

Idiopathic Intracranial Hypertension Associated with Uncontrolled Use of Weight-Loss Drugs

Imshenetskaya Tatsiana^{1*}, Ana Dvalishvili², Vladimir Ponomarev³, Volha Yarmak² and Galina Vashkevich²

¹Professor, Head of the Department of Ophthalmology, Department of Ophthalmology, Doctor of Medical Sciences, Belarusian Medical Academy of Post-Graduate Education (BelMAPGE), Minsk, Belarus

²Department of Ophthalmology, Belarusian Medical Academy of Post-Graduate Education (BelMAPGE), Minsk, Belarus

³Professor, Head of the Department of Neurology and Neurosurgery, Department of Neurology and Neurosurgery, Doctor of Medical Sciences, Belarusian Medical Academy of Post-Graduate Education (BelMAPGE), Minsk, Belarus

*Corresponding author

Imshenetskaya Tatsiana, MD, Professor, Head of the Department of Ophthalmology, Department of Ophthalmology, Doctor of Medical Sciences, Belarusian Medical Academy of Post-Graduate Education (BelMAPGE), Minsk, Belarus, Tel: +375 29 6462010; 0000-0002-9353-8664; E-mail: t.imshanetskaya@mail.ru

Submitted: 13 June 2018; Accepted: 19 June 2018; Published: 02 July 2018

Abstract

Purpose: We report a case of a patient with bilateral papilledema and Benign Intracranial Hypertension caused by uncontrolled use of drugs for self-treatment of obesity.

Methods: A 36-year-old, mildly obese female with a 7-month history of visual changes with floaters, intermittent episodes of diplopia and blurred vision, intense, debilitating, daily headaches, pulsatile tinnitus, bilateral maxillary pressure and pain. Fundus examination revealed papilledema, visual field test detects blind spot enlargement, generalized constriction, and loss of the nasal visual fields, optical coherence tomography (OCT) - increased RNFL thickness in all four quadrants, Lumbar puncture- Increased Intracranial Pressure.

Results: The diagnosis of IIH we made according modified Dandy criteria.

Conclusion: To our knowledge, this is the first report in literature of BIH caused after self-medication of overweight. Patient during a year lose 40 kg, and she manage it by uncontrolled use of drugs for weight loss.

Introduction

The current global epidemic of obesity is one of the most important challenges to our times. Our current therapeutic store for obesity is limited, by the side effects and the efficacy.

The increasing prevalence of overweight and obesity is a critical public health problem for women of childbearing age.

Idiopathic intracranial hypertension (IIH), or pseudotumor cerebri, formerly called benign intracranial hypertension, is a challenging condition with raised intracranial pressure (ICP) in the absence of identifiable cause [1]. Safavi-Abbasi, et al. stated that over 80% of patients with BIH are overweight women [2].

The annual incidence of BIH is 0.9/100,000 persons and 3.5/100,000 in females 15 to 44 years of age. It is increasing in incidence in parallel with the current epidemic of obesity [3,4]. In obese women aged 20 to 44 years who were 20% or more over ideal weight, the incidence of BIH is 19 per 100,000 [5]. More than 90% of BIH

patients are obese and over 90% are women of childbearing age. Although symptoms and signs may be recurrent in at least 10%, asymptomatic elevated intracranial pressure may persist for years [6]. The mean age at the time of diagnosis is about 30 years [7].

The symptoms of increased intracranial pressure are headache, which are recorded in almost all IIH patients, pulse synchronous tinnitus (pulsatile tinnitus), diplopia, transient visual obscurations and visual loss [8-10]. Bilateral papilledema is a common few patients have unilateral or no papilledema [11]. In some asymptomatic patients, papilledema is discovered during routine ophthalmoscopic examination. Neurologic examination may detect partial 6th cranial nerve palsy but is otherwise unremarkable.

