc diameter in size nasal to the disc was noted in the left eye (Fig. 2b) with normal disc and macula (Fig. 2A).

Laboratory investigations revealed erythrocyte sedimentation rate of 33 mm at end of one hour, normal sarcoid work up (serum calcium 8.0mg/dl, inorganic phosphorus 4.1mg/dl, total protein 6.8mg/dl, albumin 3.5gm/dl, globulin 3.3gm/dl, A/G
ratio 1.0), slightly increased serum lysozyme (540 units), serum angiotensin converting enzyme 41.8 units. Anterior chamber tap was negative for mycobacterium tuberculosis genome by PCR and acid fast bacilli were not seen on smear or subsequent culture.

Fundus fluorescein angiogram of the right eye was not possible due to the presence of vitreous haemorrhage. Left eye showed normal fluorescence temporal to the disc (Fig. 2E, 2F) and a hyperfluorescent lesion seen inferonasal to the disc (Fig. 2G) correlating with the active choroiditis lesion seen clinically. However in early phase of indocyanine green angiogram there was presence of an additional hypofluorescent lesion seen supertemporal to the macula (Fig. 2C) along with the hypofluorescent lesion present inferonasal to the disc (Fig. 2D) which was seen clinically and on fluorescein angiogram. The lesion inferonasal to the disc showed hyperfluorescence in the late phase of ICGA (Fig. 2I) and the one present supertemporal to the macula was remained hypofluorescent (Fig. 2H).

Two months later her best corrected visual acuity improved to 20/20 in right eye and 20/20 was maintained in the left eye with complete resolution of the vitritis in right eye and normal disc and macula in the right eye as well (Fig. 1b). She was asked to stop topical steroids and to continue topical antiglaucoma drops in the right eye. In consultation with chest specialist she was asked to continue two drug regime (tab Rifampicin 450mg one per day, tab Isoniazide 300mg one per day) for her systemic disease.

**Discussion:**

Indocyanine green angiography has been found to be beneficial in various posterior segment inflammatory disorders like acute posterior multiple placoid pigment epitheliopathy, birdshot retinochoroidopathy, multiple evanescent white dot syndrome, serpiginous choroiditis and Vogt Koyanagi Harada syndrome. In general, two main patterns of hypofluorescence has been described by Herbert et al in choroiditis irrespective of its activity: (i) the hypofluorescent areas to be present in all the phases of angiography due to choriocapillaries non-perfusion (ii) hypofluorescence in the early and intermediate phases of ICGA and later isofluorescence or hyperfluorescence.

Tuberculosis is one of the leading cause of infectitious posterior uveitis in India. Establishing the diagnosis and attributing it to tuberculosis is often not possible. It is based on purified protein derivative skin test, abnormal chest x-ray, isolating the organism from ocular fluid or other tissue. In the...
present case aqueous aspirate was negative for mycobacterium tuberculosis by polymerase chain reaction as the organism can remain localised in the choroid and therefore remain undetected. We however feel the case is consistent with military tuberculosis owing to the military tubercles seen on chest X-Ray. The presence of characteristic choroidal lesion and moreover complete resolution to antituberculosis therapy.

In the present case, dual angiogram revealed the area of active choroiditis in form of hyperfluorescent lesion. However, indocyanine green angiography was able to
pick up more areas of involvement, which were not seen on fundus fluorescein angiogram. It hence delineated the disease process precisely. Indocyanine green angiography can therefore be a useful adjunct in establishing the anatomical diagnosis of the disease and delineating the same.

References:

AN APPEAL

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Transpupillary Thermotherapy for Choroidal Melanoma in Asian Indian Population

Mahesh. P. Shanmugam and Rajiv Raman

Introduction:

Current treatment options for uveal melanoma include enucleation, brachytherapy, charged particle radiotherapy, local resection, laser photocoagulation and observation. In recent times, Transpupillary Thermo Therapy (TTT) has evolved as a less morbid treatment for relatively small to medium sized posterior choroidal melanoma\(^1\)-\(^6\).

In the collaborative ocular melanoma study, 25% of the small tumors that were observed without treatment increased to become medium or large tumors over a 5-year follow-up. 2 tumors increased after 5 years.\(^7\) It is thus preferable to treat small melanomas rather than observe them, especially if they show signs of activity. Small melanomas can be managed with relative ease with laser photocoagulation and TTT in contrast to the medium or large tumors, which may need brachytherapy or enucleation.

