



CASE REPORT

Metabolic acidosis during the relapse treatment of idiopathic intracranial hypertension

İdiyopatik intrakraniyal hipertansiyon relaps tedavisi sırasında metabolik asidoz

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Summary

We herein present a 40-year-old female physician who was diagnosed with idiopathic intracranial hypertension (IIH) 4 years ago. In the last years, the patient was in remission without any medications. Since the onset of COVID-19 pandemic, she has been stressfully working in the high-risk area, therefore using personal protective equipment (N95 mask, protective clothing, goggles, and protective cap) during the day for extended periods. Her headaches recurred and the patient was diagnosed with a relapse of IIH; acetazolamide and afterward topiramate were initiated, with diet treatment. Symptomatic metabolic acidosis, which is otherwise a rare side effect of the IIH treatment and not seen in her first attack even with higher doses, developed during the follow-up, presenting with shortness of breath and chest tightening. The emerging problems of IIH diagnosis and management during the COVID-19 pandemic will be discussed.

Keywords: Acetazolamide; intracranial hypertension; metabolic acidosis; papilledema; SARS-CoV-2 pandemic.

Özet

Dört yıl önce idiyopatik intrakraniyal hipertansiyon (İİH) tanısı alan, 40 yaşında bir kadın hekim hasta, son yıllarda herhangi bir ilaç kullanmadan remisyonda takip edilmekteydi. Koronavirüs hastalığı (COVID-19) salgınının başlangıcından bu yana yüksek riskli alanda ve stres altında çalışan hasta, gün boyunca uzun süreler kişisel koruyucu ekipman (N95 maskesi, koruyucu giysi, gözlük ve koruyucu başlık) kullanıyordu. Bu süreçte hastanın baş ağrıları tekrar ortaya çıktı ve İİH nüksü nedeniyle asetazolamid, ardından topiramet ve diyet tedavisi başlandı. İİH tedavisi sırasında, tedavinin çok nadir bir yan etkisi olan ve hastanın ilk atağında daha yüksek dozlarda tedavi altında olmasına karşın görülmeyen semptomatik metabolik asidoz, nefes darlığı ve göğüs sıkışma hissi ile karakterize bulgu ve semptomlar ortaya çıktı. Burada, COVID-19 salgını sırasında İİH tanısı ve yönetiminde ortaya çıkan sorunlar tartışılacaktır.

Anahtar sözcükler: Asetazolamid; intrakraniyal hipertansiyon; papilödem; metabolik asidoz; SARS-CoV-2 pandemisi.

Introduction

Although the etiology of idiopathic intracranial hypertension (IIH) is unknown and seems to be multifactorial, it affects primarily obese women of childbearing age, with recurrences in some patients. Its prevalence is estimated between 0.5 and 2/100,000 of the population.^[1] The most feared complication of IIH is permanent loss in the visual field due to long-term ischemia of the optic nerve. To assess the risk of vision loss, non-invasive optic coherence tomography (OCT) was

used in recent years along with fundoscopy and visual field examination.

Metabolic acidosis is a rare side effect of acetazolamide in the treatment of IIH.^[2] We herein report diagnostic and management difficulties of a physician in whom the stressful working conditions during the pandemic along with weight gain contributed to the reappearance of IIH symptoms and prolonged use of the personal-protective equipment (PPE) including N95 mask further complicated the management of her emerging dyspnea.