Patients with higher body mass indexes (BMIs) and recent weight gain are at increased risk [12,13]. If BIH presents in an individual who is not overweight, it is necessary to rule out associated risk factors, such as the following [12,14]. Exposure to or withdrawal from certain exogenous substances (e.g. drugs), systemic diseases

(including Lyme disease), disruption of cerebral venous flow, certain endocrine or metabolic disorders.

BIH is associated with many medical conditions, including: vitamin deficiencies and excesses, autoimmune diseases, coagulopathies, sleep apnea, obesity and iatrogenic causes [15-19].

We are reporting a case of a BIH in mildly obese women, without any other known causative factor except past uncontrolled use of drugs for self-treatment of obesity (Orlistat and Beautiful princess) and Tizanidine. There was not any clinical or diagnostic manifestation of BIH in this patient before she began taking these drugs, according her last therapeutic, ophthalmologic and neurologic examination.

Material and Methods

A 36-year-old, mildly obese female was referred with a 7-month history of visual changes with floaters, and intermittent episodes of diplopia and blurred vision which was worse in the right eye, followed by intense, debilitating, daily headaches which extended to her frontal areas bilaterally, pulsatile tinnitus, bilateral maxillary pressure and pain. Headaches were predominantly frontal in location and worse on lying down. The patient refused any trauma associated with the onset of her symptoms.

The results of the physical and ophthalmologic examination: Patient is 36 year old female, accountant. From anamnesis 3 pregnancy: 1 stillbirth, boy 4 years old suffering from vasculitis and another baby boy 2 years old without any genetic or systemic disease. The body weight 80, the height was 164, body temperature 36.6, arterial blood pressure 120/70mm/Hg, heart rate 68.

From past medical history patient suffered from obesity during past 5 years, but excessive weight gain after last baby birth.

After last baby birth patient was suffered from pain and discomfort sensation in her neck and back region. She resort city manual therapy clinic for help. There she was treated with manual therapy and Tizanidine 2mg. Patient was taking Tizanidine during month. After course of manual therapy and Tizanidine patient experience relief of her symptoms.

According FDA between January 2004 and October 2012, 1 individual taking Tizanidine reported Benign Intracranial Hypertension to the FDA.

In 2015 patient began uncontrolled use of a variety of weight-loss medications. Her body weight at this period was 120kg. She decided to take Orlistat (120 mg orally five sometimes six times a day) as medical therapy for obesity. Patient was taking this drug continuously up to 2 month. The recommended dose of Orlistat is one 120-mg capsule three times a day with each main meal containing fat (during or up to 1 hour after the meal).

According FDA between January 2004 and October 2012, 2 individuals taking Orlistat reported Benign Intracranial Hypertension.

After this she decided to take drugs of unknown origin which she buys from china distribution company. The name of drug capsule was, "Wonderful Princess". Patient was taking these drugs continuously during 3 month. We try to contact to this distribution company to know the composition of drugs, but we can't find not company

and can't get any information about this pills, because they are not registered in Belarus. After all this medications patient loss 40 kgs.

Sometime later patient was suffered with headache, nausea, vomiting, pulsatile tinnitus, transient visual obscurations and diplopia. On neurologic examination there was no localizing sign, except for sixth nerve palsy, normal level of consciousness.

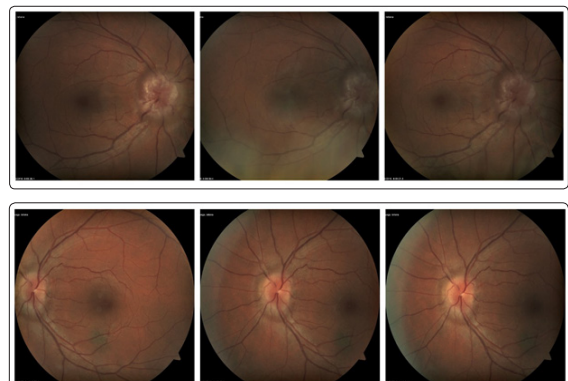
In addition, he described brief episodes of "snowy vision" inferiorly in his left eye on arising and intermittent pulsatile tinnitus. There was a history of chronic daily headache for last period without recent change. Other symptoms include lethargy and tiredness, dizziness, mood change. Her medical, surgical and family histories were unremarkable.

