

# Isotretinoin-related optic disc swelling

## Introduction

Retinoid treatment is a recognized cause of intracranial hypertension. This article presents a case of isotretinoin-related intracranial hypertension which presented to the ophthalmology services with isolated visual obscurations.

## Discussion

Isotretinoin is a synthetic vitamin A compound, or retinoid, in the form of 13-cis retinoic acid.

Isotretinoin has been available since 1982 and is currently licensed for the treatment of nodulo-cystic and conglobate acne, severe acne, scarring, acne which has

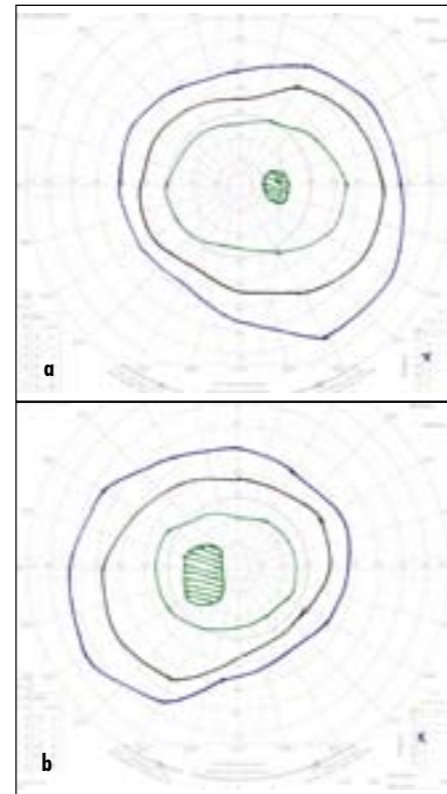
not responded to an adequate course of systemic antibacterial, or acne which is associated with psychological problems. In the UK isotretinoin should only be prescribed by, or under the supervision of, a consultant dermatologist. The mechanism of action is unknown but the drug appears to reduce sebum secretion and therefore inflammation (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2005).

Isotretinoin use is associated with many potentially serious side effects, most notably severe teratogenicity (for up to 2 years after treatment), hypertriglyceridaemia (leading to pancreatitis) and abnormal liver function

(including hepatitis) (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2005).

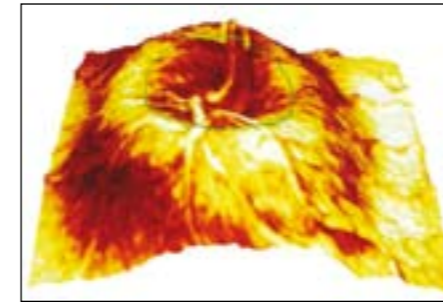
Fraunfelder et al undertook the first ophthalmic review of side effects in 1985 and reviewed 237 adverse reactions. Most common were blepharo-conjunctivitis, dry eyes, blurred vision and contact lens intolerance. Also reported were 18 cases of papilloedema and possible cases of reduced dark adaptation, inflammation and optic neuritis. These reactions can occur within

**Figure 2. Goldman visual field plots. a. Right optic disc. b. Left optic disc.**



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**Figure 3. Heidelberg retinal tomography of left optic disc.**

days or up to several years after treatment (Fraunfelder et al, 1985).

Fraunfelder et al carried out a further review of 1741 spontaneous reports of 2379 adverse ocular events in 2001. According to the World Health Organisation's (1972) definitions of causality assessment, a 'certain' relationship was found between isotretinoin and blepharo-

conjunctivitis, decreased dark adaptation and corneal opacities among others.

In 2004 a 'certain' relationship between isotretinoin and intracranial hypertension (raised intracranial pressure, normal ventricular size and swollen optic discs) was established. This is as a result of 80 cases of positive de-challenge and 12 cases of positive re-challenge being reported (Fraunfelder and Fraunfelder, 2004).

Vitamin A and other retinoids have been shown to cause intracranial hypertension but the mechanism remains unclear. A common pathway is likely, and increased CSF production with altered lipid constituents of the arachnoid villi, resulting in impeded absorption of CSF, has been suggested.

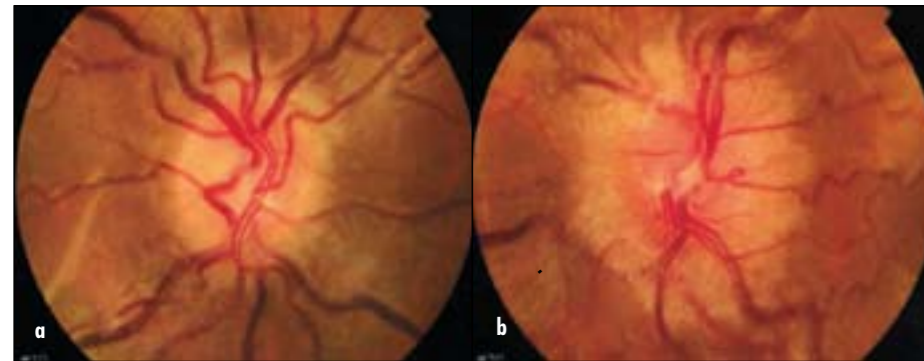
## Conclusions

Isotretinoin is a widely used drug with potentially serious side effects, many of them ocular. This case highlights the impor-

tance of taking a thorough drug history, particularly in the young, fit individuals who are often prescribed this treatment. While other causes of swollen optic discs must be considered, drug-induced intracranial hypertension must be suspected. **BJHM**

