systemic histiocytosis, infarction and acute intermittent porphyria in CNH.[2] However, postmortem examinations have not been carried out in most CNH cases. The inflammation in our patient might be compatible with an immunological disease. However, we were not able to prove the presence of an infectious agent, nor serological markers of autoimmune disease.

To the best of our knowledge, this is the first case of brain stem inflammation associated with CNH, thus expanding the range of pathology causing this rare clinical condition.

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New formulation of Botox: complete antibody-induced treatment failure in cervical dystonia

Botulinum toxin is used with remarkable success to treat various muscle and exocrine gland hyperactivity syndromes. Rarely, treatment failure due to formation of botulinum toxin antibodies (ABF) occurs.[1 2] To reduce the risk of ABF, a new formulation of Botox (in the following referred to as ''current Botox''; Allergan, Irvine, California, USA) with increased specific biological potency was introduced. Although ABF could not be detected with current Botox in a large prospective study, it has been reported recently in a patient with special immunoreactive predisposition.[3 4] We are now reporting ABF after current Botox in an immunologically unremarkable patient.

A 50-year-old woman had substantial idiopathic tonic–clonic cervical dystonia for the past 7 months. Her score on the Toronto Western Torticollis Rating Scale (TWSTRS) was 25 (Torticollis Severity Scale), 22 (Disability Scale) and 17.5 (Pain Scale).[5] Treatment was initiated with current Botox (100 MU/1.0 ml, 0.9% $NaCl/H_2O$) (table 1). Two weeks after injection series number 1, her TWSTRS score had decreased to 17 (Torticollis Severity Scale) and her overall subjective improvement, including motor symptoms and pain, was 30% of the original symptomatology. After the injection scheme was modified, her TWSTRS score on injection series 2 and 3 decreased to 5 (Torticollis Severity Scale), 7 (Disability Scale) and 0 (Pain Scale), and her overall subjective improvement rose to 90%. The target muscles then used were the left sternocleidomastoideus (60 MU), the right splenius capitis (60 MU), the right trapezius (30 MU), the left trapezius (20 MU), the right semispinalis (30 MU), the left levator scapuli (30 MU) and the left scalenii (70 MU). Side effects were not reported. On injection series 4 and 5, the therapeutic effect was stable. On injection series 6 and 7, her overall improvement declined to 40% and 20%, respectively, and partial treatment failure was concluded. On injection series 8, there was no therapeutic effect; her TWSTRS score had increased again to its pretreatment value and there was no target muscle paresis. Injection series 9 carried out with identical treatment parameters as before produced the same negative therapeutic effect. After other potential explanations were excluded, all criteria for complete antibody-induced treatment failure were fulfilled as on injection series 8.[6] Electromyography of the sternocleidomastoid muscles did not show amplitude reduction in the target muscles or denervation activity. On the mouse diaphragm assay, botulinum toxin antibody titres were negative after injection series 6, but showed a titre of >7.3 mU/ml after injection series 9.[7] As shown in table 1, during the period from injection series 1 to 8, before complete treatment failure occurred, the treatment time was 644 days; the interinjection interval was 92 (standard deviation (SD) 9) days (minimum 84 days, maximum 105 days); the single botulinum toxin dose given at each injection series was 334 (SD 47) MU (minimum 200 MU, maximum 400 MU) and the cumulative botulinum toxin dose was 2540 MU. Throughout the botulinum toxin treatment, there was no rash, eyelid oedema, dyspnoea, flu-like symptoms, muscle pain or general weakness. History of allergy was not reported.

