

The First World Report of Botulinum A Toxin Injection for Status Migrainosus

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Abstract

The author reports the first ever documented publication in the world concerning the use of botulinum toxin A (BTX-A) injection for status migrainosus. A 58-year old man had been suffering from migraine without aura for 20 years. This last attack (a very severe throbbing headache) started over the left side of his head and he had tried several medications (paracetamol, aspirin, ergotamine, mefenamic acid, and diazepam) during the attack to no avail. Physical examination revealed an acutely ill patient with an agonizing pain condition. General and neurological examinations were normal. BTX-A solution was then injected into the Fung Chou point (classical Chinese acupuncture point for migraine) in the total amount of 25 international unit. Dramatic response was observed within 1 hour of injection and status migrainosus was abort within 10 hours. He was headache-free and had no further attack of migraine for another 2 months.

Key word : Botulinum A Toxin, Status Migrainosus

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Migraine is a common neurological disorder that affects 11 per cent or more of the adult population⁽¹⁾. The past decade has seen significant advances in our understanding of the epidemiology and underlying mechanisms of migraine⁽²⁾. Several effective new acute and preventive therapies have

been introduced. Unfortunately, clinical treatment has not kept pace with scientific advances : migraine remains relatively under-recognised, under-diagnosed and under-treated⁽³⁾.

Migraine is a chronic condition characterised by episodic attacks of headache commonly

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associated with various combinations of nausea, vomiting, photophobia, phonophobia, and aura. Auras are focal neurological, usually visual, symptoms that are reported in approximately 20 per cent of attacks⁽⁴⁾.

There are no objective markers or diagnostic tests that define migraine. Therefore, early studies suffered from the drawback that differing definitions of migraine were used. However, the International Headache Society (IHS) guidelines, which were published in 1988⁽⁵⁾, have provided a standardised set of diagnostic criteria to use in migraine studies. According to these criteria, migraine without aura is characterised by attacks lasting for 4 to 72 hours. Typical headaches have at least two of the following characteristics : unilateral pain location, pulsating quality, moderate or severe intensity, and aggravation by routine physical activity. In addition, attacks are associated with nausea and with photo- and phonophobia. Migraine with aura is characterised by attacks of neurological symptoms unequivocally localised to the cerebral cortex or brainstem, which usually develop gradually over 5 to 20 minutes and last less than 60 minutes. Headache, nausea, and/or photophobia usually follow neurological aura directly or after a free interval of less than 1 hour.

The term "status migrainosus" is applied to migraine attacks when the headache does not completely disappear but continues unabated or in varying intensity for longer than 3 days⁽⁶⁾. The so-called status migrainosus seems in many cases to be due either to the injudicious use of ergotamine tartrate or to an associated tension-type headache. This complication of migraine is an example par excellence of a gap in our knowledge. In the meantime it provides a great challenge for the physician who looks after such a rare case. Antiemetics, sedatives, standard prophylactic drugs, analgesics, tryptans, and steroids provide the main group of drugs used⁽⁷⁾. We present here a new option for the successful treatment of status migrainosus with botulinum toxin A injection over the Chinese acupressure point for migraine (Fung Chou point.).

REPORT OF A CASE

A 58-year old man (HN:42-021347) had been suffering from migraine without aura for 20 years. Each attack usually started at the occipital region and then progressed to the frontal area of the same side. It was frequently accompanied by

nausea and vomiting. The headache was typically throbbing in character and lasted for 4 to 8 hours. Most attacks were aborted by paracetamol or aspirin and diazepam. He occasionally took ergotamine to relieve the very severe headache, which ranged from 2 to 4 attacks per month. He had not been prescribed calcium channel blocker or amitriptyline for migraine prophylaxis.

Four days prior to this event, the very severe throbbing headache started over the left side of his head. He took paracetamol, aspirin, ergot (cafergot[®]), mefenamic acid (Ponstan[®]), and a sedative drug (diazepam) with no relief. The attack was so severe that he had to be off work for 3 days and finally came to Siriraj Hospital for proper management.

Physical examination revealed an acutely ill patient with an agonizing pain condition. General and neurological examinations were normal. Neither of the temporal arteries were tender. Botulinum A toxin solution was then injected into the left Fung Chou point in the total amount of 25 international units (Fig. 1).

He experienced definite headache relief within 1 hour of injection. Ten hours later the headache was so much improved that he could have a long sleep during that night. The next day he was headache-free and had no further attack of migraine for another 2 months.