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Case Report

A 40-year-old female physician was evaluated 4 years ago due to her persistent headache and mild blurring in vision. Minimal papilledema was detected in fundoscopic examination. Retina nerve fiber layer (RNFL) thickness measured by OCT showed slight thinning of the optic nerve sheath. Her brain magnetic resonance imaging (MRI) and MR venography were normal. Lumbar puncture revealed a high cerebrospinal fluid (CSF) pressure of 340 mmH₂O, with normal CSF content. Biochemical tests showed a mild elevation in the erythrocyte sedimentation rate and iron deficiency anemia. Routine blood tests, including ANA and ENA screening tests and thyroid, liver, and kidney functions, procoagulant profile were all normal; rheumatology and hematology consultations were done, and treatment for iron deficiency anemia was started. She was previously diagnosed with rare episodic migraine attacks since the age of 25, with a throbbing headache accompanied by mild nausea and photophobia, and this attack profile was entirely different from the daily pressing headaches associated with IIH. Acetazolamide (increased gradually to max 1.5 g/day) and topiramate (max 100 mg/day) treatments for IIH were started. The patient lost weight with diet (body mass index of 27 decreased to 23.5), drug doses were tapered and finally discontinued due to pregnancy planning. She took hormone (estrogen and progesterone) treatment, which lasted about 2 months for in vitro fertilization, and this treatment was discontinued after failing to become pregnant. About 2 months later, in March 2020, the patient's previous headaches reappeared simultaneously with the onset of the COVID-19 pandemic in our country. The patient was working as a primary physician in the COVID-19 inpatient clinic, under heavy workload and stress, and using PPE (N95 mask, protective clothing and goggles, and headgear) for long periods throughout the day. No pathologies were detected in her repeated contrast-enhanced brain MRI. Lumbar puncture was performed, CSF pressure was 310 mmH₂O, CSF content was normal. Acetazolamide 500 mg/day and topiramate 50 mg/day were started. Acetazolamide dose was increased to 1 g/day due to the persistence of the headache. However, after 2 weeks the patient reported shortness of breath and pressure sensation in the chest aggravated with effort. Chest Computed tomography (CT) was normal, D-dimer, and repeated COVID-19 PCR tests were

Table 1. Arterial blood gas analysis, showing metabolic acidosis and hypocarbia due to compensatory hyperventilation

| Arterial blood gas | Patient's value | Range |
|--------------------|-----------------|-------------------|
| pH | 7.36 | 7.35–7.45 |
| pO ₂ | 100 | 80–100 mmhg |
| pCO ₂ | 25.8 | 35–45mmhg |
| HCO ₃ | 17.2 | 22–26 milimol/l |
| Lactate | 0.5 | 0.6–1.6 milimol/l |
| Base excess | -9.9 | -2.5–(2.5) mEq/L |

negative. Metabolic acidosis and hypocarbia due to compensatory hyperventilation were detected in arterial blood gas examination (Table 1). The patient was administered intravenous ringer lactate infusion and antacid (sodium bicarbonate) capsules. The acetazolamide dose was reduced to 500 mg/day.

Her OCT and visual field tests are shown in Figures 1 and 2. The patient's symptoms and arterial blood gas values resolved within 1 week and a strict diet program was organized.

Discussion

COVID-19 pandemic-related lifestyle may cause emerging problems in the management of IIH patients, as demonstrated in our case, who is a physician and helped us to detect the underlying cause of her symptoms, caused by IIH treatment; shortness of breath related to metabolic acidosis.

Therapeutic agents used in IIH are aimed at reducing the intracranial pressure by decreasing CSF secretion. Acetazolamide is a carbonic anhydrase inhibitor that acts in the choroid plexus, and is often well tolerated up to a dose of 1 g/day; it is considered as the first-line therapy for IIH, and is the only drug that has been supported by a randomized controlled trial.^[3] Acetazolamide had relieved the symptoms in our patient, therefore drug dose was gradually reduced and finally stopped 1 year ago, without any side effects, even though a higher dose was used. Although the benefit is evident in patients with pronounced papilledema, high doses of acetazolamide may not be tolerated and patients receiving doses higher than 1 g/day should be carefully monitored. Acetazolamide can cause other adverse effects; paraesthesia and nausea are more frequent. Although

