LETTERS TO THE EDITOR

Sympathetic ophthalmia associated with high frequency deafness

EDITOR,—Sympathetic ophthalmia with deafness has been reported rarely. We describe one such case and explore a hypothesis whereby genetic susceptibility may be associated with cross reactivity of antigens derived from common neural crest tissue.

CASE REPORT

A 72 year old woman who had previously undergone a left trabeculectomy had a fall in which she sustained a Colles fracture and a left total hyphaema. By 14 days the blood had undergone a left trabeculectomy had a fall in which she sustained a Colles fracture and a left total hyphaema. By 14 days the blood had

disappeared.

However, at 4 months post-injury, reduction of the prednisolone dose to 12.5 mg, and reduction of cyclosporin A to give a trough level of 70 µg/l, was followed by a flare of anterior uveitis in both the exciting and sympathising eyes. This responded to increased prednisolone (15 mg) and an increase in the dose of cyclosporin A to achieve a trough level of 140 µg/l. At this time the exciting eye began to display white choroidal lesions consistent with the appearance of Dalen Fuchs nodules (Fig 1). Prednisolone was gradually reduced to 12.5 mg without further complications and she ultimately achieved a visual acuity of 6/9 in both eyes. Despite treatment, her hearing loss gradually progressed to 90 dB; this has not recovered.

COMMENT

Sympathetic ophthalmia with features of Vogt-Koyanagi-Harada disease (VKH), was initially reported in the 19th century. More recently, Nirankari et al have reported one case of sympathetic ophthalmia with profound high frequency deafness which did not recover. Rao and Marak have performed a clinicopathological survey of 100 pathological specimens of eyes enucleated because of sym pathetic ophthalmia. Four of these had VKH overlap features, of which two had hearing loss. The association of sympathetic ophthalmia and deafness is clearly rare, which raises the question of what such overlap cases can teach us about the pathogenesis of VKH. Woods attempted to explain why deafness could occur in VKH, hypothesising that pigment present in the auditory labyrinth and the eye could be common targets of autoimmunity. The auditory labyrinth and the uvea are known to have a common embryological origin in the neural crest. Could a genetic predisposition facilitate the recognition of such shared antigens? Sugita et al have recently reported that cytotoxic T cells from three patients with VKH and one with sympathetic ophthalmia reacted against the MART 1 melanoma antigen (an antigen carried by skin and eye melanocytes), when presented in association with HLA-A2. Interestingly, two of their three VKH patients carried HLA-A2, HLA-B51, HLA-DR4, and a further VKH patient carried the HLA-A2, and HLA-DR4 antigens. Their sympathetic ophthalmia patient was also A2 positive, but was not positive for either HLA-B51 or HLA-DR4. Our patient was HLA typed and found to carry HLA-A2, HLA-B51, HLA-DR4.

HLA-A2 and HLA-DR4 are common and linked antigens, occurring together in approximately 33% of the population, but HLA-B51 is less common. From 537 random transplant organ donors HLA typed over 3 years, we calculated the frequency of HLA-A2, HLA-B51, HLA-DR4 in the regional population. These specificities were present together in only seven donors, giving a frequency of 1.3%. We propose that patients carrying HLA-A2, HLA-B51, and HLA-DR4 are at increased risk of damage arising in melanocytes of diverse tissues when one tissue is injured, whether in VKH or sympathetic ophthalmia.

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Accepted for publication 19 September 2000


Similarities in the packaging of cyanoacrylate nail glue and ophthalmic preparations: an ongoing problem

EDITOR,—We would like to raise concern over an ongoing problem—namely, the similarity between the packaging used for fingernail extension glue (cyanoacrylate “superglue”) and topical ophthalmic preparations.

These concerns were raised as long as 16 years ago and yet no action or progress has since been instituted by the manufacturers of these containers.

Both nail glue and ophthalmic preparations are almost identically packaged in 5–10 ml clear, round bodied, soft plastic dropper type bottles with a white non-locking twist cap which are often manufactured in the same factory. The caps are even interchangeable.

Discrimination between these products is therefore made unnecessarily difficult, particularly for patients who need to use regular topical medication—for example, glaucoma and contact lens wearers and patients who are partially sighted or blind.

Figure 1 (A) Sympathising eye: acute uveitis (pigment ring after pupillary dilatation). (B) Exciting eye: aniridia and hyphaema. (C) Exciting eye: iris pigment in trabeculectomy bleb. (D) Exciting eye: multifocal pale subretinal lesions, representing early Dalen Fuchs nodules.
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EDITOR,—Locked-in syndrome is a rare para-

ина patient with locked-in syndrome

Disconjugate vertical ocular movement

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diers of nail glue products should be forced

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Sixteen years have now passed since this issue

ramphenicol 1% ointment.

chanical removal of the glued lashes and chlo-
near abrasion.

The second case was of a 3 year old child whose brother was receiving antibiotic eye-
drops for conjunctivitis. The child imitated

drops for conjunctivitis. The child imitated

her mother’s actions by installing drops in her

own eye but used nail adhesive instead. This

led to misdirection of her eyelashes and a con-
earal abrasion.

Both children responded well to the me-

chanical removal of the glued lashes and chlo-

ramphenicol 1% ointment.

COMMENT

Sixteen years have now passed since this issue

was first raised, and we feel that the manufac-

turers of nail glue products should be forced
to address some remedial action, to ensure

that these preparations are packaged differ-

tently from therapeutic preparations in the

future.

At the very least, nail glue products should be

fitted with child safety caps to prevent any

further unnecessary anxiety and ocular trauma.