Laboratory data included a normal FBC, ESR, iron studies, antinuclear antibodies, sedimentation rate, WBC count, red blood cell count, hemoglobin and hematocrit, platelet count and fasting blood glucose. Antinuclear antibody and rheumatoid factors were negative. Antineutrophil cytoplasmic antibody test (C-ANCA, P-ANCA) negative. Urine tests-normal. Anticardiolipin antibody of IgG and Ig Misotype in serum negative. Investigatory laboratory studies were normal including complete blood count, comprehensive metabolic panel, lipid profile, thyroid function studies, coagulation studies, serum cyanocobalamin levels, serum rapid plasma reagin, toxoplasmosis antibody titer, cytomegalovirus deoxyribonucleic acid polymerase chain reaction and Two-tiered diagnostic tests for Lyme disease enzyme-linked immunosorbent assay (ELISA) and the Western blot.

Ophthalmologic examination revealed visual acuity of 20/20 in both eyes; Optic nerve ultrasonography (ONUS) detected a wide optic nerve sheath. Fundus examination revealed signs of papilledema: Disc hyperemia, nerve fiber layer swelling which obscured the normal disc margins and the disc was grossly elevated. The visual field test detects blind spot enlargement, generalized constriction and loss of the nasal visual fields, especially inferonasal.

Optical coherence tomography (OCT) - increased RNFL thickness in all four quadrants. Color vision tests within normal ranges. Pupils were briskly reactive with no relative afferent papillary defect.

CT or MRI scanning: the ventricles were normal in size, findings without evidence of thrombosis. Thin section computed tomogram sections of the orbits show enlarged optic nerve sheaths of the optic nerve sheath and reversal of the optic nerve head. Magnetic resonance venography (MRV) within normal ranges.



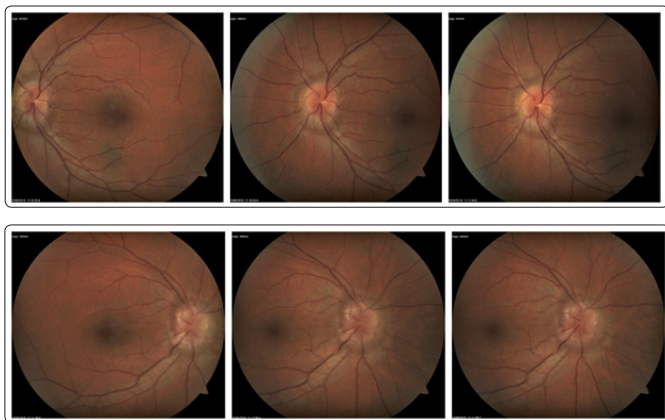


Figure: Idiopathic Intracranial Hypertension

Results

The diagnosis of BIH was made according modified Dandy criteria: 1. Symptoms of raised intracranial pressure (headache, nausea, vomiting, transient visual obscurations and papilledema) 2. No localizing signs with the except of sixth nerve palsy 3. The patient is awake and alert 4. Normal CT/MRI findings without evidence of thrombosis 5. LP opening pressure of >25 cm H₂O and normal biochemical and cytological composition of CSF 6. No other explanation for the raised intracranial pressure [20,21].

The most important neurologic manifestation in BIH is papilledema. Visual field loss occurs in almost all cases of IIIH. In a prospective study of IIIH, visual loss in at least one eye (other than enlargement of the physiological blind spot) was found in 96% of patients.