British Medical Association, Royal Pharmaceutical Society of Great Britain (2005) *British National Formulary*. No.49. British Medical Association, Royal Pharmaceutical Society of Great Britain, London  
 Fraunfelder FT, LaBraico JM, Meyer SM (1985) Adverse ocular reactions possibly associated with isotretinoin. *Am J Ophthalmol* **100**(4): 534-7  
 Fraunfelder FT, Fraunfelder FW, Edwards R (2001) Ocular side effects possibly associated with isotretinoin usage. *Am J Ophthalmol* **132**(3): 299-305  
 Fraunfelder FW, Fraunfelder FT (2004) Adverse ocular drug reactions recently identified by the National Registry of Drug Induced Ocular Side Effects. *Ophthalmology* **111**(7): 1275-9  
 World Health Organisation (WHO) (1972) *International Drug Monitoring: The role of National Centres*. The WHO Technical Report series No. 498. WHO, Geneva

**Figure 1. a. Right optic disc. b. Left optic disc.**



## Case Report

A 19-year-old Asian woman presented to eye casualty via her optician. She complained of a 3-week history of an intermittent 'misty' patch in her left vision. This lasted less than 5 seconds at a time and occurred more frequently in the mornings. There were no other symptoms and she was systemically well.

The patient was currently in the 11th week of a 16-week course of oral isotretinoin for recalcitrant acne, but was on no other medication. She had been using oral tetracycline until 1 year previously.

Examination revealed visual acuities of right 6/6, left 6/9 with pharmacologically dilated pupils. Clinical examination was unremarkable (including normal ocular movements, visual fields to confrontation, colour vision and cranial nerves) with the exception of grossly swollen optic discs, left greater than right (Figure 1).

The isotretinoin therapy was stopped and blood tests, Goldman visual fields (Figure 2), Heidelberg retinal tomography (Figure 3), computed tomography (CT) scan of the head and electro-diagnostic tests (EDTs) were arranged.

Fields showed an enlarged left blind spot but no other abnormality. Blood tests showed elevated cholesterol, alkaline phosphatase and alanine aminotransferase levels. CT head scan revealed no intracranial abnormality and EDTs were normal. Neurology review corroborated a diagnosis of drug-induced raised intracranial pressure and lumbar puncture was felt to be unnecessary.

Eleven weeks later the patient was asymptomatic with a clear reduction in the swelling of both discs. Liver function tests and Goldman visual fields were returning to normal. The patient remains asymptomatic and under regular review.

## IN THE PUBLIC'S VIEW

### Divine intervention?

The *Independent on Sunday*, in its first tabloid edition (although they call it 'compact'), asked of bird flu, 'Why weren't we warned?' Have they been asleep? The media have been full of 'Experts warn of pandemic' stories all year. I'm fed up of them. The newspaper quoted experts predicting two million deaths in this country; let's hope they are as far out as the estimates a couple of years ago of 136 000 due to die from variant Creutzfeldt-Jakob disease.

All that needs to be said so far is that flu occurs in pandemics a few times per century; there hasn't been a big one recently, so one is due. End of story really. We might just as well complain continually that governments are unable to stop tectonic plates grinding against one another and causing earthquakes. Earthquakes are a story when they happen, not in-between. When it happens, the flu pandemic will be a worthy story, but so far in the whole of Asia, where people live among their poultry, there have been only 60 deaths, and no evidence yet of enhanced transmission between people. When that happens, jumbo jets will do the rest. You can forget about migrating birds.

Bird flu is a medical story that surfaces regularly but without coordination. Who knows what makes one editor think it important on Monday in this newspaper, and another editor on Tuesday on that TV channel, with a mid-week lull before more at the weekend on the radio? At the end of the first week in October there was nationwide coverage of the successfully tested vaccine for cervical cancer – a true medical breakthrough. Vying for the front pages was George Bush's divine prompting to invade Iraq, explained by a cartoonist as a mishearing of the instruction to 'work in Tie Rack'. Only the *Sun* ignored both stories, preferring cricketer ('Ashes hero') Kevin Pietersen's relationship with the model Caprice.

The newspapers did not imply that the vaccine signalled the beginning of the end for cancer. The *Daily Express* was hopeful about other cancers caused by viruses and listed them, though its headline 'Miracle of new cancer vaccine' was overstated. The *Daily Telegraph* and the *Times* linked the story with restrictions on the availability of expensive new anti-neoplastic agents, the *Times* in an editorial titled 'Whatever works'. That is nonsense – whatever works?

– and the subtitle 'Step by costly step, science is defeating cancer' was little better. The last sentence of a sober *Independent* editorial summed it up best. After mentioning the most common solid tumours, it said, 'Great as the news is on cervical cancer, it does not signal the dawn of a new era.'

Doctors are fond of blaming the media for exaggerating research findings but the media often don't have to look far for encouragement. The US Food and Drug Administration is in turmoil after its commissioner resigned suddenly, to be replaced by a urologist, Andrew von Eschenbach, 'who has exasperated [National Cancer Institute] researchers by making it a goal to end suffering and death from cancer by 2005 – an improbable aim he describes as "within our grasp"' (Anon, 2005). Von Eschenbach is apparently a family friend of George Bush, so maybe he knows something that we don't. **BJHM**

Anon (2005) In need of rehab. *Nature* **437**: 789-90

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