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Accepted for publication 31 October 2000

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Disconjugate vertical ocular movement in a patient with locked-in syndrome

Editor,—Locked-in syndrome is a rare para-

tic state in which voluntary movements are

affected. This uncommon de-erent state

results in quadriplegia, loss of gestural or vocal

communication with a defect in horizontal eye

movements. However, consciousness and ver-

tical eye movements are spared, which enable

the patient to communicate by way of ocular

movement, either conjugate upward or down-

ward.

Here, we report an unusual case of locked-in syndrome presenting disconjugate

vertical and torsional ocular movement, mim-

icking seesaw nystagmus (SSN).

CASE REPORT

A 30 year old man was brought to the emer-

gency room. He was unable to move his extremites and all verbal communication was not

possible because he could not speak.

Increased deep tendon reflex with bilateral extensor toe signs were noted. He could open

his eyes. Visual acuity was uncheckable. Visual

field appeared to be normal by a threatening
test. Pupil size was equal and light reflex was

prompt. Funduscopic examination did not

show any remarkable findings.

On command, he showed conjugate vertical

eye movements but he could not make hori-

zontal gaze. Instead, full conjugate hori-

zontal leftward deviation was obtained with
cold water irrigation in the left ear, but nystag-

mus to the opposite side was absent. Caloric

stimulation on the right ear was not

performed because eardrum perforation was

suspected. Doll’s eye manoeuvre showed full

range of horizontal eye movements except for

the adduction of the left eye, presumably due
to left internuclear ophthalmoplegia. Conver-

gence for near target was not possible. When

the patient was asked to look to the right side,

the right eye moved upward with intorsion,

and at the same time, left eye moved

downward and extorsion. It appeared to be a

half cycle of SSN. When the patient was asked
to look to the left side, the reverse half cycle

of SSN was observed—the left eye moved

upward with intorsion whereas right eye

moved downward with extorsion. Horizontal

gaze was limited, although there seemed to

be minimal movement. The eyes that moved

downward didn’t cross above the midline (Fig

1A, B).

In addition to the above findings, intermittent irregular jerky eye movements

were detected. These also consisted of elevation with intorsion of one eye and

synchronous depression and extorsion of the other eye. They appeared in a

clustered pattern containing

four to five cycles of SSN, beating at

between 0.5 and 1 Hz. Whether this

phenomenon was purely voluntary or involuntary

was not confirmed. It had persisted for 1 month.

Brain MRI revealed an extensive infarct in the ventral pons (Fig 1C).
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Accepted for publication 7 November 2000


Conjunctival CD5+ MALT lymphoma

EDITOR,—Primary ocular non-Hodgkin’s lymphoma (NHL) may occur in the conjunctiva, eyelids, and lacrimal glands, but the majority occur in the orbit.1 Most primary ocular NHL are of B cell origin, either of the follicular, diffuse small, or mixed cell type.1

According to the Revised European American classification of lymphoid neoplasms (REAL classification)2 the most common ocular NHL, arising from mucosa associated lymphoid tissue (MALT) and the marginal zone of lymph follicles, is included in the group of extranodal peripheral B cell lymphomas.1 Histopathological features of marginal zone lymphoma (MZL) of the MALT type consists of a diffuse and parafollicular growth pattern and the presence of lymphoepithelial lesions.3 The tumour cells express monotypic surface Ig (sIg) and sometimes cytoplasmic Ig (cIg) (usually IgM), moreover the pan B cell antigens CD19, CD20, CD22, and CD79a.4 Typically, they are negative for CD5, CD10, and CD23.

Characteristically, MZL of the MALT type affects older patients and may remain localised for years,5 while disseminated disease involving bone marrow and peripheral blood is rare.3 Localised tumours may be cured with local irradiation, whereas disseminated stages of the disease are not curable and transformation into a large cell NHL may occur.4

We report a case of conjunctival MZL of the MALT type with an unusual clinical appearance, an CD5+ immunophenotype, and a history of idiopathic non-specific anterior uveitis.

CASE REPORT

A 79 year old man was referred to our hospital with a 3 month history of right eye discomfort and an epibulbar mass below the upper eyelid. Ophthalmological examination of the right eye revealed a reddish palpable tumour, 1.5 cm in diameter, located in the upper conjunctiva (Fig 1C). The extraocular movements were normal. Cornea and anterior chamber appeared clear; however, cortical and nuclear opacities were noted in the crystalline lens. Posterior segment examinations showed areas of confluent drusen and retinal pigment epithelium atrophy, with a normal optic disc. The patient’s left eye had suffered from a severe anterior uveitis 30 years earlier and some recurrences, resulting in subsequent phthisis bulbi. Slit lamp examination revealed a low flare without cells in the anterior chamber, an indication of persisting vascular damage, moreover posterior synechiae. Lens opacification and age related macular degeneration were similar to the right eye. Because of the age related macular degeneration and the cataract visual acuity was “only” 20/100. For the right eye, for the phthisis left eye counting fingers/1 metre. The intraocular pressure was normal for the right eye (17 mm Hg), but hypotonic for the left eye (7 mm Hg). Because the uveitis was not due to any systemic or ocular disorder (characterised by blood chemistry tests and anterior chamber tap) it has to be diagnosed as idiopathic non-specific uveitis.