Medical and surgical treatment of patients with idiopathic intracranial hypertension is often challenging, requiring integration of the history, examination and clinical course. The most important factor is usually the amount and progression of visual loss. Next in importance is the severity of the patient's symptoms with regard to how much they are disrupting the patient's activities of daily living. In case-control studies, no association is found between IIIH and multivitamin, oral contraceptive, corticosteroid or antibiotic use [22,23]. However, case reports associating some drugs appear convincing: nalidixic acid, nitrofurantoin, indomethacin or ketoprofen in Bartter's syndrome, vitamin A intoxication, isotretinoin, thyroid replacement therapy in hypothyroid children, lithium and anabolic steroids [24-32].

Idiopathic intracranial hypertension is reported only by a few people who take Tizanidine Hydrochloride. 1,119 people who have side effects while taking Tizanidine hydrochloride from FDA and social media. Among them, 1 has Idiopathic intracranial hypertension.

We predispose it could be play triggering role for development IIIH. From past medical history patient was using a variety of drugs for weight-loss. She decided to take orlistat (120 mg after every 8 hours) as medical therapy for obesity. Patient was taking this drug continuously up to month.

We found that Between January 2004 and October 2012, 2 individuals taking Orlistat reported Benign Intracranial Hypertension to the FDA. The drug capsules named as "Wonderful princess" is not registered in Belarus. Patient was taking these drugs continuously during 2 months.

To our knowledge, this is the first report in literature of IIIH caused after self-medication of overweight. Our patient during a year loses 40 kg, and she manage it by uncontrolled use of orlistat and drugs of unknown origin from china. (with unknown composition). The recommended dose of Orlistat is one 120-mg capsule three times a day with each main meal containing fat (during or up to 1 hour after the meal). Our patient was taking this drug five or six time during a day.

Before 2015 a thorough medical history and physical exam of patient was without any characteristic sign or symptom of IIIH. She had done MRT during this period and it was without pathological changes.

It is very important to lose weight correctly. But there are a lot of cases that persons try to lose weight fast and easy, results most of this cases are dramatic.

References

1. Corbett JJ, Savino PJ, Thompson HS, Kansu T, Schatz NJ, et al. (1982) Visual loss in pseudotumorcerebri. Follow-up of 57 patients from five to 41 years and a profile of 14 patients with permanent severe visual loss. *Arch Neurol* 39: 461-474.
2. Safavi-Abbasi S, Di Rocco F, Nakaji P, Feigl GC, Gharabaghi A, et al. (2008) "Thrombophilia due to factor V and factor II mutations and formation of a duralarteriovenous fistula: case report and review of a rare entity," *Skull Base* 18: 135-143.
3. Durcan FJ, Corbett JJ, Wall M (1988) The incidence of pseudotumorcerebri. Population studies in Iowa and Louisiana. *Arch Neurol* 45: 875-877.
4. Radhakrishnan K, Ahlskog JE, Cross SA, Kurland LT, O'Fallon WM (1993) Idiopathic intracranial hypertension (pseudotumorcerebri). Descriptive epidemiology in Rochester *Arch Neurol* 50: 78-80.
5. Durcan FJ, Corbett JJ, Wall M (1988) The incidence of pseudotumorcerebri. Population studies in Iowa and Louisiana. *Arch Neurol* 45: 875-877.
6. Corbett JJ (2006) Problems in the diagnosis and treatment of pseudotumorcerebri. *Can J Neurol Sci* 10: 221-229.
7. González-Hernández A, Fabre-Pi O, Díaz-Nicolás S, López-Fernández JC, López-Veloso C, et al. (2009) [Headache in idiopathic intracranial hypertension] 17-20.
8. Giuseffi V, Wall M, Siegel PZ, Rojas PB (1991) Symptoms and disease associations in idiopathic intracranial hypertension (pseudotumorcerebri): a case-control study. *Neurology* 41: 239-244.
9. Wall M, George D (1991) Idiopathic intracranial hypertension. A prospective study of 50 patients. *Brain* 114: 155-180.
10. Frisén L (1982) Swelling of the optic nerve head: a staging scheme. *J Neurol Neurosurg Psychiatr* 45: 13-18.
11. Wall M (2008) Idiopathic intracranial hypertension (pseudotumorcerebri). *Curr Neurol Neurosci Rep* 8: 87-93.
12. Daniels AB, Liu GT, Volpe NJ, Galetta SL, Moster ML, et al. (2007) Profiles of obesity, weight gain, and quality of life in idiopathic intracranial hypertension (pseudotumorcerebri). *Am J Ophthalmol* 143: 635-641.
13. Miller NR, Newman NJ (1999) Pseudotumorcerebri (benign intracranial hypertension). In: Walsh and Hoyt's Clinical Neuro-Ophthalmology 1: 523-538.
14. A Sismanis (2003) "Pulsatile tinnitus," *Otolaryngologic Clinics of North America* 36: 389-402.
15. DK Binder, JC Horton, MT Lawton, McDermott MW (2004)