Uveal melanoma is relatively rare in Asian Indians and most patients present initially with large tumors necessitating enucleation. We treated 6 Asian Indian patients with small choroidal melanoma with TTT and present our results.

Patients and methods:

A retrospective analysis of the case records of six patients with choroidal melanoma treated with transpupillary thermotherapy at our tertiary care centre between 1998 to 1999 was done. Individual tumor characteristics are outlined in table 1. 2 patients had been treated with diode laser photocoagulation earlier. The pupil was dilated with phenylephrine 5% and Tropicamide 0.25% eye drops prior to treatment. Topical Lignocaine HCl 4% or retrobulbar injection of Lignocaine HCl 2% was used for anesthesia. Transpupillary thermotherapy was performed using infrared diode laser at 810nm (Oculight SL Diode photocoagulator with operating microscope adapter) through a contact lens (Mainster lens: Ocular instruments, Bellevue, WA, USA.). A 2.0mm spot size was used and the power was titrated to achieve a mild graying of the tumor at the end of one minute.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Age</th>
<th>Eye</th>
<th>Location</th>
<th>SRF</th>
<th>Drusen</th>
<th>Pigment</th>
<th>Dimensions (Ht x V x H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>72</td>
<td>OS</td>
<td>Fovea just spared</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>4.3 x 9.2 x 10.6 mm</td>
</tr>
<tr>
<td>2</td>
<td>67</td>
<td>OD</td>
<td>Subfoveal</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3.4 x 12.8 x 10.4 mm</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>OD</td>
<td>1DD ST to disc</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2.5 x 5.9 x 7.1 mm</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>OS</td>
<td>Just SN to disc</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>4.2 x 9.1 x 9.3 mm</td>
</tr>
<tr>
<td>5</td>
<td>37</td>
<td>OS</td>
<td>1DD IT to disc</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3.3 x 7.4 x 12 mm</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>OS</td>
<td>Just IT to disc</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2 x 5.1 x 5.1 mm</td>
</tr>
</tbody>
</table>
Using the adjusted power and 2.0mm spot size, entire surface of tumor including 1-1.5mm of clinically normal chorioretina around the margins of the tumor was treated by overlapping spots of one-minute duration. The location of the tumor, pre and post treatment dimensions of the tumor on ultrasonography, treatment parameters, adjunctive treatment used before and after transpupillary thermotherapy and complications of therapy were noted on each follow up.

Results:

Average age at presentation of the choroidal melanoma in this subset of patients was 49.3 ± 17.3 years (range: 20 –72yrs ) with a male preponderance (M: F 5:1). Mean follow-up was 11.5 ± 5 months (range: 2-22 months). The mean pretreatment height of the tumor was 2.9 ± 0.78mm and the basal diameter 9 ± 2.3mm. In 4 cases the tumor was located within 1 disc diameter of the disc and in 2, the tumor was located in the foveal and parafoveal areas respectively. Mean laser power used was 885 ± 230.98MW, for an average duration of 16.83±7.41minutes (Table 2). 5 of 6(83.3%) tumors showed signs of regression after TTT (mean post treatment height: 1.18±1.09mm) (Fig. 1-5). One patient (case 4) did not respond to treatment and underwent enucleation. The tumor residue was treated with diode laser photocoagulation (Iridex Oculight) in 2 patients and 3 patients underwent further TTT. The average time to achieve a flat scar was 17 months. There was no evidence of metastatic disease in any of the patients to date.