ABF can be partial or complete, as in our patient, depending on the balance between botulinum toxin and botulinum toxin antibodies. The risk of ABF is increased with short interinjection intervals and high botulinum toxin single doses.[8] It is also increased by the low specific biological potency of the botulinum toxin preparation used—that is, by a low biological potency in relation to a high load of botulinum neurotoxin as caused by partial inactivation of the neurotoxin during manufacturing. With current Botox, the specific biological potency could be increased from 4 MU/ng neurotoxin-non-toxic protein complex of previous Botox to 20 MU/ng neurotoxin-non-toxic protein complex.[3] As a consequence, the risk of ABF in patients with cervical dystonia could be reduced from about 5% to <1%.[3] However, a case recently reported indicates that current Botox does not eliminate the risk of ABF entirely.[4] With single doses of 48 MU botulinum toxin, only interinjection intervals as long as 98.3 (SD 36.1) days, only three injection series applied and administration of a cumulative botulinum toxin dose of only 96 MU. Suspicion of a special immunoreactive predisposition of this patient arose, especially since a similar case of ABF after Dysport has been reported previously.[9] In the current patient, the treatment time was 644 days, the interinjection interval 92 (SD 9) days, the single botulinum toxin dose 334 (SD 47) MU and the cumulative botulinum toxin dose 2540 MU. With these unremarkable treatment parameters and no apparent special immunoreactive predisposition, this case indicates that current Botox can produce ABF not only in immunologically exceptional patients but also in unremarkable ones.

Table 1 Treatment protocol

Injection series	Time (days)	Interinjection interval (days)	Single dose (mouse units Botox)	Subjective improvement (% of original symptomatology)	Remarks
1	0		200	30	NR
2	98	98	300	50	NR
3	182	84	400	90	NR
4	287	105	300	90	NR
5	378	91	300	90	NR
6	478	100	300	40	PTF MDA: negative
7	562	84	340	20	PTF
8	644	82	400	0	CTF
9	728	84	400	0	CTF MDA: >7.3 mU/ml

CTF, complete treatment failure; MDA, mouse diaphragm assay; NR, normal response; PTF, partial treatment failure.

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BOOK REVIEWS

From basic pain mechanisms to headache

Edited by Jes Olesen, Troels S Jensen. Published by Oxford University Press, Oxford, 2006, £85.00 (hardback), pp 261. ISBN 978-0-19-856981-7

We cannot doubt that headache is painful, but in many hospitals and university centres, there seems to be remarkably little academic or even clinical interchange between neurologists seeing patients with headache syndromes and anaesthetists running pain clinics, let alone with the basic scientists working in the field. The approaches needed seem to be different; in particular, patients with headache require a doctor to provide a diagnosis, whereas the diagnosis in patients attending pain clinics is usually well established. However, in both cases, the treatments offered are empirical and owe little to our understanding of the pathophysiology of neuropathic pain.

In the latest book in his series based on the annual research seminars in Copenhagen, Professor Jes Olesen, assisted by Dr Troels Jensen, has attempted to bridge this gap by seeking contributions from experts in experimental pain, as well as from experts in the clinical assessment, diagnosis and management of specific headache and other pain syndromes.

From my clinical perspective, some of the early chapters written by basic scientists seem to plunge very deep, very quickly, exemplifying the persistent gulf between the disciplines. Perhaps the most valuable parts of the book are those on specific pain syndromes, particularly trigeminal neuralgia, the allodynia accompanying migraine, and the new, particularly helpful concept of morphine-induced pain by the facilitation of brain stem modulating pathways, which may go some way to explain the chronic headache so often seen in regular users of codeine. It is a sign of the difficulty, for example, that the various contributors cannot decide whether migraine should be classified with the inflammatory neuropathic syndromes or not.

This book is a brave attempt at a particularly challenging goal—it is perhaps inevitable that the different backgrounds of the contributors are reflected in the approaches they adopt in their chapters. I believe this text will be of value to both neurologists and pain experts, although a lot more research work is needed before clinical treatment ceases to be empirical and becomes fully grounded in the basic science of pain modulation.

