Disappearance of eyelid xanthelasma following oral simvastatin (Zocor)

The major risk factors for coronary heart disease include smoking, elevated blood pressure, and elevated serum cholesterol. Risk reduction starts with identification of those at risk and then alteration of factors such as discontinuation of smoking, lowering of blood pressure, and reduction of serum cholesterol. Patients who should have blood cholesterol testing include those with family history of premature coronary heart disease or hyperlipidaemia, personal history of coronary heart disease, or clinical evidence of elevated lipids with features of xanthelasma, corneal arcus under age 50 years, and cutaneous xanthomas at any age.1 Two of the latter clinical features are ophthalmic and detection relies on the ophthalmologist.

Xanthelasma appear as multiple yellow placcoid lesions in the pericocular skin and represent a concentration of lipocytes in the dermis.2 There are numerous methods to manage the cosmetic appearance of xanthelasma, which typically involves surgical excision or laser ablation.3 We report a novel approach to management using oral cholesterol lowering medication and patience.

Case report

In 1992, a 68 year old male smoker with a history of hypertension and elevated serum cholesterol was referred for evaluation of a newly diagnosed iris mass. On examination, the visual acuity was 20/20 in both eyes. The mass was diagnosed as a benign iris nevus and observation was advised. Coincidental bilateral medial canthal and upper and lower eyelid xanthelasmas were detected (fig 1A). The largest xanthelasma measured 16 mm in diameter. Observation was advised with tentative plan for surgical excision in the future. The patient was advised to continue his antihypertensive medications and anticoagulant medication (oral simvastatin (Zocor) 20 mg once daily). At the 6 month follow up the iris nevus was stable and the xanthelasmas persisted. Yearly examinations were advised. The patient did not return for 10 years. Surprisingly, the xanthelasmas had completely resolved, leaving no clinical trace of subcutaneous lipid (fig 1B). He continued on his medications and serum cholesterol was normal.

Comment

In the Lipids Research Clinics Program Prevalence Study, xanthelasma and corneal arcus were associated with increased levels of serum cholesterol and low density lipoprotein cholesterol (LDL-C), especially in young males.4 People with either lesion had increased odds of having type IIa dyslipoproteinaemia. Adjusted odds ratios for ischaemic heart disease in participants with xanthelasma and corneal arcus were generally increased. The study concluded that the clinical findings of xanthelasma or corneal arcus, especially in young people, helped to identify those with plasma lipoprotein abnormalities.5

Management of patients with elevated LDL-C include both low cholesterol diet and cholesterol lowering medications, the most popular of which are the statins. There are currently five statin drugs on the market in the United States and these include lovastatin (Mevacor, Altocor), simvastatin (Zocor), pravastatin (Pravachol), fluvastatin (Lescol), and atorvastatin (Lipitor). The major effect of these medications is to lower LDL-C by slowing down the production of cholesterol and by increasing the liver's ability to metabolise the LDL-C in the blood. Statins reduce LDL-C by approximately 40% and produce a modest increase in high density lipoprotein-cholesterol (HDL-C). These medications are given daily in the evening to take advantage of the fact that the body makes more cholesterol at night. Statins reduce measured blood LDL-C within 4–6 weeks. In a study of 20 536 patients, this resulted in long term reduction in coronary heart disease, stroke, and mortality.6

Simvastatin is derived synthetically from a fermentation product of Aspergillus terreus. Simvastatin is hydrolysed to an inhibitor of an enzyme responsible for cholesterol synthesis. In the Multicenter Anti-Atheroma Study, simvastatin slowed the progression of atherosclerosis, measured by vascular stenosis diameter on angiography, and decreased significantly the development of new lesions.7

To our knowledge, there have been no previous reports on the effect of statins on eyelid xanthelasma. A PubMed search for keywords “statin and xanthelasma” and simvastatin and xanthelasma yielded no relevant publications. The management of eyelid xanthelasma includes surgical excision, microsurgical inverted peeling, laser inverted resurfacing, photovaporisation using carbon dioxide laser, and application of bichloracetic acid. Patients with the highest recurrence rate are those with elevated cholesterol. These local treatments do not address possible systemic associations. By observations in this report, we suggest that serum cholesterol be evaluated and if elevated, oral statin combined with dietary cholesterol restriction might result in resolution of xanthelasma over time, but, more importantly, reduction of patient cardiac risk.