Orbital magnetic resonance imaging (MRI) showed a supraequatorial lesion that surrounded the right eyeball (Fig 1A and B). Computed tomography (CT) scans demonstrated an intact bone structure of the orbit and no abnormalities were seen in the remaining skull, body or abdomen. As extensive as possible the anterior, visible part of the epibulbar lesion was surgically resected (Fig 1C and D), formalin fixed and paraffin

![Figure 1](http://www.bjo.bmj.com/fig/1a.png)  (1A) Orbital magnetic resonance imaging (MRI) shows a supraequatorial and epibulbar tumour (arrow) with extension to the deep orbit of the right eye (arrowheads). (1B) On equatorial sectional plane, MRI revealed tumour masses surrounding the optical nerve (arrowheads). The optical nerve appears not to be infiltrated. (1C and 1D) The epibulbar mass are immunoreactive for the B cell marker CD79a (left), whereas only few intermingled normal T cells express CD3 (right). Immunoreactive cells are indicated by a red membranous signal. APAAP technique, counterstaining by haematoxylin, magnification ×400. (2B) Monoclonal antibody MIB1 recognises a relatively low tumour growth fraction of about 10%. Proliferating cells are indicated by a red nuclear or cytoplasmic signal. APAAP technique, counterstaining by haematoxylin, magnification ×400. (2C) Most primary ocular NHL are of B cell origin, either of the follicular, diffuse small, or mixed cell type.1
embodied sent to the pathology department of Justus-Liebig-Universität Giessen, Germany, for immunohistological studies (Fig 2). Immunohistochemistry was done on the routinely formalin-fixed, paraffin embedded biopsy specimen after microwave pretreatment. Sections were pretreated with 10 mM citrate buffer (pH 6.0) for 10 min and endogenous peroxidase was blocked with 3% hydrogen peroxide solution. Sections were incubated with the following primary antibodies: CD5, CD20, CD43, CD79a, PAX5, CD3, CD56, CD10, CD45RO, CD200, CD21, CD138, Vimentin, and Bax. After rinsing in PBS, the sections were incubated with the secondary antibody and visualized using a DAB reaction for CD10, CD23, and CD30 were negative.

General physical examination of the patient showed no abnormalities. There were no lymphadenopathy or hepatosplenomegaly. Peripheral blood smears as well as bone marrow aspiration biopsy showed no signs for a disseminating lymphoma. All haematological and biochemical parameters were within the normal range. The exception of slightly elevated tyrosine kinase (8 U/l) and β2-microglobulin levels (2.9 µg/l) suggestive for intensified cell growth. In conclusion, the final diagnosis of a low malignant conjunctival MALT lymphoma was established and confirmed by the German reference centre (Prof M-L Hansmann, University of Frankfurt). The patient underwent radiotherapy (40 Gy) of the right orbit (fractionated to 5 × 2 Gy/week). After radiotherapy, the lesion decreased markedly. No recurrence of the orbital lesion or any systemic involvement was noted during the follow up period of 18 months.

COMMENT

The immunophenotypic profiles of low grade B cell NHL are complex and still under investigation. Especially the T cell antigen CD5 is of interest. B cell NHL are complex and still under investigation. Especially the T cell antigen CD5 is of interest. Since CD5+ B cells were found in the lymph glands, lymphoepithelial lesions were not detected by VS38c and reactivity for CD10, CD23, and CD30 was negative.

Since increased numbers of CD5+ B cells are found in blood of patients with autoimmune diseases, CD5+ B cells are thought to exert an immunoregulatory function. Whether CD5 expression is relevant to the prognosis of patients with MALT lymphoma is controversial.

The association of MALT lymphomas with diverse autoimmune disorders, especially Sjögren’s syndrome and Hashimoto’s thyroiditis is well known. Until now, the pathogenetic link of this relation is not clear, but an influence of a long standing inflammation and a change of immunological lymphoid subtypes is discussed to promote the development of MALT lymphoma. Perhaps there is also a (autoimmune) correlation of anterior uveitis (of the contralateral eye) and MALT lymphoma, as demonstrated here, but it cannot be proved and is perhaps incidental.

The differential diagnoses of our patient are MZLs, bearing the unusual CD5+ phenotype, chronic lymphocytic B cell leukaemia (B-CLL), and mantle cell lymphoma (MCL).

The last were excluded because of different morphological and phenotypic features. Furthermore, B-CLL and MCL are usually widespread at diagnosis showing diffuse lymphadenopathy, substantial lymphocytosis, and bone marrow involvement. Both diseases are non-aggressive and less malignant than MALT lymphoma and usually not curable. Although there was an extended growth from the epibulbar conjunctiva towards the deep orbit, our patient showed a localised stage of the disease, an indolent clinical course, and a favourable response to radiotherapy. Thus, we demonstrated an exceptional case of a conjunctival MZL of the MALt type with unusual CD5+ phenotype.

We thank Drs Irina Fenic, Joachim Woenckhaus, Karsten Küstenfeld, and Christian Vorwerg for critical reading of this manuscript.
not in his father and brother, suggesting that both conditions might belong to the same spectrum of a single genetic disorder. Microcephaly and lymphoedema (MIM152950) was first described by Leung in 1985 in five individuals in a four generation family. There was no mental retardation. Congenital lymphoedema has also been described in three other isolated cases of microcephaly-chorioretinopathy. In the present family, the microcephaly and lymphoedema of the feet in patients 1 and 2 was associated with mental retardation as well as chorioretinopathy. This suggests that the three disorders previously distinguished could be the variable expression of a single genetic condition.

Ophthalmological findings reported in the autosomal dominant syndrome of microcephaly-chorioretinal dysplasia syndrome (MIM156590) include chorioretinal dysplasia, myopic astigmatism, and retinal dystrophy. Chorioretinal dysplasia represents the most common ocular abnormality seen in all patients of this report. Microphthalmia as seen in the proband has been reported before. Closed angle glaucoma secondary to a persistent primary hyperplastic vireous (PHPV) has not been described. The spectrum of eye anomalies seen in the three patients of a single family clearly indicate the wide variety of ocular abnormalities that can be associated with a single genetic entity. Feingold and Bartoshesky and Limwongse et al suggested before that the three entities might represent the variable expression of a single entity. The clinical variability in the expression of this syndrome is remarkable. The proband of the present family had a severe multiple malformation syndrome, with anomalies of the heart, skeleton, and eyes. The presence of marked lymphoedema of the feet suggested the diagnosis which was confirmed upon examination of his brother and father, who had milder manifestations with microcephaly and developmental delay. Interestingly, the eye anomalies had not been diagnosed in either of them, and in addition the pedal oedema had disappeared. This suggests that all children with microcephaly, a careful eye examination is warranted.