DISCUSSION

Status migrainosus is a very disturbing condition and is defined as the attack of migraine that lasts more than 72 hours whether treated or not. Headache in status migrainosus is continuous throughout the attack or interrupted by headache free intervals lasting less than 4 hours and the interruption during sleep is disregarded. By this definition a patient with status migrainosus suffers from severe headache and needs all sorts of treatment to abort the attack. There are no large series or double-blind treatment trials in status migrainosus, although reports on the treatment of isolated acute migraine include many patients with status migrainosus⁽⁸⁻¹¹⁾. Many subjects respond to one regimen better than another. The choice of treatment modality depends on the preference of the physician, the condition of the patient, and presence or absence of medical contraindication to various agents. They include dihydroergotamine⁽¹²⁾, metoclopramide⁽¹²⁾, phenothiazine^(10,13), corticoste-

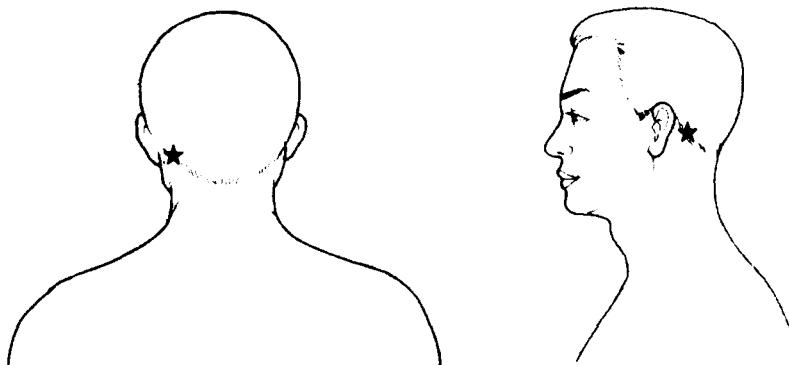


Fig. 1. Diagrammatic picture showing Fung Chou point for botulinum toxin A injections.

roids(14), nonsteroidal antiinflammatory drugs(14), intravenous lidocaine(15), and sumatriptan(16-18).

Factors that are thought to be responsible for triggering status migrainosus include emotional stress, depression, abuse of medications, anxiety, diet, hormonal factors, and multiple nonspecific factors. Management of these problems were thought to be important in avoiding status migrainosus. Our patient had fulfilled the criteria of status migrainosus and he had tried several medications during the attack to no avail. Botulinum A toxin injection was thus injected into the classical Chinese acupuncture point for migraine headache (i.e. the Fung Chou point). Dramatic response was observed within 1 hour of injection and status migrainosus was aborted within 10 hours.

Botulinum toxin type A (BTX-A) has been used clinically for a number of disorders believed to be due to overactive striated or smooth muscles, such as focal dystonia (e.g. blepharospasm, torticollis, occupational cramp, foot dystonia, etc)(19-23), hemifacial spasm(24-26), spasticity (e.g. post stroke spasticity, post head injury, post-encephalitis, multiple sclerosis, brain or spinal cord tumours, radiation encephalopathy, metabolic and toxic encephalopathies, etc)(27-30), rectal sphincter spasm with fissure(31), urinary dyssynergia, and achalasia(32). Benefits have also been reported for hyperhidrosis(33), hypersalivation, and hand sweat-

ing, showing that BTX-A can inhibit overactive nonmotor as well as motor peripheral acetylcholine neurones. In addition to reducing muscle hyperactivity and spasm, BTX-A treatment often reduces the pain associated with muscle spasm such as cervical dystonia, achalasia and rectal fissures. Preliminary evidence suggests that it can also be beneficial in the treatment of chronic low back pain and cervical pain associated with muscle spasm(34). The booming of BTX-A for cosmetic purposes to reduce facial wrinkles as a cosmetic indication is now widely accepted especially crow feet, frontal furrows and infraorbital wrinkles(35).

Several recent open-label, noncontrolled studies reported that treatment of patients with BTX-A markedly reduced migraine frequency and symptoms(36,37). There are also several studies of BTX-A treatment for tension-type headache both pilot and double-blind, placebo controlled studies which have persistently shown the benefit for treatment and prophylaxis(38-40).

In Thailand, the author has carried out BTX-A injection in an open label study of 21 headache patients which demonstrated the efficacy of this treatment(41). The author believes this report is the first ever documented publication in the world concerning the use of BTX-A injection for status migrainosus.