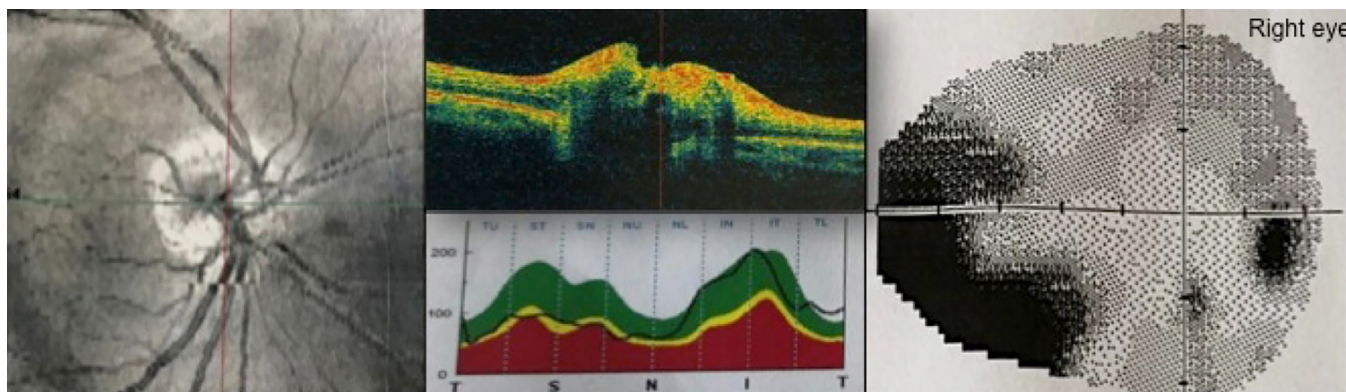


Figure 1. Fundoscopic examination revealed a minimal papilledema in the nasal part of the right optic disc. RNFL thickness in the superior quadrant was significantly thinner. Humphrey Visual Fields demonstrated enlargement of the blind spot and peripheral nasal scotoma which was detected previously. Funduscopy photograph (left). Spectral domain (SD) optical coherence tomography (OCT) cross-section image through the optic nerve head (middle, above). The extent on the retinal nerve fiber layer is shown between the red (internal limiting membrane [ILM]) and green lines. SD-OCT retinal nerve fiber layer (RNFL) thickness line graph shows RNFL thickness values (middle, below). Humphrey visual field 24–2 grey scale image (right).

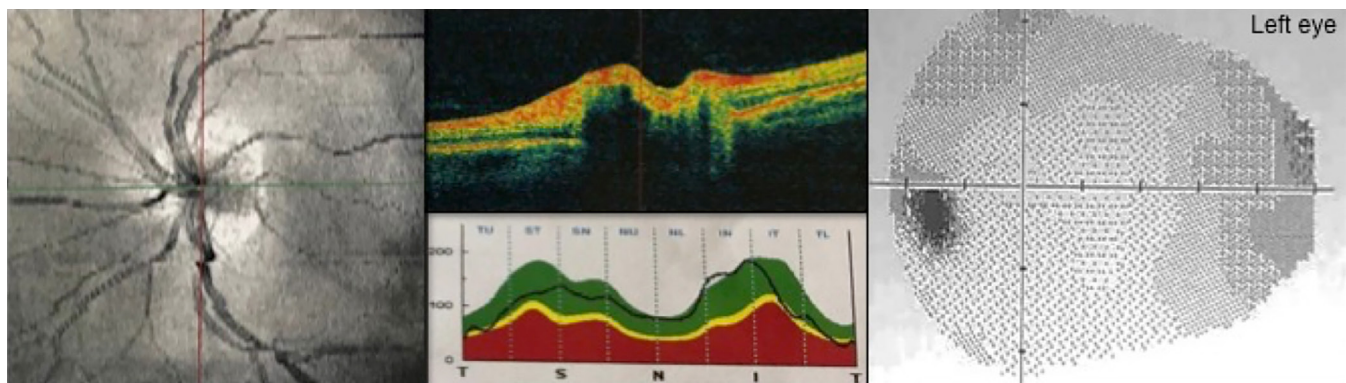


Figure 2. Fundoscopic examination revealed a minimal papilledema in the nasal part of the left optic disc. RNFL thickness was normal in all quadrants. Visual field test result was normal.

metabolic acidosis is a known side effect, in our experience the number of patients followed with symptomatic metabolic acidosis is very low. Besides, we did not encounter any problems in her first attack with the same or even higher dosages.