In a sporadic patient with microcephaly, chorioretinal dysplasia, and mental retardation the clinical distinction between and autosomal dominant and recessive inheritance is not possible. However, the association with pedal lymphoedema could indicate probable autosomal dominant inheritance, since this has not been described in the autosomal recessive families.

Koen De Vriendt is a senior clinical investigator of the Fund for Scientific Research-Flanders (Belgium) (FWO). This paper was presented at the EPOG meeting Cambridge in September 2000 by I Casteels.
with BANFF 2B rejection, and given intravenous methylprednisolone 500 mg on the first day, tapered over 5 days to prednisone 30 mg/day. Creatinine level rose to 2.4 on day 35, and OKT3 (5 mg/day, intravenous) was begun.

On the fifth day of OKT3 therapy, the patient complained of right eye discomfort and redness. Over 2 days, the discomfort worsened and visual acuity fell, to 6/24+ on the right and 6/9 on the left. Marked conjunctival injection, keratic precipitates, iris vessel congestion, white cells in the anterior chamber, hypopyon, and trace anterior vitreous cells were present in the right eye. Inflammation obscured fundus details, but anterior uveitis was not detected by B-mode ultrasonography. The left eye exhibited conjunctival injection without intraocular inflammation.

Anterior chamber paracentesis from the right eye revealed white blood cells and no organisms. Cultures of aqueous humour and conjunctival swab were negative. Topical prednisolone 1% every 2 hours and hyoscine (scopolamine) 0.25% twice daily were begun in the right eye, and OKT3 was discontinued. Three days later, acuity improved to 6/18, conjunctival injection decreased, and the hypopyon resolved. Prednisolone drops were tapered and, within 5 days, vision improved to 6/6 in both eyes and OKT3 was discontinued. Swabs cleared. Over the next week, topical medica-
tions were tapered, then discontinued, with- out return of inflammation.

COMMENT

OKT3 is implicated as a cause of anterior uveitis in our patient because of onset of inflammation soon after initiating OKT3 therapy, accelerated resolution of inflammation following discontinuation of OKT3, and lack of identifiable infectious aetiologies. We did not further pursue a cause and effect relation through OKT3 rechallenge because renal status had improved. It is unclear whether OKT3 acted alone or in combination to induce uveitis. This type of synergistic drug interaction is reported for rifabutin induced uveitis, which may be potentiated by concur-
rent administration of fluconazole.5

The adverse effects of OKT3 include optic neuritis, abducens nerve palsies, conjunctivitis, scleritis, and blindness presumed due to photoreceptor toxicity.6 Non-inflammatory uveitis in patients taking OKT3 is not reported or known to the manufacturer.

While efficacy of OKT3 against allograft rejection is based on suppression of CD3+ T lymphocytes, OKT3 side effects may result from stimulation of separate immune path-
ways. For instance, aseptic meningitis and encephalitis may result from activation by OKT3 of non-CD3 T cells that then attack neural antigens.7 OKT3 induces a cytokine release, in which interleukin-6, tumour necrosis factor, and other mediators are released by lymphocytes; these agents are also implicated in uveitis.8 Production of anti-
OKT3 and other antibodies, and complement activation, also occur with OKT3 therapy, and may contribute to inflammation by immune complex formation with ocular or other antigens.9 Although vitritis may develop dur-
ing immune recovery in patients with AIDS and retinitis,10 it is unlikely that enhanced immune activity associated with acute rejection is relevant in our patient, since uveitis began only after additional immunosuppres-
sive therapy was given. A direct toxic effect of OKT3 in ocular tissues has not been reported.

In conclusion, severe anterior uveitis occurred during treatment with OKT3, and resolved with OKT3 withdrawal and topical therapy.

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Accepted for publication 31 October 2000

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Maxillary sinus non-Hodgkin's lymphoma with orbital and intraocular involvement in the acquired immunodeficiency syndrome

EDITOR,—In spite of its rare occurrence there is a well established association between the acquired immune deficiency syndrome (AIDS) and lymphoma, which most of the time is a highly malignant B cell type affecting the central nervous system (CNS).1 Rare cases of lymphomas involving para-

cal sinus, orbit, and intraocular structures have been described. This report describes a case of primary lymphoma of the maxillary sinus with orbital and intraocular secondary involvement.

CASE REPORT

A 28 year old man with AIDS presented with right proptosis and recurrent sinitis. His CD4+ count was 3 cells x10^3/l and viral load 1 343 145 copies. Skull and orbital computed tomograph (CT) scans demonstrated right maxillary sinus opacification, mild right propt-
osis, and an anterior superotemporal mass in the right orbit. Cerebral image was unremark-
able. The ocular examination disclosed right eye proptosis, ptosis, and a visible mass on the temporal area of superior right lid, restricting the spontaneous lid opening (Fig 1). There was bilateral lid oedema but no mass could be found on the left side. Right eye movements were restricted. Papillary reflexes were normal in both eyes, and visual acuity reached 6/12 right eye and 6/6 left eye. Fundus examination revealed a left choroidal lesion measuring approximately 1 disc diameter superior to the disc (Fig 2). Lid infiltration prevented right fundus examination, but a B-scan