REFERENCES

1. Scher AI, Stewart WF, Lipton RB. Migraine and headache : A meta-analytic approach. In: Crombie IK, ed. *Epidemiology of pain*. Seattle : IASP Press, 1999: 59-70.
2. Silberstein SD, Lipton RB, Goadsby PJ. Headache in clinical practice. Oxford : ISCS Medical Media, 1998.
3. Lipton RB, Diamond S, Reed M, et al. American Migraine Study II: Prevalence, burden and health care utilization for migraine in the United States. *Headache* 2000; 40: 427 (Abstract).
4. Pryse-Phillips W, Findlay H, Tugwell P, Edmeads J, Murray TJ, Nelson RF. A Canadian population survey on the clinical, epidemiologic and societal impact of migraine and tension-type headache. *Can J Neurol Sci* 1992; 19: 333-9.
5. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalgia* 1988; 8 (Suppl 7): 19-28.
6. Cough JR, Diamond S. Status migrainosus : Causative and therapeutic aspects. *Headache* 1983; 23: 94-101.
7. Blau JN. Ed. Migraine. Clinical, therapeutic, conceptual and research aspects. London : Chapman and Hall, 1987: 201.
8. Callaham M, Raskin N. A controlled study of dihydroergotamine in the treatment of acute migraine headache. *Headache* 1986; 26: 168-71.
9. Jones J, Sklar D, Dougherty J, White W. Randomized double-blind trial of intravenous prochlorpromazine for the treatment of acute headache. *JAMA* 1989; 261: 1174-85.
10. Lane PL, Ross R. Intravenous chlorpromazine-preliminary results in acute migraine. *Headache* 1985; 25: 302-4.
11. Saadah H. Abortive headache therapy in the office with intravenous dihydroergotamine plus prochlorperazine. *Headache* 1993; 32: 143-6.
12. Raskin NH. Treatment of status migrainosus : The American experience. *Headache* 1990; 30 (Suppl 2): 550-3.
13. Lane PL, McLellan BA, Baggoley CJ. Comparative efficacy of chlorpromazine and meperidine with dimenhydrinate in migraine headache. *Ann Emerg Med* 1989; 18: 260-5.
14. Gallagher MR. Emergency treatment of intractable migraine. *Headache* 1986; 26: 74-5.
15. Reutens DC, Fatovich DM, Stewart-Wynne EG, Prentice DA. Is intravenous lidocaine clinically effective in acute migraine? *Cephalgia* 1991; 11: 245-7.
16. Jauslin P, Goadsby PJ, Lance JW. The hospital management of severe migrainous headache. *Headache* 1991; 31: 658-60.
17. Goadsby PJ, Zagami AS, Donnan GA, et al. Oral sumatriptan in acute migraine. *Lancet* 1991; 338: 782-3.
18. The Subcutaneous Sumatriptan International Study Group. Treatment of migraine attacks with sumatriptan. *N Engl J Med* 1991; 325: 316-21.
19. Poungvarin N. Prevalence of dystonia and occupational cramps in Thailand. In: Kimura J, Shiba-saki H, eds. *Recent advances in clinical neurophysiology*. Amsterdam: Elsevier, 1996: 921-32.
20. Poungvarin N, Devahastin V, Viriyavejakul A. Treatment of various movement disorders with botulinum A toxin injection: An experience of 900 patients. *J Med Assoc Thai* 1996; 78: 281-8.
21. Poungvarin N, Viriyavejakul A. Botulinum A toxin treatment in spasmotic torticollis : Reports of 56 patients. *J Med Assoc Thai* 1994; 77: 464-70.
22. Poungvarin N. Writer's cramp : The experience with botulinum toxin injection in 25 patients. *J Med Assoc Thai* 1991; 74: 239-47.
23. Poungvarin N, Devahastin V, Chaisevikul R, Prayoonwiwat N, Viriyavejakul A. Botulinum A toxin treatment for blepharospasm and Meige syndrome: Report of 100 patients. *J Med Assoc Thai* 1997; 80: 1-8.
24. Poungvarin N, Viriyavejakul A, Komoltri C. Placebo-controlled double-blind cross-over study of botulinum A toxin in hemifacial spasm. *Parkin Related Disord* 1995; 1: 85-8.
25. Poungvarin N, Viriyavejakul A. Two hundred and fifty patients with hemifacial spasm treated with botulinum toxin injection. *J Med Assoc Thai* 1992; 75: 199-203.
26. Poungvarin N, Viriyavejakul A. Two hundred and fifty patients with hemifacial spasm treated with botulinum toxin (Abstract). *Mov Disord* 1990; 6 (Suppl 1): 67.
27. Poungvarin N, Vachalathiti R. Botulinum treatment for post-stroke spasticity : Low dose regimen (Abstract). *Eur J Neurol* 1996; 3 (Suppl 2): 23.
28. Viriyavejakul A, Vachalathiti R, Poungvarin N. Botulinum treatment for post-stroke spasticity : Low dose regime. *J Med Assoc Thai* 1998; 81: 413-9.
29. Simpson DM, Alexander DN, O'Brien CF, et al. Botulinum toxin type A in the treatment of upper extremity spasticity : A randomized, double-blind, placebo-controlled trial. *Neurology* 1996; 46: 1306-10.
30. Snow BJ, Tsui JK, Bhatt MH, Varelas M, Hashimoto SA, Calne DB. Treatment of spasticity with botulinum toxin : A double-blind study. *Ann*

Neurol 1990; 28: 512-5.

