



Not so benign intracranial hypertension

Kathleen B Digre

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regularly and available free on the internet. It provides summaries of the disease that are written by experts and contact details of patient support groups. The website is widely used by healthcare professionals, but glossaries are also available, to explain genetic terms or medical terminology, with links to reputable medical sites on the internet. A similar directory and website provided by the National Organisation for Rare Disorders (www.rarediseases.org) provides information and links with patients' support groups in North America.²

Doctors recommending a support group will find that it is very helpful for many families, who will come in contact with other families and share their problems. However, the encounter can be stressful for patients whose condition was diagnosed recently and for their families as it may bring them face to face with patients who have severe manifestations of the disease. Doctors should first review the information given by the patients' group and discuss this problem with families before recommending the resource.

Patients without a diagnosis cannot be helped by this resource as support groups aim to help those with specific diseases. So what about children in whom there clearly is some form of a rare syndrome, yet no diagnosis has been made? They are not left without support as there is a group—Syndromes without a Name—for undiagnosed syndromes listed on the directory.

If the rare disease is caused by a single gene disorder an excellent resource for information is provided by the National Institutes for Health in the United States. Online Mendelian Inheritance in Man (www.ncbi.nlm.nih.gov/omim/) provides detailed clinical reviews for 14 184 single gene disorders, together

with the latest genetic research. The information provided on this site is being updated continually and is reviewed by experts. The site also provides a comprehensive list of references, which can then be accessed through a link to PubMed. More adventurous and curious users may explore the links to genetic databases in the fruit fly, mouse, and other animal species. This internet resource is a practical example of how the human genome mapping project is disseminating genetic information and can benefit physicians from various specialties.

What is rare for the generalist may be common for the specialist. Regional genetic services cover populations of around three million and therefore develop clinical expertise in many rare inherited disorders. Direct contact with or referral to the clinical genetic staff will answer specific questions and provide more support and access to diagnostic testing. A list of the regional genetic centres is provided on Contact a Family's website.

Where textbooks have not provided an answer about a rare inherited disorder many answers are now available with relative ease of access beyond textbooks.

Michael A Patton *professor*

Department of Medical Genetics, St George's Hospital Medical School, London SW17 0RE

Competing interests: MP is an honorary member of the medical advisory board of Contact a Family and medical director of the Birth Defects Foundation.

- 1 Patton MA, Wraith E, ed. *The Contact a Family Directory of specific conditions and rare syndromes in children*. London: Contact a Family, 1991.
- 2 Gruson E, ed. *The NORD guide to rare disorders*. Philadelphia: Lippincott, Williams and Wilkins, 2002.

Not so benign intracranial hypertension

Condition needs to be diagnosed before patients develop visual symptoms

That a common antibiotic, doxycycline, used to treat malaria, acne, and other infections could cause increased intracranial pressure is not a recent revelation.¹ Other tetracyclic antibiotics such as minocycline and tetracycline have caused intracranial hypertension.

Benign intracranial hypertension is a syndrome of signs and symptoms of increased intracranial pressure without causative lesions on images obtained by magnetic resonance imaging or computed tomography.² The disorder is controversial from its name to its putative pathophysiology, but it should be considered when anyone taking doxycycline begins to complain of a new headache.

The first controversy surrounding the disorder is the name—benign intracranial hypertension. For over 100 years the condition has been known as pseudotumour cerebri or benign intracranial hypertension.³ Corbett and Thompson, following the lead of Buchheit, made a plea to replace "benign" with "idiopathic,"⁴ to set apart the idiopathic form of increased intracranial pressure from symptomatic forms, and to dispel the notion that the condition is totally benign.

What to call this syndrome is far from settled, but at present we diagnose the primary or idiopathic form in individuals in whom no cause can be found after careful questioning and clinical evaluation. The secondary forms of intracranial pressure should be characterised as intracranial hypertension due to venous thrombosis, or intracranial hypertension due to medication, such as doxycycline.