References

New onset diplopia: 14 years after retinal detachment surgery with a hydrogel scleral buckle

In 1979, the hydrogel explant (Miragel, Waltham, MA, USA) was introduced as a scleral buckling material in the surgical management of retinal detachment. It was widely used in the 1980s and early 1990s as it was initially believed to be well tolerated, less prone to infection, and easy to manipulate. However, long term complications related to swelling and fragmentation of the explant have been reported over recent years, resulting in discontinuation of its use in 1999.

Case report
A 36 year old healthy man presented on 2003 with symptoms of mild right ocular discomfort. Past ocular history included a right retinal detachment repair 14 years previously, using a 907 (3 x 5 mm) Miragel scleral buckle (Miragel, Medical Instruments Research Associates, Waltham, MA, USA), sutured to the inferior sclera. On examination, visual acuity was 20/120 right and 20/20 left. There was no diplopia or limitation of eye movements. What was thought to be a small conjunctival cyst was noted inferiorly but, otherwise, the ocular examination was unremarkable and the retina was secure.

A year later (2004), he presented with increasing marked right ocular discomfort and diplopia in all fields. His visual acuity was unchanged, but there was marked restriction of elevation and reduction in adduction of the right eye and binocular diplopia in all fields of gaze. A tense swelling of the inferior conjunctiva was noted (fig 1, top), intraocular pressure was normal, and the retina was flat.

Intraoperatively, exploration revealed no conjunctival cyst, but a large encapsulated scleral buckle. The explant was friable, gel-like, and translucent, but could be removed like, and translucent, but could be removed easily. Computed tomography (CT) (fig 1, bottom) demonstrated a right orbital circumferential soft tissue mass surrounding lower half of the globe and a small area of calcification on the inferotemporal sclera.

In our case, there was a profound increase in the explant volume during a 14 year period. The resulting diplopia and restriction of extraocular movement as well as the clinical evaluation mimicked a giant orbital inclusion cyst. The correct diagnosis was only made intraoperatively. Scleral thinning and necrosis as seen in our case has been reported previously, resulting in intraoperative vitreous leak after removal of the expanded explant. In our patient, there was an area of thinned sclera, but the surrounding calcification and the early removal of the explant prevented vitreous leak.

It is important to note that patients who have undergone scleral buckling with hydrogel explants before 1995 are at risk of developing this complication. Symptoms of progressive diplopia, pain, and restriction of extraocular muscle movement in these patients should also raise the possibility of explant expansion. The assistance of a retinal surgeon may sometimes be required because of the increased risk of scleral thinning and leakage of liquid vitreous intraoperatively.

References

Inverse globe retraction syndrome complicating recurrent pterygium

Often larger and more aggressive than the original lesion, recurrent pterygia can cause visual symptoms that are most often secondary to their mechanical effects on the cornea. We report a case of inverse globe retraction syndrome (that is, retraction during abduction) due to the restrictive effect of a recurrent pterygium and the management of this complication.

Case report
A 28 year old man without a medical history or ocular symptoms underwent pterygium excision to his left eye with a superotemporal conjunctival autograft and intraoperative mitomycin C. Three weeks postoperatively, he noted a feeling of pressure in the left eye...
and diplopia during left gaze. Two months postoperatively she presented to us and her ophthalmic examination was significant for the following—left eye: 2 mm enophthalmos relative to right eye, recurrence of the pterygium, globe retraction during left gaze secondary to a leaft effect from the recurrent pterygium, and minimal abduction deficiency (fig 1). One month later, his examination was stable and surgery was scheduled. Intraoperatively forced ductions showed –1 (on a scale of 1 to 4) limitation of abduction in the left eye. The left eye was positioned in abduction and a 3 mm vertical incision was made in the nasal conjunctival 3 mm posterior to the limbus. A 5–6 mm graft of amniotic membrane (locally procured and kept frozen before use) was sutured in the conjunctival autograft with adjunctive mitomycin C; however, because aggressive recurrence is still possible initial pterygium surgery should only be performed for patients with significant cosmetic and/or functional concerns. For the management of inverse globe retraction syndrome complicating recurrent pterygium in this case, the use of amniotic membrane as a tissue spacer permitted excellent functional improvement.