Table 2 : Treatment parameters with anatomical & visual results

<table>
<thead>
<tr>
<th>S.No</th>
<th>Ht. Before Tt</th>
<th>Pre Tt Vn</th>
<th>Power (mw)</th>
<th>Spot size</th>
<th>Duration</th>
<th>Ht. at last Visit</th>
<th>Post Tt Vn</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.6mm</td>
<td>.6/18</td>
<td>800-1000</td>
<td>2mm</td>
<td>15min</td>
<td>flat</td>
<td>.6/9</td>
</tr>
<tr>
<td>2</td>
<td>3.4mm</td>
<td>.6/60</td>
<td>500</td>
<td>2mm</td>
<td>25min</td>
<td>1.7mm</td>
<td>.3/60</td>
</tr>
<tr>
<td>3</td>
<td>2.5mm</td>
<td>.2/60</td>
<td>1000</td>
<td>2mm</td>
<td>25min</td>
<td>2.2mm</td>
<td>.3/36</td>
</tr>
<tr>
<td>4</td>
<td>4.2mm</td>
<td>.6/9</td>
<td>1200</td>
<td>2mm</td>
<td>27min</td>
<td>Enucleated</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2.7mm</td>
<td>.6/18</td>
<td>800-1000</td>
<td>2mm</td>
<td>10min</td>
<td>2mm</td>
<td>.6/30</td>
</tr>
<tr>
<td>6</td>
<td>2mm</td>
<td>.6/36</td>
<td>810</td>
<td>1.2mm</td>
<td>10min</td>
<td>flat</td>
<td>.6/60</td>
</tr>
</tbody>
</table>

Fig 1 :Comparison of height of the tumor before & after Tt.
Schnelder et al evaluated treatment of choroidal melanoma in 17 patients either using transpupillary thermotherapy alone (6 eyes) or combined brachytherapy and transpupillary thermotherapy (11 eyes). All tumors exhibited a reduction of tumor height after a mean follow up of 14.25 months. Godfrey et al have also shown 71.4% tumors regressed with TTT over 8.7 months. Shields et al reported a reduction of tumor height from 2.8mm to 1.7mm in 100 patients, six months after TTT. Tumor regression occurred in 94% cases with an average of three sessions of treatment. Other studies have also shown the efficacy of TTT in tumors with a mean height of 2.76mm and basal diameter of 6.83mm. In our series 83.3% of tumors with a mean height was 2.9mm and basal diameter 9.0 mm responded favorably to TTT.

**Discussion**

Hyperthermia has a relative selective effect on neoplastic tissue. The impaired cooling system of the tumor due to the absent or aberrant vascular channels makes the tumor act like a heat sink. Journee-de-Korver et al first described intermediate hyperthermia within the temperature range of 45-60 °C resulting in necrosis up to a depth of 3-4 mm of the tumor, whereas hyperthermia above 60°C (temperature achieved in laser photocoagulation) resulted in limited superficial penetration. This ability of TTT to penetrate to a depth of 3-4 mm, makes it an ideal treatment modality for small melanomas.

Hyperthermia has been used to enhance the effect of radiation in the treatment of choroidal melanomas. Oosterhuis et al have combined brachytherapy with TTT to treat thicker tumors (mean height:: 8.4mm). Schnelder et al evaluated treatment of choroidal melanoma in 17 patients either using transpupillary thermotherapy alone (6 eyes) or combined brachytherapy and transpupillary thermotherapy (11 eyes). All tumors exhibited a reduction of tumor height after a mean follow up of 14.25 months. Godfrey et al have also shown 71.4% tumors regressed with TTT over 8.7 months. Shields et al reported a reduction of tumor height from 2.8mm to 1.7mm in 100 patients, six months after TTT. Tumor regression occurred in 94% cases with an average of three sessions of treatment. Other studies have also shown the efficacy of TTT in tumors with a mean height of 2.76mm and basal diameter of 6.83mm. In our series 83.3% of tumors with a mean height was 2.9mm and basal diameter 9.0 mm responded favorably to TTT.
One patient who did not respond to TTT (case 4) had an amelanotic tumor, lacking adequate pigment to absorb laser energy. Shields et al have also shown that amelanotic tumors do not respond well to TTT, until retreated with indocyanine green as an adjunct to enhance laser absorption. Godfrey et al found that increasing the power alone does not have the desired result in amelanotic tumors. In addition, this eye which was enucleated had a medium sized tumor composed of epithelioid cells on histopathological examination establishing its higher malignant potential.

3 patients in our series had decreased vision after TTT, because of the proximity of the tumor to the optic nerve or macula. Visual acuity may improve in some cases with absorption of subretinal fluid in an extra macular tumor, but most submacular or peripapillary tumors lose vision due to heat related damage. Shields et al reported a stable or improved vision in 58% cases while Godfrey et al reported reduced vision in 43% cases. Other complications associated with TTT are retinal vascular occlusions, scarring with tractional changes, thermal papillitis, minimal subretinal or vitreous hemorrhage.