Moreover, her second drug topiramate has many different mechanisms of actions, including carbonic anhydrase enzyme inhibition. Topiramate can cause metabolic acidosis, although not as much as acetazolamide. In addition, since topiramate is a first-line agent for migraine prevention, it can provide additional benefits for IIH patients with migraine-like headaches along with its effect of loss of appetite.^[4] The fact that our patient had a history of episodic migraine made her suitable for the selection of topiramate, also helped her for weight control. Thus the current management plan was reasonable and same with her previous IIH treatment but it resulted in severe dyspnea related to metabolic acidosis, reversed by dose reduction along with decreasing the use of N95 mask.

The symptoms of metabolic acidosis are mainly related to the underlying disorder and compensatory hyperventilation is an important clinical sign, which is often misinterpreted as a primary respiratory disorder.^[5] Given the high contamination risk of COVID-19, these symptoms of headache and dyspnea could easily be misdiagnosed in a health-care worker.

During the pandemic many headache centers avoided in-person outpatient visits, therefore IIH is one of the risky headache syndromes because it depends on close neuro-ophthalmological diagnostic work-up. The risk of COVID-19 presenting primarily with headache is another concern, especially in a physician.^[6] High levels of stress and heavy workload, along with a previous migraine history, which could be aggravated by PPE, could have been misleading in our case. Therefore, the importance of funduscopy and in-person visits should not be neglected in the pandemic era for IIH diagnosis.

Spectral domain OCT provides reliable and quantitative evaluation of the structural changes due to papilloedema in the long-term, by measurement of the RNFL thickness, total retinal thickness, optic nerve volume and retinal ganglion cell layer thickness, despite the potential for some misinterpretations. A significant structure-function relationship was observed between visual field loss and macular and RNFL thickness measurements.^[7] In our case, a correlation was observed in the visual field test and RNFL thickness measurements, supporting our follow-up findings.

PPE has been used widely in the emerging severe acute respiratory syndrome coronavirus SARS-CoV-2 and it is clear that the use of N95 masks is essential. N95 face mask is generally well tolerated, has minimal adverse effects such as tightness of the mask and difficulty of breathing.^[8] A study investigating the effect of N95 masks on headaches seen in healthcare providers showed that headaches were more common in those who wore masks longer than 4 h.^[9] The etiopathogenesis of N95 facial mask-related headaches may possibly be associated with hypoxemia, hypercapnia, mechanical factors, or stress. A shorter period of wearing a facial mask can reduce the frequency and severity of these headaches. Our patient has used masks for prolonged periods, which may have triggered headaches, however, the relationship with metabolic acidosis seemed rather elusive. Moreover, she had also migraine diagnosis, further complicating the differential diagnosis. It was reported that a previous history of migraine was present in a substantial proportion (23.9%) of patients with IIH, together with migraine-like headache profiles, suggesting the involvement of shared mechanisms in pain pathways.^[10]

The pathophysiology of IIH has not been fully characterized. The proposed main mechanism is CSF dysregulation, however metabolic, inflammatory and endocrinological perspectives are also thought to play a role.^[11,12] Intracranial hypertension has been reported in women using hormonal contraception and during pregnancy. Also, the combination of risk factors such as obese phenotypes, insulin resistance, hypertriglyceridemia (dyslipidemia), and hypertension in IIH patients suggest that they may be at risk for metabolic syndrome; this point has gained special importance in the COVID-19 pandemic era, due to changing lifestyle, leading to weight gain. In our patient, the use of hormone therapy 2 months ago may have contributed to the recurrence of the IIH along with weight gain due to changing unhealthy lifestyle in the pandemic era.

Conclusion

In conclusion, IIH patients need special attention during the pandemic due to emerging differential diagnostic problems besides lifestyle changes provoking headaches. We also want to emphasize that a rare but significant side effect of acetazolamide treatment is metabolic acidosis, which needs to be kept in mind.

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