- “Ideopathic intracranial hypertension,” *Neurosurgery* 54: 538-551.
16. M Jindal, L Hiam, A Raman, D Rejali (2009) “Idiopathic intracranial hypertension in otolaryngology,” *European Archives of Oto-Rhino-Laryngology* 266: 803-806.
 17. A Sismanis (1998) “Pulsatile tinnitus: a 15-year experience,” *American Journal of Otolaryngology* 19: 472-477.
 18. Jennum, SE Borgesen (1989) “Intracranial pressure and obstructive sleep apnea,” *Chest* 95: 279-283.
 19. V Biousse, A Ameri, MG Bousser (1999) “Isolated intracranial hypertension as the only sign of cerebral venous thrombosis,” *Neurology* 53: 1537-1542.
 20. WE Dandy (1937) “Intracranial pressure without brain tumor: diagnosis and treatment,” *Annals of Surgery* 106: 492-513.
 21. JL Smith (1985) “Whence pseudotumorcerebri?” *Journal of Clinical Neuro-Ophthalmology* 5: 55-56.
 22. Ireland B, Corbett JJ, Wallace RB (1990) The search for causes of idiopathic intracranial hypertension. A preliminary case-control study. *Arch Neurol* 47: 315-320.
 23. Giuseffi V, Wall M, Siegel PZ, Rojas PB (1991) Symptoms and disease associations in idiopathic intracranial hypertension (pseudotumorcerebri): a case-control study. *Neurology* 41: 239-244.
 24. Deonna T, Guignard JP (1974) Acute intracranial hypertension after nalidixic acid administration. *Arch Dis Child* 49: 743.
 25. Mushet GR (1977) Pseudotumor and nitrofurantoin therapy [letter] *Arch Neurol* 34: 257.
 26. Konomi H, Imai M, Nihei K, Kamoshita S, Tada H (1978) Indomethacin causing pseudotumorcerebri in Bartter’s syndrome. *N Engl J Med* 298: 855.
 27. Larizza D, Colombo A, Lorini R, Severi F (1979) Ketoprofen causing pseudotumorcerebri in Bartter’s syndrome. *N Engl J Med* 300: 796.
 28. Feldman MH, Schlezinger NS (1970) Benign intracranial hypertension associated with hypervitaminosis A. *Arch Neurol* 22: 1-7.
 29. Spector RH, Carlisle J (1984) Pseudotumorcerebri caused by a synthetic vitamin A preparation. *Neurology* 34: 1509-1511.
 30. Van Dop C, Conte FA, Koch TK, Clark SJ, Wilson-Davis SL, et al. (1983) Pseudotumorcerebri associated with initiation of levothyroxine therapy for juvenile hypothyroidism. *N Engl J Med* 308: 1076-1080.
 31. Saul RF, Hamburger HA, Selhorst JB (1985) Pseudotumorcerebri secondary to lithium carbonate. *JAMA* 253: 2869-2870.
 32. Shah A, Roberts T, McQueen IN, Graham JG, Walker K (1987) Danazol and benign intracranial hypertension. *Br Med J [ClinRes]* 294: 1323.

Copyright: ©2018 Imshenetskaya Tatsiana. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.