31. Maria G, Cassetta E, Gui D, Brisinda G, Bentivoglio AR, Albanese A. A comparison of botulinum toxin and saline for the treatment of chronic anal fissure. *N Engl J Med* 1998; 338: 217-20.

32. Annese V, Basciani M, Borrelli O, Leandro G, Simone P, Andriulli A. Intrasphincteric injection of botulinum toxin is effective in long-term treatment of esophageal achalasia. *Muscle Nerve* 1998; 21: 1540-2.

33. Naumann M, Flachenecker P, Brocker EB, Toyka KV, Reiners K. Botulinum toxin for palmar hyperhidrosis. *Lancet* 1997; 349: 252.

34. Knusel B, Grant M, Loesser JD. Intramuscular injection of botulinum toxin type A (BOTOX) in chronic low back pain associated with muscle spasm. Poster presented at The American Pain Society Meeting; November 1998; San Diego, California. Poster number 672.

35. Moy RL. Why devote an issue to botulinum toxin? Special issue. Denervation techniques for facial rejuvenation. *Dermat Surg* 1998; 24: 1167-254.

36. Binder W, Brin MF, Blitzer A, Schenrock L, Diamond B. Botulinum toxin type A (BTX-A) for migraine : An open label assessment (Abstract). *Mov Disord* 1998; 13 (Suppl 2): 241.

37. Silberstein S, Methew N, Saper J, Jenkins S; for the BOTOX Migraine Clinical Research Group. Botulinum toxin type A as a migraine preventive treatment. *Headache* 2000; 40: 445-50.

38. Schulte-Mattler WJ, Wieser T, Zierz S. Treatment of tension-type headache with botulinum toxin : A pilot study. *Eur J Med Res* 1999; 4: 183-6.

39. Smuts JA, Baker MK, Smuts M, Stassen JMR, Rossouw E, Barnard PWA. Prophylactic treatment of chronic tension-type headache using botulinum toxin type A. *Eur J Neurol* 1999; 6 (Suppl 4): S99-S102.

40. Rollnik JD, Tanneberger O, Schubert M, Schneider U, Dengler R. Treatment of tension-type headache with botulinum toxin type A : A double-blind, placebo-controlled study. *Headache* 2000; 40: 300-5.

41. Poungvarin N, Prayoonwiwat N, Senanarong V, Nilanont Y, Danchaivijitr C. Treatment of headache with botulinum toxin A injection : An open label study of 21 patients. *Intern Med J Thai* 2001; 17: 105-10.

รายงานแรกในโลกที่ฉีดสารใบทุลิnmทอกซิน เอ เพื่อรักษาภาวะ Status Migrainosus

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ผู้เขียนได้เสนอรายงานการฉีดสารใบทุลิnmทอกซิน เอ เพื่อรักษาภาวะ status migrainosus ในชายไทยอายุ 58 ปี ที่ได้รับการวินิจฉัยว่าเป็นโรคปวดศีรษะไมเกรนมากนาน 20 ปี โดยผู้ป่วยมีอาการปวดศีรษะซึ้งแบบบุบ ๆ ติดต่อกันนานา 3 วัน ซึ่งยาหลายชนิดที่ผู้ป่วยรับประทานได้แก่ พาราเซตามอล, แอลสไพริน, ergotamine, mefenamic acid และ diazepam ไม่สามารถบรรจันอาการปวดศีรษะได้เลย การตรวจร่างกายผู้ป่วยไม่พบความผิดปกติใด ๆ ในทางระบบประสาทแต่ผู้ป่วยมีอาการปวดศีรษะมากและทุรนทุราย จึงได้รับการฉีดสารใบทุลิnmทอกซิน เอ จำนวน 25 หน่วยสากล ที่บริเวณท้ายทอยด้านซ้าย (ตำแหน่ง Fung Chou ซึ่งเป็นตำแหน่งฝังเข็มรักษาโรคปวดศีรษะไมเกรน ในต่างจังหวัด) อาการปวดศีรษะของผู้ป่วยเลิกลงอย่างมากภายใน 1 ชั่วโมง และ 10 ชั่วโมงต่อมาหายลับนิบ ผู้ป่วยไม่ปวดศีรษะอีกเลยในตลอดเวลา 2 เดือนถัดมา ผู้รายงานเชื่อว่ารายนี้เป็น status migrainosus รายงานแรกของโลกที่ได้รับรักษา ด้วยการฉีดสารใบทุลิnmทอกซิน เอ

คำสำคัญ : ใบทุลิnmทอกซิน เอ, ภาวะ Status Migrainosus

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