Figure 1  The patient’s appearance at presentation in (A) primary gaze, (B) right gaze, (C) left gaze. There is relative enophthalmos in the left eye that increases during left gaze. During right gaze, adduction in the left eye occurs with less effort than abduction in the right eye.

Comment
Inverse globe retraction syndrome is rare. It has been reported as being caused by medial rectus abnormality, innercational misdirection, and secondary to restriction from traumatic tissue capture in the medial orbital wall. The current case demonstrates another cause for the syndrome, globe restriction as a result of a leak effect from aggressive pterygium recurrence. The risk of pterygium recurrence after initial pterygium removal is minimised by the technique of conjunctival autograft with adjunctive mitomycin C; however, because aggressive recurrence is still possible initial pterygium surgery should only be performed for patients with significant cosmetic and/or functional concerns. For the management of inverse globe retraction syndrome complicating recurrent pterygium in this case, the use of amniotic membrane as a tissue spacer permitted excellent functional improvement.

Figure 2  The patient’s appearance 6 weeks after amniotic membrane placement in (A) primary gaze, (B) right gaze, (C) left gaze. There is no longer globe retraction left eye during left gaze. During right gaze, adduction in the left eye occurs with effort similar to that needed for abduction in the right eye.

patients, although difficulty with figure-ground discrimination cannot be excluded.

Posterior cortical atrophy is a clinical and radiological diagnosis based upon the presence of occipitoparietal abnormalities with initially preserved occipitotemporal (face and colour recognition) and anterior cerebral function. It is thought to be as a result of Alzheimer’s disease, in most cases, although the syndrome has been described with other pathologies—for example, subcortical gliosis, Creutzfeld-Jakob disease, and progressive multifocal leukoencephalopathy. Although it is rare, it should be suspected in any patient presenting with visuospatial or visuospatial disabilities in the absence of any signs on standard ophthalmological examination. Screening tests for higher visual function deficits can then be employed.

The corollary of this is that a patient with an established diagnosis of dementia should be tested for disorders of higher visual function, because a patient with otherwise mild cognitive deficits may still be driving.

**References**


**Radial optic neurotomy in combined cilioretinal artery and central retinal vein occlusion**

Combined cilioretinal artery and central retinal vein occlusion (CRVO) is a rare clinical finding first described by Oosterhuis. The pathogenesis of this condition is not well established and remains controversial. Most reports postulate that the initial CRVO causes an elevation of the intraocular pressure, which induces a precedently reduced perfusion pressure at the arterial side. Since the perfusion pressure of the cilioretinal artery is lower than the central artery, it becomes relatively occluded. Recently, Oprenacak et al. described radial optic neurotomy (RON) involving pars plana vitrectomy (PPV) and radial incision of the optic nerve to treat CRVO. We report this new surgical approach in a patient with combined cilioretinal artery occlusion and CRVO.

**Case report**

A healthy 64 year old woman complained of unilaterally blurred vision for the past 3 days. Her visual acuity (VA) was 20/200 in the right eye (RE) and 20/20 in the left eye (LE). The anterior segment in both eyes was unremarkable on slit lamp examination. Fundus examination RE demonstrated a whitening of the macula corresponding to an area supplied by a cilioretinal artery. The retinal veins were dilated, accompanied by adjacent retinal haemorrhages (fig 1A). The fundus of the left eye appeared normal. Fluorescein angiography (FA) RE revealed a delayed arteriovenous (AV) perfusion time of 13 seconds. Systemic evaluation of the patient did not reveal any general disease. Although treated systemically with corticosteroids and low dose heparin for 4 weeks, she developed CRVO with severe disc oedema, extensive dilatation of the retinal veins, radial orientated intraretinal haemorrhages, and cotton wool spots (fig 1B). On FA there was a reduced perfusion time of the cilioretinal artery in addition to the typical
signs of CRVO (fig 2A). Based on positive results of RON in CRVO, we offered this treatment to our patient. After she signed an informed consent, RON was performed with two radial cuts at the nasal edge of the optic disc. After 2 days disc oedema was significantly reduced with sharp visible disc margins. Two months postoperatively the retinal haemorrhages, cotton wool spots, and disc oedema had improved and her VA improved to 20/25 RE (fig 1C). FA demonstrated a physiological AV perfusion time of less than 3 seconds and no signs of an occluded cilioretinal artery (fig 2B).