The other major controversy concerns the cause of intracranial hypertension. One group posit that all forms of intracranial hypertension, idiopathic and secondary, are due to venous occlusion, or venous hypertension.⁵ However, others have shown that changes in the venous sinuses including venous hypertension may be secondary to the intracranial hypertension itself. King showed that if pressure of cerebrospinal fluid is reduced the venous hypertension disappears.⁶

How doxycycline causes intracranial hypertension is not known; however, case reports abound of increased intracranial pressure associated with drugs including tetracycline,⁷ minocycline⁸ and doxycycline.⁹ Proposed mechanisms by which "cyclines" (tetracycline, doxycycline, minocycline) cause intracranial

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A list of drugs associated with increased intracranial pressure appears on bmj.com

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hypertension include the drugs' interference with the energy dependent absorption mechanism by affecting cyclic adenosine monophosphate at the arachnoid granulations.⁸ Although no clear genetic link exists to increased intracranial pressure, a genetic predisposition was proposed when dizygotic twin sisters developed the disorder. Both were taking tetracycline for acne. One was symptomatic with papilloedema, headache, and intracranial hypertension, while the other was found to have asymptomatic papilloedema after her twin had received her diagnosis.¹⁰ Most of what we know about benign intracranial hypertension concerns the idiopathic form. More common than previously recognised, idiopathic intracranial hypertension occurs in 10-20/100 000 obese women. This means that idiopathic intracranial hypertension is as common among obese women as multiple sclerosis. The disorder affects women (7:1), who present with symptoms of intracranial hypertension (headache, diplopia, whooshing noises in the head) and signs of intracranial hypertension (papilloedema, palsy of the sixth cranial nerve). Ninety per cent of the patients are obese.³

In contrast, intracranial hypertension due to the tetracycline antibiotics (including doxycycline) occurs in both sexes, at almost any age, and without concomitant obesity. The symptoms and signs of intracranial hypertension, however, are the same. How quickly a person develops intracranial hypertension after ingesting doxycycline is unknown, but in the largest review of intracranial hypertension induced by minocycline, some participants had used the drug for up to a year before developing symptoms whereas others became symptomatic within two weeks.⁹ Some dispute whether tetracyclines cause intracranial hypertension at all since so many individuals are treated with the drug every year without developing intracranial hypertension. However, individual cases have been reported where stopping the drug resolved symptoms and signs of intracranial hypertension, and restarting the drug brought recurrence of intracranial hypertension.¹¹

No matter whether the disorder is idiopathic or secondary, it is known to be anything but benign. Corbett et al found that idiopathic intracranial hypertension often persists up to 41 years after the initial diagnosis, and that over 25% of patients have severe visual loss.¹² Patients with secondary forms of intracranial hypertension such as those using doxycycline are also not immune to visual loss. In 12 patients with minocycline induced intracranial hypertension 25% had notable visual field loss.⁹ Therefore, patients who complain of headache after using doxycycline should be examined carefully, including their visual acuity, and formal testing of the visual fields. Funduscopy after dilating the pupils to look for papilloedema is mandatory.

Treatment of the primary and secondary forms of intracranial hypertension is similar—reduce intracranial hypertension. While there are no randomised controlled trials to guide the choice of treatment most practitioners recommend acetazolamide and weight loss to treat primary idiopathic hypertension. In the

secondary forms, correcting the underlying mechanism, for example, treating the venous thrombosis, or stopping the causative medication is indicated. If visual loss progresses despite optimal medical therapy (usually acetazolamide, methazolamide, or furosemide (frusemide) in adequate doses), consideration of optic nerve sheath fenestration or lumbar peritoneal shunt is warranted to prevent further visual loss.³ Risk factors for visual loss include a delay in diagnosis due to failure to diagnose the disorder, inadequate treatment, and delayed treatment.³ The outcome of increased intracranial pressure due to doxycyclines is generally good if recognised early, before vision has been affected seriously.

Despite the many controversies, intracranial hypertension due to use of doxycycline does occur. Practitioners prescribing the tetracyclic antibiotics should be aware of the syndrome of increased intracranial pressure, and pay particular attention to the ocular fundus for papilloedema. Appropriate referral for visual testing including visual fields should be made, and treatment directed at stopping the drug, and instituting symptomatic treatment that lowers the intracranial pressure.

Kathleen B Digre *professor of neurology and ophthalmology*

University of Utah, Departments of Neurology and Ophthalmology, Salt Lake City, Utah 84132 USA (Kathleen.digre@hsc.utah.edu)

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Correction

Tobacco, coffee, and Parkinson's disease

An error occurred in the authors' names in this editorial (15 March, p 562). The name of the second author should have been Catharine Gale, not Chris Gale, and she should have been listed as the first author. We apologise for this editorial error.