Laser photocoagulation has a poor depth penetration and has to be applied in multiple sittings to treat small melanomas. TTT has a better depth penetration thereby obviating the need for multiple treatments. In addition, it can be used to treat tumors that are larger than that can be treated with laser photocoagulation but too small to employ brachytherapy. Brachytherapy is associated with severe complications such as radiation retinopathy, papillopathy, cataract, dry eye etc., in addition to the need for surgery to apply and remove the plaque. TTT avoids these complications and is a viable alternative in small and selected medium sized tumors.

However, long term effects of TTT are as yet unknown and heat induced damage to ocular structures may not become clinically evident for months or years, similar to radiotherapy. TTT alone cannot be used to treat most medium and large tumors or those situated in the periphery. Current recommendations for TTT are melanomas < 4 mm in height and < 7 mm in basal diameter.

This is the first report to evaluate the role of TTT for choroidal melanoma in Asian Indian patients. This report also assumes significance as \( I_{25} \) Brachytherapy for treating melanomas is as yet not available in India and some of the tumors that may need brachytherapy may alternatively be managed with TTT.

Reference:

Degraded stereopsis as a presenting sign of Convergence Insufficiency

S.Jayarajini and Shrikant R Bharadwaj

Introduction

Convergence insufficiency, characterized by receded near point of convergence and a larger exodeviation for near than for distance, is by far the most commonly encountered binocular vision ailment in an orthoptic clinic. Convergence insufficiency is an anomaly in which both the accommodation and vergence system and their complex interplay thus have to be thoroughly examined before arriving at the diagnosis of convergence insufficiency. Case report details are the presentation, examination, treatment and outcome of a patient with convergence insufficiency.

Case Report

A 27-year-old Ophthalmologist was referred to the Orthoptic Clinic of Sankara Nethralaya with chief complaints of double vision when performing eye surgery. He had no complaints with vision for distance and near.

Ocular examination showed distance acuities of 6/5 and near acuities of N6 in both eyes with his existing myopic and astigmatic correction. Subjective and objective refraction revealed a minor and insignificant change in the astigmatic correction in the left eye. No diplopia or suppression was reported with Snellen acuity and Worth–4-Dot test. Anterior and posterior segments of both eyes were normal. Orthoptic evaluation showed normal extra ocular motility. Cover test with the spectacles revealed an orthophoria for distance and an exophoria with an intermittent divergent squint (IDS) for near. These were substantiated by the phoria measures for both distance and near. The near point of convergence (NPC) was receded both objectively (16 cms) and subjectively (14cms). Relative amplitudes were also reduced when compared to a normal age matched individual (NRA: +2.50DS; PRA: -1.50DS). The normal Negative relative accommodation is +1.75DS to +2.00DS and the normal Positive relative accommodation is -2.25DS to -2.50DS. Dynamic retinoscopy showed a lag of accommodation of +1.00DS OU. The vergence limits, as measured by synoptophore, were also borderline (table 1). Binocular accommodative facility was within normal limits (17 cycles /min) Stereopsis threshold measured by the Random Dot stereopsis method showed a degraded stereopsis threshold of 80 arc sec (table: 4). These findings suggested a diagnosis of convergence insufficiency and depleted fusional vergence ranges. The patient was advised to undergo vergence training (one sitting per day lasting 15 minutes on synoptophore) for 10 days and home vision therapy exercises for improving convergence (Cat-card exercises and Pencil push-up exercises – 2 times per day lasting 15 minutes each) until the next visit.

<table>
<thead>
<tr>
<th>DUCTION</th>
<th>BLUR</th>
<th>BREAK</th>
<th>RECOVERY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adduction</td>
<td>+15°</td>
<td>+20°</td>
<td>+14°</td>
</tr>
<tr>
<td>Abduction</td>
<td>-5°</td>
<td>-1°</td>
<td>-1°</td>
</tr>
</tbody>
</table>

Table 1: Vergence ranges in first visit

The patient felt much better after 10 days of vergence exercises but still had problems while performing surgeries. There was no change in the phoria status when compared to the last visit. The near point of convergence had improved both subjectively and objectively (8cms). The lag of accommodation remained the same but the accommodative facility improved to 26 cycles per min when compared to the first visit. It was interesting to note an improvement in the vergence ranges especially in the “Break” values of the abduction–adduction testing (Table2). A remarkable
improvement in the stereopsis threshold from 80 arc sec to 20 arc sec was also noted (Table 4). The patient was asked to continue home vision therapy (2 times a day lasting 15mins. each) until the next follow-up.