Figure 2 Left fundus showing choroidal lesion measuring approximately 1 disc diameter superior to the disc.
COMMENT
Classically, the AIDS associated lymphomas are of the B cell type and involve the CNS and the abdominal cavity, as opposed to the preferential ganglion involvement seen in immune competent patients. Such cases usually develop at advanced disease stage. Primary maxillary sinus lymphomas are rare, as is secondary orbital involvement. Malignant parasanal sinus tumour secondarily involves the orbit in 45% of the cases, but lymphomas are uncommon. Primary and secondary orbital lymphomas are rare, and bilateral occurrence is very unlikely. Rare cases of intraocular primary lymphomas were also previously described. Our patient had bilateral involvement of the sinuses, orbit, and intraocular structures, which was suspected by CT scan, and although we didn’t obtain a specimen from the choroidal lesions for histological confirmation, the disappearance of the left lesion and the scarring on the right fundus just after treatment supports lymphoma as the diagnosis for the intraocular lesion. The immunohistochernistry was CD20 (L26) positive, and negative for all the other markers (CD3, CD30, Lambda, Kappa, S-100 protein, HMB-45), confirming the B cell origin.

Non-Hodgkin’s lymphoma in HIV infected patients tends to be of high grade malignancy, being very aggressive most of the times, with a mean survival of around 8 months. Our patient died after 3 months in spite of initial good response to chemotherapy.

Lymphoma treatment is still controversial. Radiotherapy has demonstrated good results for treatment of both systemic disease and in cases of orbital and intraocular involvement. On the other hand, chemotherapy has been good for systemic disease but has not been successfully used for intraocular disease. Interestingly, our patient had a significant improvement after chemotherapy, but that was shortly followed by an intense reactivation, which was probably due to the high grade of malignancy.

Lymphomas associated parasanal sinus, orbital, and intraocular lymphomas are considered to be very rare tumours, and even though their incidence has decreased in the HAART era, clinicians should be aware of this potential manifestation of non-Hodgkin’s lymphoma.

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Accepted for publication 1 November 2000


Pythium insidiosum keratitis confirmed by DNA sequence analysis

EDITOR,—Pythium insidiosum is an unusual but serious ocular pathogen. Although the organism grows as a mycelium in tissue, it is not a member of the fungal kingdom and its identification can be a challenge for a routine laboratory. We report a case of Pythium keratitis in which the organism was confirmed by nucleic acid sequencing.

CASE REPORT
A 32-year-old man was referred from Kuala Lumpur having suffered with intractable keratitis of the left eye for 4 weeks. He gave a history of diabetes, disposable contact lens wear, and swimming in the Kelang River. Routine microbiological investigations had been negative. At presentation to Flinders Medical Centre, he was on topical antibiotic, antifungal, and anti-amoebic medication. He had a large epithelial defect, a deep stromal infiltrate approaching the limbus, and hypopyon (Fig 1, top). His visual acuity was hand movements approaching the limbus, and hypopyon (Fig 1, top). His visual acuity was hand movements. The drops were stopped and corneal scrapings were taken. Gram and Giemsa stains were negative. A biopsy was performed the following day and hyphae were observed in sections. A filamentous organism appeared in cultures of the original scrapings. There was no response to continued antifungal treatment and a penetrating graft was performed 4 days after the biopsy. Postoperatively, the patient received oral tiranazonazole and topical natamycin. Prednisolone phosphate drops were introduced 10 days later. Twice in the first 3 weeks after surgery the patient returned to theatre for an anterior chamber washout of proliferative material invading from the peripheral cornea (Fig 1, bottom). Hyphae were seen in these specimens, but cultures were negative. The patient returned to Malaysia and, 7 months postoperatively, had a clear graft, useful vision in the eye, and no recurrence of infection.

The histopathology revealed a florid keratitis with necrotic stroma and degenerate neutrophils and monocytes. Massive numbers of hyphae were seen in silver-stained sections, particularly in the anterior stroma (Fig 2, top). Hyphae were also observed penetrating Descemet’s membrane. The organisms were not stained by the periodic acid-Schiff (PAS) method, also commonly used in suspected fungal infection, giving these sections the appearance of Swiss cheese (Fig 2, bottom).

Colonies grew rapidly on the primary fungal medium (plain Sabouraud’s agar, 28°C). They were white with a yellowish tinge, unusually flat, and difficult to cut and separate from the agar. Few septae and no spores were seen. The isolate was sent to a reference laboratory under suspicion of being a zygomycete. However, no further taxonomic clues were induced by standard measures so a molecular approach was employed. The methods have been described. Initially, a 510 base pair segment of the 18S ribosomal RNA gene was amplified (universal primers NS1 and NS2) and sequenced (Model 373A DNA sequencer, Applied Biosystems Inc). A search of databases (GenBank, EMBL) revealed homology to oomycetes. The isolate was then incubated for 48 hours in water containing autoclaved grass. Motile zoospores were observed, indicative of P. insidiosum. Other characteristic consistent with this identification were colony morphology, optimal temperature of growth (35°C), hyphal diameter (4–6 μm), and molecular blasts.

Figure 1 Pythium insidiosum keratitis. Top, the patient at presentation. Bottom, proliferative material in the anterior chamber after corneal transplantation.

Figure 2 Histopathology of the excised cornea (×625). Top, silver stain. Bottom, PAS. The organisms have not stained with PAS; their presence is indicated by the spaces in the section.
intercalary swellings in viable hyphae, vesicles at the end of spore discharge tubes, and spores germinating by means of germ tubes.  

To confirm the identification, the internal transcribed spacer (ITS) region defined by primers ITS1, the 5.8S gene and ITS2) was amplified. The 900 base pair product was sequenced by a direct double stranded DNA cycle method using primers 1–6 as detailed except for the substitution of primer 3 with 3c (5'-GCCAGTTCGGTGTTAGGACATT). The sequences were checked between complementary strands and shown to be 99.0% homologous with P insidiosum reference strain CBS777.84 using CLUSTAL V software (CA Lèvesque, personal communication). In comparison, the sequence was ~95% homologous with other Pythium species and ~90% homologous with other genera of oomycetes (BLAST database, NIH, Bethesda, MD, USA).