Comment

Combined cilioretinal artery occlusion and CRVO are discussed as a separate clinical entity in the literature, and its treatment by RON has not been described. Opremcak et al postulated that a surgical decompression of the optic disc and scleral ring by RON may contribute to an improved venous perfusion in CRVO. Our patient demonstrated additional signs of an arterial occlusion with delayed filling of the cilioretinal artery in the macula, which may induce permanent functional loss. The underlying pathomechanism of CRVO remain unknown, current discussions lean towards an intraluminal occlusion by a thrombus, increased extravasal pressure, or a combination of both as possible causes. In addition the therapeutic effect of RON is also questionable. It remains unclear as to whether RON causes a decompression of the optic disc increasing the ocular blood flow or induces the formation of new chorioretinal shunt vessels. In our case the goal of RON was to reduce the capillary pressure, therefore increasing the perfusion in the cilioretinal artery and thus improving central vision. Patients with combined occlusive AV disease may benefit from RON by improving their haemodynamic perfusion pressure, retinal anatomy, and consecuitive central visual function.

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References


MAILBOX

Value based medicine

In a fine recent editorial, Drs Melissa and Gary Brown raised issues at the nexus of health policy and clinical science. As utility assessment is relatively new to the visual sciences, understanding both the assumptions behind this work and the consequences of relaxing those assumptions is essential for the conduct of high quality research and appropriate interpretation of the results.

The use of community elicited utilities (that is, including people without the disease in the elicitation study) in economic valuation should be given more than minimal consideration. Meta-economic evaluations are intended to inform health policy makers by assessing the value society places on the cure or prevention of disease. Community based utilities typically reflect larger estimates of utility loss than those elicited from patients and result in a more favourable analysis of the cost-effectiveness of new interventions than those relying on patient elicited utilities. At the same time, estimating community elicited utilities requires the development of easily understood scenarios to assist community members in understanding the disease or condition with which the disease, after leading investigators prefer to rely on patient elicited utilities. Rather than dismiss the community elicited approach, economic evaluation in ophthalmology would be greatly facilitated by development of a catalogue of community elicited utilities related to old disease developed through the standard gamble or time trade-off methods or responses to health status questionnaires that include algorithms to estimate health utilities.

While the Browns caution against the use of functionality based health related quality of life instruments (for example, the NEI-VFQ) in economic evaluation, we would like to offer an alternative explanation for this concern. Most disease specific instruments are based in psychometric theory and designed to measure change in the patient’s self reported health status in investigator defined domains. Domain scores do not reflect the importance the respondent assigns to the activities, but scoring algorithms developed by the instrument designer. The result is a metric that is often meaningful to clinicians but does not reflect the value the patient or society places on the health state. This limits generalisability across disease groups, as well as investigators’ ability to comment on the most efficient method to screen for, or treat, an ophthalmic condition affecting multiple areas of physical, mental, or emotional function.

Finally, the standard gamble elicitation method should not be dismissed handily. More frequent use of the time trade-off reflects the method’s intuitive appeal rather than theoretical superiority. As opposed to the time trade-off in which the anchor event (typically, death, blindness, etc) occurs early in the future, in the standard gamble the event is immediate. This provides an estimate of the person’s risk preference unconfounded by time. The time trade-off consistently results in higher estimates of utility loss than the standard gamble, potentially resulting in an overestimation of the cost-effectiveness of treatment or prevention.