<table>
<thead>
<tr>
<th>DUCNTON</th>
<th>BLUR</th>
<th>BREAK</th>
<th>RECOVERY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adduction</td>
<td>+21°</td>
<td>+31°</td>
<td>+28°</td>
</tr>
<tr>
<td>Abduction</td>
<td>-5°</td>
<td>-1°</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Vergence ranges in second visit

One month later the patient showed significant improvement in his performance with the operating microscope. Orthoptic evaluation during this session revealed an orthophoria for both distance and near confirmed Maddox rod findings. The near point of convergence had further improved up to 5 cms. (Objectively and subjectively). A significant improvement in both the near points of accommodation and the relative accommodation (NRA: +3.25DS ; PRA: -5.00DS) was noted. The accommodative facility showed a small and insignificant decrease since the last visit. The response accommodation was same as the last visit (Lag values of OD: +0.75DS; OS: +1.00DS). Similar to the last visit, the “Break” values showed the maximum change when compared to the previous visits, although an overall increase

<table>
<thead>
<tr>
<th>DUCNTON</th>
<th>BLUR</th>
<th>BREAK</th>
<th>RECOVERY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adduction</td>
<td>+20°</td>
<td>+36°</td>
<td>+30°</td>
</tr>
<tr>
<td>Abduction</td>
<td>-7°</td>
<td>-4°</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Vergence ranges in third visit

Discussion

Convergence insufficiency is generally regarded as a syndrome which includes an exodeviation of the eyes at near point, relatively little or no deviation of the eyes with distance fixation, a relative deficit of the positive relative convergence and a receded near point of convergence.1 Studies on vergence anomalies places convergence insufficiency as the leading cause of aethenopia and ocular fatigue2, with the incidence rate ranging from 1.75% to 25% in American population.3,4 This deficiency can often present as other vergence anomalies such as convergence excess, divergence insufficiency, divergence excess and false

<table>
<thead>
<tr>
<th>Test parameters</th>
<th>First visit</th>
<th>Final visit</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cover test</td>
<td>Orthophoria for distance; IDS for near</td>
<td>Orthophoria for both distance and near</td>
<td>Orthophoria for both distance and near</td>
</tr>
<tr>
<td>Near point of convergence</td>
<td>Subjective: 14 cms Objective: 16 cms</td>
<td>Subjective: 5 cms Objective: 5 cms</td>
<td>Subjective: 8 cms Objective: 8 cms</td>
</tr>
<tr>
<td>Near point of accommodation</td>
<td>Push up : 12 cms Push out : 12 cms. OD:+1.00DS OS:+1.00DS</td>
<td>Push up : 8 cms Push out : 8 cms. OD:+0.75DS OS:+1.00DS</td>
<td>Push up:13cms Push out:13cms OU: +0.75DS to +1.00DS</td>
</tr>
<tr>
<td>Lag of accommodation</td>
<td>NRA:+2.50DS PRA:-1.50DS</td>
<td>NRA:+3.25DS PRA:-5.00DS</td>
<td>NRA:+1.75DS to +2.00DS PRA:+2.25DS to -2.50DS</td>
</tr>
<tr>
<td>Relative accommodation facility</td>
<td>17 cycle/minute</td>
<td>23 cycle/minute</td>
<td>12 cycles/min</td>
</tr>
<tr>
<td>Stereopsis thresholds</td>
<td>80 arc seconds</td>
<td>20 arc seconds</td>
<td>40 arc seconds</td>
</tr>
</tbody>
</table>

Table 4: comparison of the various test parameters in the first and final visit
convergence insufficiency and thus should be approached with caution. The various oculomotor parameters should be thoroughly analyzed before the treatment modality is decided upon.

The end-point of convergence is Diplopia, which marks the exhaustion of both the accommodative and fusional convergence limits (effect of tonic and proximal convergence is negated). The demand on convergence is met either by the accommodative convergence or by the fusional convergence. Deficiency in one of the two components is usually compensated by the other for the maintenance of normal binocular vision.