**COMMENT**

*P. insidiosum* is an aquatic, filamentous organism that produces heterokont, biflagellate zoospores, placing it as an oomycete in the kingdom *Chromista*. The only other human pathogen in this kingdom is *Rhinosporidium seeberi*, the agent of rhinosporidiosis. Oomycetes have a diploid genome and a cell wall consisting of cellulose compounds and glycan, features which distinguish them from the fungal groups of the kingdom Fungi. The identification of an oomycete in our patient can explain the PAS result and the lack of response to antifungals, there being no chitin or ergosterol in the cell wall, respectively. In response to antifungals, there being no chitin or ergosterol in the cell wall, respectively. In addition to our genetic approach to confirming the identification, serological tests have been developed in Bangkok and at the Centers for Disease Control, Atlanta.

Oomycetes play an important part in the decomposition and recycling of decaying matter. Some species are parasitic on crops and fish. In mammals, *P. insidiosum* causes a granulomatous disease (“swamp cancer”) in several species including horses and dogs. A number of cases of human pythiosis have been reported, mostly subcutaneous infections and arthritis in thalassaemic patients in farming communities of South East Asia. With respect to the eye, *P. insidiosum* has been responsible for periorbital infections in Australia and the USA and corneal ulcers in Thailand, Haiti, and New Zealand. Some patients have had no other medical history. Contact lens wear, exposure to river water, and diabetes were possible predisposing factors in our patient.

No cases of *Pythium* keratitis have been cured medically. A boy with facial pythiosis was cured without surgery by a 1 year course of terbinafine and itraconazole. For the cornea, however, it would be difficult to imagine a successful outcome given the destructive nature of the organism, the slow response if any to most antimicrobial agents, the probable delay in identification, and the need to prevent further tissue invasion. Transplantation may be the best option.

The introduction of corticosteroids in the treatment of fungal keratitis and, presumably, *Pythium* infection, must be approached with great caution. We gave prednisolone in the hope of reducing inflammation in the grafted cornea without encouraging a recurrence of the disease. It was fortunate that, apparently, no infectious elements had been left in the eye.

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Accepted for publication 23 October 2000

Refractive, keratometric, and topographic determination of astigmatic axis after penetrating keratoplasty

EDITOR,—We read with interest the article by Sarhan et al on the effect of divergence between refractive, keratometric, and topographic determination of astigmatic axis on suture removal after penetrating keratoplasty. The authors make some fundamental errors in their use of vectors for the calculation of mean astigmatism and have failed to refer to the dependence of astigmatism on the overall refractive power. As clearly discussed by several authors,1–4 it is inappropriate to analyse astigmatism without analysing the overall change in refractive power. The authors state that the two groups (agreement and disagreement) were comparable before suture removal in the preoperative vector of astigmatism but do not present the mean presuture removal vector. The authors appear to calculate a mean of the scalar component of astigmatism. Vectors have both direction and magnitude and cannot be averaged in this way; doing so leads to erroneous and incorrect conclusions. It is also of concern that no post-suture leads to erroneous and incorrect conclusions. The authors need to determine what to what extent the direction and degree of change in astigmatism was in the direction of the suture removed and how this differed between the two groups. The presence of pseudophakia is also relevant, since there may be an influence from non-corneal astigmatism. A table including details of each subject’s refractive and keratometric data or refractive data are presented. It is also of concern that no post-suture means or comparison of these data have been carried out.1–4

The fundamental advantage of the Jaffe formula is its inherent consistency between refractive and keratometric changes and its sound mathematical basis.5 The authors of the letter make the valid comment that natural changes in refraction, keratometry, and topography might occur as part of the natural evolution of the cornea after penetrating keratoplasty. This is correct but again a very theoretical consideration. In practice, in the presence of significant post-keratoplasty astigmatism, most corneal surgeons will not wait and hope for natural progression to obviate the error. Intervention in the form of suture removal is undertaken between 4–6 months post-graft in order to influence the existing astigmatism. Such intervention does indeed influence the astigmatism, usually favourably. Rate of change of astigmatism following cataract extraction. Trans Am Ophthalmol Soc 1983;vol 81:201–3.


Reply

EDITOR,—Kaye and colleagues make valid though theoretical comments regarding vector analysis in the evaluation of post-keratoplasty astigmatism. We did use a software program for vector analysis based on the Jaffe and Clayman1 method of analysis of the vectors. Several formulas2–4 have been adopted to determine surgically induced astigmatism by vector analysis and further modifications have been carried out.1–4 The authors need to deter-
Argon laser and trichiasis: a helpful tip

Editor.—Trichiasis is a posterior misdirection of eyelashes. Owing to constant corneal irritation it can give rise to discomfort, recurrent infection, corneal ulceration, and pannus formation. Several modalities of treatment exist which include electrolysis, cryotherapy, and argon laser thermoablation. Argon laser offers the advantage of being a relatively simple, virtually painless method of destroying the eyelash follicle. It is especially useful when there is a need to limit contiguous tissue inflammation and destruction—for example, ocular pemphigoid. Argon laser can be precisely applied to the follicle with or without topical anaesthesia. A beam size of 50 μm, for a duration of 0.1 second and energy levels of 400–500 mW is normally used in our clinic.

Thermoablation depends on the absorption of argon laser by pigment. In our experience, patients with chronic trichiasis, who have undergone repeated removal of eyelashes with other available methods, have pale hypopigmented lashes which do not absorb sufficient laser energy. This makes it difficult and sometimes impossible to get a result in spite of increasing the energy levels. Recently, we have used a blue marker pen to mark the base of the offending eyelash with the result that argon laser is better absorbed by the blue pigment. Once there is initial uptake subsequent shots down the lash root can be easily completed.