We hope that our comments will help future work to be pragmatic and theoretically sound. This is necessary if we are to properly characterise the appropriateness of our methods as well as the value of our findings.

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Authors’ reply
We thank Drs Kymes and Frick for their excellent letter regarding utility analysis as a health related quality of life instrument. We agree that the use of primarily function based quality of life instruments such as the NEI-VFQ-25 may result in missing many important variables in the quality of life arena, as well as limit applicability across all diseases. In contrast, preference based quality of life instruments, such as utility analysis, are applicable across all diseases and encompass all variables that comprise quality of life, as well as the weighting of those variables. Of great additional importance is the fact that preference based instruments can be used in healthcare economic analyses, especially utility analysis. Therefore, most function based instruments have not been successfully used.

Concerning the use of time trade-off and standard gamble utility analysis, we have found that the time trade-off methodology is easier for patients to comprehend and also is more sensitive to milder health states since there is risk aversion to the consequence of immediate death associated with the standard gamble variant. Froberg and Kane have also shown that the time trade-off method of utility has greater test-retest reliability, intra-rater reliability and inter-rater reliability than standard gamble methodology. In our experience, time trade-off utilities generally demonstrate better construct validity and a wider range between pre-intervention and post-intervention values than standard gamble utilities, thus resulting in more favourable cost utility analysis, rather then less favourable analyses.

With regard to quality of life respondents, we remain firm in our adherence to the fact that a basic pillar of value based medicine is the use of utility values obtained from respondents with a health state in question. We have found that utility value diminution in patients who actually have age related macular degeneration ranges from 10% to 75% greater than the decrement estimated by treating ophthalmologists for the same condition. This has been noted as well for non-ophthalmological health states. We disagree that community utility values generally overestimate the degree to which a disease decreases quality of life. In contrast, we and others have noted that community and provider participants asked to evaluate the quality of life associated with a health state using utility value analysis generally underestimate the decrement in quality of life compared to patients with that health state. In essence, patients who have lived with a health state are those best able to ascertain the quality of life associated with that health state. And it is usually worse than others imagine.

In conclusion, we thank Kymes and Frick for their interest and comments and look forward to additional awareness in the arena of value based medicine. As increasing numbers of those who allocate healthcare resources become aware that value based medicine allows for higher quality care (by incorporating quality of life parameters that evidence based clinical trials often ignore) and the most efficient use of resources, it will have a considerably greater role in the delivery of cost effective, quality healthcare. When that takes place, all will benefit.

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Cystoid macular oedema with trypan blue use
We read with interest the article by Gouws et al. on the apparent increased incidence of cystoid macular oedema (CMO) in phaco-emulsification patients when trypan blue was used to stain the anterior capsule. Trypan blue has been commonly used in anterior and posterior segment surgeries. However, studies on the use of trypan blue, both in the anterior and posterior segments, did not show apparent toxicity. Thus, it would be appreciated if the authors could clarify whether other ophthalmic con-founders were assessed in their study, including: (1) other causes of CMO such as diabetes, uveitis, and prostaglandin use; (2) operating time since phototoxicity from the operating microscope cannot be ignored; (3) whether the operation time is expected to be longer; (4) whether all patients received a fundus examination with dilated pupil after the operation. If these were only performed in patients with suboptimal visual acuities, the incidence of CMO may be underestimated.

Finally, we concur with the authors’ view of minimising any theoretical toxicities of trypan blue. It is our routine to actively remove trypan blue with the bimanual irrigation aspiration system as soon as the anterior capsule has been stained. It has been very effective and the potential toxicities may be reduced.

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Authors’ reply
We thank Lam et al. for their interest. In response to their comments, as stated in the article and demonstrated in figures 1B and C, the effect persists when co-morbidity such as diabetes is removed. Both groups’ surgery was performed by the same surgeon who did not have juniors attached to the list.