Dynamic retinoscopy on the first visit revealed a decreased accommodation of +2.00DS (OU) for a demand of +3.00DS. The accommodative convergence was thus decreased and an additional strain on the fusional vergence system was put to meet the demands on convergence. Borderline vergence ranges during the evaluation revealed a poor fusional vergence range. Thus, the demand on convergence was not sustained, thereby leading to diplopia and degradation in Stereopsis thresholds. This probably was the reason for the poor performance of the patient with surgical microscopes. The lag values however should be interpreted with caution. Convergence insufficiency is usually associated with low lag values (increased response accommodation) to compensate for the poor fusional reserves. The 40cm unfused dynamic retinoscopy would tend to exhibit a normal or high lag because, monocularly, the accommodation may be unaffected by convergence.5

Orthoptic evaluation on the subsequent visits revealed an improved near point of convergence and vergence values (Graph1). The lag of accommodation remained the same pointing a steady state of accommodative convergence. The improved near point of convergence was more because of the fusional vergence involvement. This is in accordance with the study done by Daum.6 The result is further corroborated by the improved “break values” in adduction. The Stereopsis thresholds improved near point of convergence and improved fusional reserves (Graph2).

Low relative amplitudes of accommodation, as measured in the initial evaluation do not essentially imply low accommodative thresholds. Poor fusional reserves can often cause a Diplopia to occur even before the sustained blur is obtained.5 Further, presence of an accommodative facility of 17cycles / min contradicts a poor accommodative reserve. The phoria status improved over the course of treatment. Schor accounted for changes in phoria position because of slow fusional vergence7 and this probably explains the change in the phoria status.

Treatment of convergence insufficiency largely depends upon two things:
1. Full compensation of heterophoria, which is not likely to cause any symptoms.
2. Partial compensation of heterophoria, which is likely to cause symptoms.
Thus, treatment is indicated only in those conditions in which the heterophoria is not fully compensated. The success rate in treatment of exodeviations has been found to be generally very good in latent and most intermittent deviations treated with orthoptics, especially those of convergence insufficiency. It is interesting to note that orthoptics can influence slow fusional vergence. The data in this paper confirm that orthoptics can affect the heterophoria value because of effects on the slow fusional vergence system. Orthoptics is usually effective at strengthening the vergence system and had only an insignificant effect on the normal portion of the system. Treatment, thus should be aimed at improving both the facilities and aid a harmonious interaction of the two systems. An improvement in the AC/A component and other ocular parameters following orthoptic treatment and a subsequent decrease in their facility after one year of therapy. This suggests that the treatment provided to improve the patient’s condition should not be stopped upon achievement of desired results but should be tapered slowly for maintenance of the same.

References
within or across databases. Numerous human genetics and molecular biology databases are currently providing such links.

The human genome database is a compilation of various databases, which gives information on the various aspects of the human genome. These databases can be used to compare and analyze our observed data. Chromosomal abnormalities, mutation analysis, linkage analysis and information regarding hereditary disorders can be got from these databases.

In this paper we discuss how we explored the web to compile the human genomic databases so that it can be effectively used in our laboratory. In our laboratory, we are working to understand the fundamental genetics of various eye genetic disorders like

![Figure 1: Human genome related World Wide Web sites.](image)
age-related cataract, angle closure glaucoma, diabetic retinopathy, retinoblastoma, retinitis pigmentosa and other retinal degenerative disorders. We also searched for DNA software programs that can be identified and downloaded so that it can be useful for genetic studies.

Methodology:
The details about various human genome databases and the free software tools are obtained by browsing the Internet with the help of the various search engines like www.google.com, www.yahoo.com, www.metacrawler.com, www.netcrawler.com and www.altavista.com. For the search we used keywords like DNA databases, human genome database management and research genetics. This search and analyses took four weeks between start and completion.

Results and Discussion: On search we found that 106 independent databases were related to the human genome. The databases were on various aspects of human genome like chromosomal location of genes, disorders associated with chromosomal abnormality, single gene disorders, structure of the gene, domains in the gene, current research on various hereditary disorders etc. Thus obtained databases were classified into clinical and laboratory related databases. The clinical databases were linked only to ocular disorders and were further sub-classified into academic and patient related genetic databases. The databases giving information on the current research on ocular genetic disorders were included in the academic section while those information oriented towards patients’ education were included in the patient related database sections. These databases also help the clinician to counsel the patients. The laboratory related search focused on the databases with software tools, which can be used for submitting DNA sequences, finding out mutation, human genome loci, polymorphism, probes, genetic maps, citations and references. Various databases obtained are dealt in the following sections and a list is provided in Figure 1.