In conclusion, we have found the simple and inexpensive technique of marking eyelash bases useful in increasing the efficacy of argon laser photoepilation.

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Optokinetic nystagmus in patients with central field defects

Editor.—We read with interest the article by Valmaggia et al. who studied optokinetic nystagmus (OKN) in patients with macular degeneration. They noted abnormalities of OKN gain only in patients with large central scotomas. Therefore, an intact macula seems not to be necessary for the generation of OKN. This implicitly suggests an important role of the peripheral retina in eliciting an OKN. In this context, it is interesting to note that we observed an inverted OKN in some patients with defects of the central visual field. This suggests an important role of the peripheral retina to induce an OKN in the inversed direction, countering the OKN in the classic direction. In this central-peripheral interaction, we proposed an important role for spatial-selective attention. It would be very interesting to find a method to monitor direction of attention simultaneously with OKN.

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Unfavorable Results of Eyelid and Lacrimal Surgery: Prevention and Management


Dr Mauriello has relied on his vast clinical experience to put together an authoritative treatise on the prevention and management of problems in eyelid and lacrimal surgery. Each chapter in the three large sections—esthetic eyelid and midface surgery, functional eyelid surgery, and lacrimal surgery—has contributions by one set of authors and is preceded by introductory comments from the editor. The authors describe in detail their approaches to the very specific complications associated with particular surgical interventions.

The uniqueness of the text lies in its layout, as Dr Mauriello has enlisted the assistance of colleagues in various subspecialties of ophthalmic plastic surgery, head and neck surgery, and dermatological surgery to ophthalmology. Each chapter is deliberately intended to bring a diverse range of views on these topics. A concluding editorial nicely summarises the expert commentary from each chapter.

Although this text can be read and enjoyed by a wide audience of medical practitioners, it will be most appreciated by ophthalmologists, ophthalmic plastic surgeons, plastic surgeons, and others performing surgery in the pericu- lar region. The eyelid surgery sections are par- ticularly timely and well outlined, covering essential topics such as endoscopic forehead elevation, laser resurfacing, and congenital blepharoptosis surgery. A wide spectrum of lacrimal disorders from infancy to adulthood are also described, including the management of lacrimal sac tumours, Relevant histopathol- ogy, neuroimaging, and schematic diagrams serve to emphasise surgical or anatomical principles where necessary. The scope of the text may be expanded for residents in the early stages of their training, but it does provide some indication of the breadth of knowledge and surgical techniques that need to be mastered in order to optimise functional and aesthetic surgical results. The intraopera- tive photographs, with meticulous attention to detail, provide careful instruction as to how to carry out surgical techniques with maximum success yet minimal complications. For surgeons embarking on a career in ophthalmic plastic surgery, or for established surgeons interested in optimising surgical results, this text is a welcome addition to any collection of surgical literature.

DAN DEANGELIS

Neuro-ophthalmology Review Manual


The Neuro-ophthalmology Review Manual is the 5th edition of a well established favourite. The intention, as with previous editions, is to provide a readable compendium of “no nonsense” neuro-ophthalmology for neuro-ologists, neurosurgeons, and ophthalmologists. The first edition of the book was envisaged as a coaching manual for the US Board examinations, but subsequent editions have been expanded in the hope of providing, in addition, a practical guide to the management of patients in the clinic and on the wards.

Apart from the senior author (Lanning B Kline) there are six contributing authors. The text of 280 pages is divided into 20 chapters, two of which on the pharmacology and performances of higher visual function are completely new. The other chapters cover the full range of neuro-ophthalmic subject matter, including the major problems of disorders of eye movement, visual fields, pupils, and the optic disc. There are also chapters on the trigeminal nerve, the facial nerve, eyelid disorders, headache, carotid artery disease, and hysteria and malingering. The chapters are not formally referenced, but it is supplemented with bibliography of books, chapters, and original articles. The information is in note format, with line diagrams and a few tables.

Generally speaking an enormous amount of information is condensed into each chapter, but is readily accessible because of the layout. Mostly the information is clinically useful, with an emphasis on lists of differential diagnoses and pointers towards the diagnosis of individual conditions. Clinical data are heavily on clinical diagnosis, with little detail on laboratory tests, imaging, etc, and virtually none on management. For this reason on occasion some of the information seems rather arcane, and seems to predate the modern imaging era.

Examination candidates will find the dogmatic approach in some chapters—for example, “The six syndromes of the sixth nerve” or “The five syndromes of the fourth nerve”—very helpful in evolving a rigorous examination technique for topical diagnosis, as well as a useful way of retaining a lot of information. On the other hand any ophthalmologist would find it useful to be reminded of the essentials of, for example, disorders of the facial nerve or of higher visual function when confronted with such a patient in the clinic.

All in all this book is a mine of useful information. It is comprehensive and covers the vast majority of practical neuro-ophthalmic scenarios, which may confront the ophthalmologist. It can be recommended as a revision aid for the Part 3 membership exam. It would be a useful quick reference book for both the ophthalmic casualty and the neuro-ophthalmology clinic.

JOHN S ELSTON

BOOK REVIEWS
NOTICES

National prevention of blindness programmes and Vision 2020
The latest issue of *Community Eye Health* (36) discusses national prevention of blindness programmes. For further information please contact *Community Eye Health*, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EL. (Tel: (+44) (0) 20-7608 6909/ 6910/6923; fax: (+44) (0) 7250 3207; email: eyeresource@ucl.ac.uk) Annual subscription £25. Free to workers in developing countries.