R Peatfield

Amyotrophic lateral sclerosis, 2nd edn

Edited by Robert H Brown, Michael Swash, Piera Pasinelli. Published by Informa Healthcare, 2006, £85.00 (hardcover), pp 362. ISBN 1-84184-463-2

Amyotrophic lateral sclerosis, through its first edition, has become the standard text for clinicians and researchers in the field of amyotrophic lateral sclerosis (ALS)/MND, and with this new edition, which retains many of the strengths of the first, it is likely to remain so. The fact that treatment receives an allocation of 29 pages whereas genetics (clearly implicated in only 10% of cases of this relatively rare disease) gets 100 pages reflects the state of the ALS world rather well. Bridging the ''translational medicine'' gap between our ever-increasing knowledge of the basic phenomena observed in genetic and cellular models and what is actually happening in the disease process in patients with sporadic ALS (and ultimately providing treatments) unfortunately remains an aspiration rather than a reality.

The balance of the book in this edition has shifted slightly, away from clinical description and even more towards research. The opening chapter on the clinical spectrum of motor neurone disorders is a useful account of the different forms of motor neurone degeneration (including those at the fringes of most people's clinical practice, like shellfish poisoning), but the opportunity to map out in detail for neurologists the natural history and clinical features of different clinical subtypes of ALS, which can cause much diagnostic confusion, has been missed. The chapter on epidemiology is comprehensive, if a little uncritical, in a subject in which much of the research is methodologically challenged.

Specific chapters devoted to imaging, peripheral neurophysiology and traumatic masturbatory syndrome provide a comprehensive survey of the different techniques in development as diagnostic and prognostic markers. A chapter on clinical approaches to disease monitoring and prognostication, which are probably as good as any investigative technique in helping patients, would have provided an appropriate balance. The massive increase in interest in ALS as a multisystem neurodegenerative disease is reflected in an extremely useful chapter on cognitive aspects. Much of the rest of the book is devoted to reviews of the main pathways implicated in ALS, such as oxidative stress, apoptosis and mitochondrial dysfunction, which are good but fairly standard accounts that can be found elsewhere. A stimulating exception is the truly integrative and readable chapter from Wills and Brown on insights to be gained from the molecular biology of ageing.

This excellently presented book is still the best available on the subject, but I would make a plea to the editors of future editions not to let the exponentially increasing load of scientific literature on ALS squeeze further the basic clinical description of the disease, which must remain the starting point for all research on ALS.

K Talbot

Clinical neuroimmunology, second edition, 2005

Edited by Jack Antel, Gary Birnbaum, Hans-Peter Hartung, Angel Vincent. Published by Oxford University Press, Oxford, 2005, $265.00 (hardback). ISBN 0-19-851068-0

The editors and authors should be congratulated on completing the task of producing the second edition of *Clinical neuroimmunology*. The contents live up to its title and cover a wide spectrum of conditions falling within the remit of clinical neuroimmunology and more. A generous number of chapters are dedicated to basic science and animal models of immune-mediated disorders. The book starts with an introductory chapter on immunology and separate chapters on the principles of autoimmunity and immunotherapy. This is followed by chapters relevant to neuroimmunology, which include the organisation and development of the central nervous system (CNS), immune properties of the CNS, the role of the immune response in tissue damage and repair, neural immune interactions in autoimmune disease, immunological properties of the peripheral nervous system, genetics of immune-mediated neurological diseases, principles of immune–virus interactions in the nervous system, immunity to bacterial infections and animal models of neurological disease.

Not unexpectedly, the lion's share of the book goes to multiple sclerosis and related disorders, with chapters on acute disseminated encephalomyelitis, the pathology and immunology of multiple sclerosis, imaging the immunobiology of multiple sclerosis, effects of immune mediators on neurophysiological function in multiple sclerosis, myelin repair in multiple sclerosis and immune-directed treatments in multiple sclerosis. The last chapter is testament to how far we have advanced with the treatment of multiple sclerosis and includes some of the emerging treatments that are considerably more effective than the current licensed multiple sclerosis disease-modifying treatments.

There are several excellent chapters on immune-mediated disorders of the peripheral nervous system. These include chapters on the