The www.hgmp.mrc.ac.uk gives information on the current human genome research. The Human Genome Project (HGP) is an international research effort to characterize the genomes of human and selected model organisms through complete mapping and sequencing of their DNA, to develop technologies for genomic analysis, to examine the ethical, legal and social implications of human genetics research, and to train scientists who will be able to utilize the tools and resources developed through the HGP to pursue biological studies that will improve human health. The gslc.genetics.utah.edu/index.html - GSLC also called the Genetic Science Learning Center helps people understand how genetics affects our life and society. It gives information on basic genetics, genetic disorders, the genetics related to the society and the thematic units. The www3.ncbi.nlm.nih.gov/Entrez/ (NCBI) - is a database on sequence retrieval from hyperlinked protein, nucleic acid, protein structure and genome mapping databases. The www.hgmp.mrc.ac.uk also gives information on each chromosome and the centers associated with it. The “www.gdb.org/gdb/hgp” is a Human Genome Project resource. The is one of the most important database that holds data on human genome loci, polymorphism, mutation, probes, genetic markers, Gen Bank, citations and contacts.

The “www.genome.wustl.edu” database collects records of chromosome abnormalities from over 70% of the laboratories performing routine cytogenetic analysis in the UK. The records contain the karyotype of the sample, the primary reason for referral, the type of tissue sampled and the presence of a cell line/stored tissue. The Integrated Genomic Database (IGB) is an example of a molecular biology data warehouse. Database federations and data warehouses usually provide full query facilities and insulate users from the component databases via their global schemas. Multidatabase systems are collections of loosely coupled databases, which are not integrated using a global schema.
The bioinformatics.weizmann.ac.il/udb/- The Unified Database (UDB) presents an integrated map for each chromosome, based on data integrated from various radiation hybrid, linkage and physical mapping resources. With the help of sequenced enhanced UDB we can get information on a region in a specified chromosome, about markers and cytogenetic bands.

Software tools for DNA analysis: These databases provide programs which can be used in DNA analysis like searching for motifs, patterns in DNA sequences, analysis of microarrays, selection of nucleotide probes etc. Wordup (www.area.ba.cnr.it/pub/embnet/software/Wordup)- This is a fast and sensitive method designed to isolate short nucleotide sequence, which has non-random statistical properties and may thus be biological active. Coresearch (www.gsf.de) - This program Coresearch is used to identify and delimitate consensus elements (e.g. protein binding sites) in a set of unaligned nucleic acid sequences. The www.tigr.org- (The Institute for Genomic Research) - this database provides over 15 free softwares for different uses like, MUMmer- this is a system for aligning whole genome sequences. Using an efficient data structure the system rapidly aligns sequences, which contains millions of nucleotides. TIGR Multiple Experiment Viewer- This software is a JAVA application used to allow the analysis of microarray data to identify patterns of gene expression and differentially expressed genes. Genesplicer- It is a fast and flexible system used for detecting splice sites in the genomic DNA of various eukaryotes. GlimmerM- This is a gene finder based on a dynamic programming algorithm that considers all possible exons for inclusion in a gene model and chooses the best of these combinations. “www.cybergenome.com” -There are a lot of softwares available in this sites like Primer3: (www-genome.wi.mit.edu/cgi-bin/primer/primer3_www.cgi) is primer selection software from MIT that considers oligo melting temperature, size, GC content, and primer-dimer possibilities; PCR size, and possible constraints within the source sequence. It was developed at Whitehead Institute and Horward Hughes Medical Institute. DNA Tools (www.cybergenome.com/tools/software.html) is a program package for routine handling and analysis of DNA and protein sequences. The package includes general facilities for sequence and contig editing, restriction enzyme mapping, translation, repeat identification, advanced options for searching sequences and their headers. With the help of this software several thousand sequences can be loaded and analyzed in a single project. Trace Viewers: ABI chromatogram viewers for Windows and MAC platforms. PDRAW32 This is a DNA annotation software tool for making annotated plasmid maps. It also sequences editing, virtual digestions, and analysis of sequences. DNA for Windows: is a compact and easy to use DNA analysis program, ideal for small scale sequencing projects. AnnHyb - (www.annhyb.free.fr) is a comprehensive DNA analysis and edit tool which allows sequence retrieving directly form the server, sequence editing with proof reading, restriction analysis, translation etc. Another software that is available free of cost on the net for the identification of restriction sites for various restriction enzymes in the given genomic sequence is called as WEBCUTTER 2.0 - (www.firstmarket.com/cutter/cut2.html). COPE - is an environment on pedigree management and drawing. This environment is intended as a facility for epidemiologists and statisticians to share their familial data through the networks. www.bimas.dcert.nih.gov/sw.html - This website also houses a lot of molecular biology softwares used for various purposes. Comprehensive Genomic Sequence Analysis Packages: These are a growing set of programs for manipulating and analyzing “genetic” data. Linkage Analysis Tools -These programs are used to analyze pedigrees for linkage between a diseased trait and a number of marker loci from BIMAS. Linkage analysis software used in gene mapping work is available at “linkage.rockefeller.edu”. Primer Selection Tools This is a computer program developed to aid in selecting oligonucleotide primers for DNA
sequencing and for the polymerase chain reaction. The www.bioinformatics.org gives information on the latest developments in bioinformatics. The bioinfo.weizmann.ac.il/: From this site information is obtained on bioinformatics and computational biology. It is basically an educational website, which gives details on sequence analysis. The www.isb-sib.ch/: this is the Swiss Institute of Bioinformatics, which educates on bioinformatics and has the state of art facilities for this purpose. DNA software is also available on bioinformatics at www.sibc.ac.cn.