Not all patients had dilated fundus examination postoperatively. Clinically significant cystoid macular oedema (CMO) is unlikely in patients with visual acuities of 6/12 or better although subclinical CMO can be demonstrated in up to 20% with fluorescein angiography.
BOOK REVIEW

The History of Moorfields Eye Hospital, Volume III


Like John Mortimer’s book of a similar title this third volume of the history of Moorfields Eye Hospital is an affectionate but critical look back at the hospital that has been a major influence in many ophthalmologists’ training and subsequent practice. The volume is written in a positive upbeat style but also describes some of the faults and difficulties that have beset it in the past four decades. In a complex organisation such as a hospital there are inevitable inefficiencies and problems with personalities but the author has wisely stuck to the facts and has plotted the course of the management of the hospital in a very readable way; he has sensibly avoided petty confrontations and offers a lucid outline of the course of Britain’s flagship ophthalmic hospital.

The two previous histories of Moorfields described times past when ophthalmic practice changed only gradually and political upheaval was minor. The current author has been in the unique position of being involved with Moorfields throughout the 40 years he describes. Given the turmoil, both professional and managerial, that has engulfed the delivery of health care during this period he was fortunate that many of the individuals involved with the hospital were available for interview, thus providing first hand accounts of the good and bad times that affected the hospital. The various chapters outline lucidly the clinical and political changes of the time; Moorfields represents in microcosm all the influences to which NHS consultants of all disciplines have been subjected. One special feature of the period described is that it also covers the first 40 years following the foundation of the Institute of Ophthalmology and the not always easy relationship between the hospital and the institute is recorded both openly and tactfully.

The book comprises a number of chapters outlining the various aspects of the hospital development—for example, clinical, managerial, financial, etc. The first chapter is an overview involving all aspects of the hospital during the 40 years from 1963 to 2003. It provides a concise synopsis of all the forces bearing on the hospital; not only clinical but also in terms of research, teaching, and political upheaval. Indeed, for those younger ophthalmologists entering the profession at the present day the book offers a concise overview of those political influences that have shaped the lives of the NHS and its staff during recent decades.

As the author points out in his preface the subsequent chapters take up the issues raised in the first chapter and analyse them in more detail. If one, therefore, picks up the book and reads it cover to cover there is a strong repetitive element but it was not really the author’s intention that the book should necessarily read in this way. Each of the later chapters is written in a stand alone fashion dealing with clinical progress, academic development, research, teaching, and finance so that some repetition is inevitable. The major characters in the story of Moorfields development are given due weight; particularly Professor Barrie Jones, under whose influence Moorfields progressed from a rather slow moving organisation to the establishment of all the subspecialist services we know today.

Apart from rather a large number of medical metaphors such as “calm waters,” “stormy seas,” and a few petty errors of detail, such as dates, this volume is a good read, particularly if approached as the author intended. He himself has made major contributions to the standing of Moorfields Eye Hospital and the book is written in the typically clear and polished style, reminiscent of his own scientific contributions.

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CORRECTIONS

In the letter entitled, Norrie disease and peripheral venous insufficiency (Br J Ophthalmol 2004;88:1475) the ordering of the authors was incorrect. The correct order is Michaelides M, Luthert PJ, Cooling R, Firth H, Moore AT. The journal apologises for this error.

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Owing to an author error the name of one of the authors of the paper entitled, Long term effect on IOP of a stainless steel glaucoma drainage implant (Ex-PRESS) in combined surgery with phacoemulsification, which appeared in the April issue of the journal (Br J Ophthalmol 2005;89:423–9) was omitted (S Gandolfi). The author list should be C Traverso, F De Feo, A Messas-Kapal, P Denis, S Levartovsky, E Selmel, F Badalà, Z Zagorski, A Bron, S Gandolfi, M Belkin. S Gandolfi is at the Clinica Oculistica, University of Parma, Italy.

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Worldwide clinical trials for new technique for early detection of eye disease

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For further information on the congress and committees, scientific program and coordinators of different areas are available at the congress website www.ophthalmology2006.com.br

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This retrospective study on a unique cohort of patients provided us with the opportunity to demonstrate a potential side effect with the use of trypan blue. A prospective trial is required to control for all the variables and confirm or refute our findings.