Second Sight
Second Sight, a UK based charity whose aims are to eliminate the backlog of cataract blind in India by the year 2020 and to establish strong links between Indian and British ophthalmologists, will be sending volunteer surgeons to India early in 2001. Details can be found at the charity website at www.secondsight.org.uk or by contacting Dr Lucy Mathen (lucymathen@yahoo.com).

2nd Interdisciplinary Symposium on the Treatment of Autoimmune Disorders 2001
The 2nd Interdisciplinary Symposium on the Treatment of Autoimmune Disorders 2001 will take place on 7–9 June 2001 at the University Hospital, University of Kiel, Kiel, Germany. Further details: Prof Dr Med Michael Sticherling, Department of Dermatology, University of Kiel, Schittenhelmstrasse 7, D-24105 Kiel, Germany (tel: +49-431 597 1512; fax: +49-431 597 1611; email: msticherling@dermatology.uni-kiel.de).

European Intensive Program of Disease and Imaging of the Fundus
The European Intensive Program of Disease and Imaging of the Fundus under the auspices of the European Program Socrates will be held 2–12 July 2001 at the Clinique Ophthalmologique Universitaire, 40 avenue de Verdun, 94010 Créteil, France. Further details: Béatrice Rousseau (tel: (33 1) 45 17 52 22; fax: (33 1) 45 17 52 66).

American Institute of Ultrasound in Medicine—Millennium Ultrasound Course Series
A course entitled “Obstetrical and Gynecological Ultrasound” will be held in New York City, NY, on 24–26 August 2001. Further details: Stacey Bessling, Public Relations Coordinator, AIUM, 14750 Switzer Lane, Suite 100, Laurel, MD 20707-5906, USA (tel: 301-498-4100; email: sbessling@aium.org).

14th World Congress of the International Society for Laser Surgery and Medicine
The 14th World Congress of the International Society for Laser Surgery and Medicine is to be held on the 27–30 August 2001 at Sri Ramachandra Medical College and University Hospital, Chennai, India. The American Society of Lasers in Medicine and Surgery has indicated that it will designate the 14th World Congress of ISLSM as its society’s co-sponsoring meeting. A pre-conference course and separate sessions in ophthalmology will be held as a part of this international meeting. Further details: Dr B Krishna Rau, President, 14th World Congress of the International Society for Laser Surgery and Medicine, Department of Surgery, D2 Ward, Sri Ramachandra Medical College and Research Institute, Porur, Chennai - 600 116, India (tel: 91-44-4765856; 4768027-28, 8527776, 8594804; fax: 91-44-8594578, 4767008; email: krishnar@iiasmd01.vsnl.net.in and website: www.medindia.net/islsm2001).

31st Cambridge Ophthalmological Symposium
The 31st Cambridge Ophthalmological Symposium will be held 3–5 September 2001 at St John’s College Cambridge. The subject is Retinal Detachment. Further details: COS Secretariat, Cambridge Conferences, The Lawn, 33 Church Street, Great Shelford, Cambridge CB2 5EL, UK (tel: 01223 847464; fax: 01223 847465; email: b.ashworth@easynet.co.uk).

1st Asia Pacific Forum on Quality Improvement in Health Care
The 1st Asia Pacific Forum on Quality Improvement in Health Care will be held from 19–21 September 2001 in Sydney, Australia. Presented by the BMJ Publishing Group (London, UK) and Institute for Healthcare Improvement (Boston, USA), with the support of the Commonwealth Department of Health and Aged Care (Australia), Safety and Quality Council (Australia), NSW Health (Australia) and Ministry of Health (New Zealand). Further details: quality@bma.org.uk; fax +44 (0) 7383 6869.

41st St Andrew’s Day Festival Symposium on Therapeutics
The 41st St Andrew’s Day Festival Symposium on Therapeutics will be held on 6–7 December 2001 at the Royal College of Physicians of Edinburgh. Further details: Ms Eileen Strawn, Symposium Co-ordinator (tel: 0131 225 7324; fax: 0131 220 4393; email: e.strawn@rcpe.ac.uk; website: www.rcpe.ac.uk).

4th International Conference on the Adjuvant Therapy of Malignant Melanoma
The 4th International Conference on the adjuvant therapy of malignant melanoma will be held at The Royal College of Physicians, London on 15–16 March 2002. Further details: Conference Secretariat, CCI Ltd, 2 Palmerston Court, Palmerston Way, London SW8 4AJ, UK (tel: +44 (0) 20 7720 0600; fax: +44 (0) 20 7720 7177; email: melanoma@confcom.co.uk; website: www.confcom.co.uk/Melanoma).

XXIXth International Congress of Ophthalmology
The XXIXth International Congress of Ophthalmology will be held on 21–25 April 2002 in Sydney, Australia. Further details: Congress Secretariat, C/- ICMS Australia Pty Ltd, Box 2609, Sydney, NSW 2001, Australia (tel: +61 2 9241 1478; fax: +61 2 9251 3552; email: ophthalm@icmsaust.com.au; website: www.ophthalmology.aust.com).

International Society for Behçet’s Disease
The International Society for Behçet’s Disease was inaugurated at the 9th International Congress on Behçet’s Disease. Professor Shigeaki Ohno represents the ophthalmology division (Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, Sapporo, Japan: tel: +81-11-716-1161 (ext 5944); fax: +81-11-736-0952; email: sohno@med.hokudai.ac.jp). The 10th International Congress on Behçet’s Disease will be held in Berlin 27–29 June 2002. Further details: Professor Ch Zouboulis (email: zoubbere@zedat.fu-berlin.de).

CORRECTION

A mistake occurred in a letter to the editor by Badenoch et al published in the April issue of *BJO* (2001;85:502–3). In the last sentence of the third paragraph under the heading “Case report” the hyphal diameter is given as 4–6 mm; this should be 4–6 µm.