This study gives an insight on human genome databases available on the net. Various search engines were used to identify different DNA databases. One hundred and six databases giving information on various aspects of human genetics were collected and classified. Twenty software programs, which will be useful in molecular biology research, were found and these can be downloaded free of cost. These databases and the software programs can be used in any laboratory oriented towards human genome research.

Reference:
Introduction:

Human genetics is the study of inheritance in Man. Genetic disorders compared to heart or lung diseases are rare in a population, but when 10,000 different single gene disorders and various other complex or multifactorial diseases are put together, they form a major group in health and disease. Genetic studies have helped to identify the genes responsible for deadly diseases like breast cancer, retinoblastoma, Alzheimer’s, Huntington, Duchenne Muscular dystrophy etc. The gene discovery is opening the doors for prevention and better management of genetic diseases. The field of genetics is complex, rapidly growing and a deluge of new information is gained every day. The amount of information to be studied is colossal. The field of human molecular genetics is relatively new but what we know now has been gathered over the last 30 years. The massive data that is generated in the field is not only stored efficiently but also is available in the public domain for free access and retrieval.

A database is a data repository that provides a centralized and homogenous view of data for multiple applications. The data in a database are structured according to a database definition, called schema, specified in a data definition language and are manipulated using operations specified in a data manipulation language. Data definition and manipulation languages are based on a data model that defines the semantics of the constructs and operations supported by these languages. Comprehensive studies on molecular biology data often involve exploring multiple molecular biology databases, which entails coping with the distribution of data among these databases, the heterogeneity of the systems underlying these databases, and the semantic (schema representation) heterogeneity of these databases. Early attempts to manage heterogeneous databases were based on revolving heterogeneity by consolidating these databases either physically, through integration into a single homogenous database, or virtually, by imposing a common definition language, data model, or even data base management system (DBMS), upon heterogeneous databases. These attempts failed because they required a very difficult to attain degree of cooperation and a costly replacement of applications that were already based on existing databases. The most effective way of coping with heterogeneous databases is to allow them to preserve their autonomy, that is, their local definitions, applications, and policy of exchanging data with other databases.

Approaches to managing heterogeneous databases include connecting them using the World Wide Web (WWW), organizing them into database federations or multi database systems, and constructing warehouses. The World Wide Web is officially described as a “wide area hypermedia information retrieval initiative aiming to give universal access to a large universe of documents”. The World Wide Web uses the Internet to transmit hypermedia documents between computer users internationally. Heterogeneous databases can be connected via WWW hypertext links at the level of individual data items. Data retrieval in such systems is limited to selecting a starting data item within one database and then following hyperlinks between data items.