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A case of idiopathic intracranial hypertension associated with PCOS

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Summary

Idiopathic intracranial hypertension (IIH) is a rare neurologic disorder. It is also known as pseudotumor cerebri. The incidence of IIH is one to two per 100,000 population annually. The higher incidence is in obese women from 15 to 44 years. The main symptoms are headache and visual loss. It mostly affects women of childbearing age who are overweight or obese. There are many theories of pathogenesis of IIH, but precise pathogenesis is unknown. One of the causes of IIH is intracranial venous sinus thrombosis. It can cause increased cerebrospinal fluid (CSF) pressure by obstruction of venous outflow and blocking of CSF absorption. In polycystic ovary syndrome (PCOS) patients, thrombogenic tendency is increased due to increased aromatization of testosterone to estradiol which could induce estrogen-mediated thrombophilia. The authors present a 14-year-old girl with PCOS stigma who presented with a severe headache and papilledema. These symptoms were not improved by standard medical therapy of IIH and PCOS, but improved after laparoscopic ovarian drilling. The authors report it with a review of the literature.

Key words: PCOS; Idiopathic intracranial hypertenstion; Laparoscopic ovarian drilling.

Introduction

Idiopathic intracranial hypertension (IIH) sometimes called benign intracranial hypertension (BIH) or pseudotumor cerebri (PTC), is a neurological disorder that is characterized by increased intracranial pressure in the absence of a tumor or other neurologic disease. Symptoms are headache, nausea, vomiting, pulsatile tinnitus, double vision, and other visual symptoms [1]. If untreated, it may lead to swelling of the optic disc in the eye, which can progress to loss of vision [2]. Therefore, the main treatment goal of IIH is to prevent or arrest progressive visual loss [3].

IIH is diagnosed with a lumbar puncture and brain scan to rule out other causes [4]. Some patients respond to lumbar puncture or medication, while others require surgery to relieve the pressure. This condition may occur in all age groups, but is most common in young women, especially those with obesity [5].

The cause of IIH is unknown, but, three theories exist as to why the pressure might be raised in IIH: an excess of cerebrospinal fluid (CSF) production, increased volume of blood or brain tissue, or obstruction of the veins that drain blood from the brain. The venous obstruction might cause blood flow from the brain to be impaired or congested. Congestion of venous blood may result from a generally increased venous pressure, which has been linked to obesity and intracranial venous sinus thrombosis. PCOS may be associated with facilitated development of IIH through an increased tendency to thrombosis [6]. The authors report a case of IIH associated with PCOS.

Case Report

A 14-year-old girl whose body mass index (BMI) was 20.61 kg/m^2 within normal range visited Department of Ophthalmology with complaint of dry eye and visual disturbance. Magnetic resonance (MR) orbit image showed no remarkable abnormal finding. Under the impression of optic neuritis, steroid therapy was started (methylprednisolone one g/day for three days, and then predinisolone 60 mg/day), however, her symptoms got worse and one month later, new symptoms, headache, and nausea appeared.

On further evaluations, slit-lamp biomicroscopy confirmed papilledema (Figure 1). Lumbar puncture revealed that the CSF opening pressure was increased to 34 cmH_2O, cerebrospinal fluid (CSF) composition was normal range, and no bacteria and virus was found in CSF culture. Radiologic imaging studies such as brain magnetic resonance imaging (MRI) with magnetic resonance angiography (MRA) and venography showed no abnormal finding. Through these findings, IIH was diagnosed [4].

General IIH therapy was begun. CSF drainage was performed and medication (acetazolamide, 750mg a day) was commenced. After treatment, headache and eye ball pain were improved slightly but papilledema did not improve. She was hospitalized and discharged repeatedly due to headache, eye ball pain, and high intracranial pressure. Due to her gynecologic symptom, irregular menstrual interval (35 to 70 days), gynecologic evaluation was requested. Her menarche occurred at 11 years of age. On transrectal ultrasound examination, both ovaries were polycystic with more

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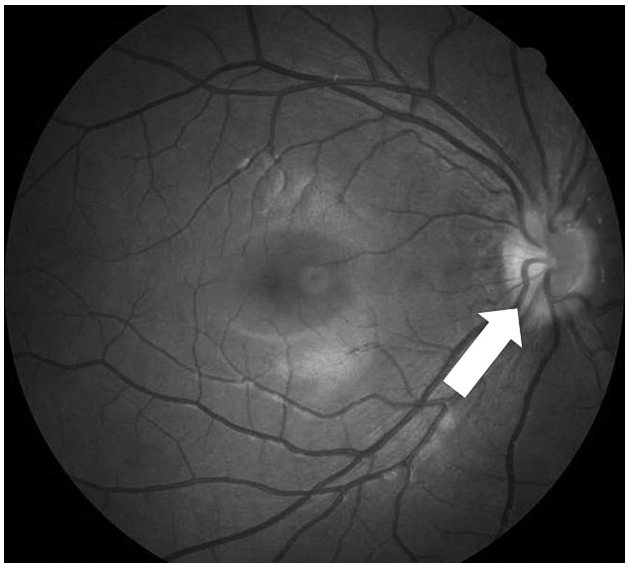

Figure 1. — Slit-lamp biomicroscopic finding of right eye. Fundus photographs showing papilledema (arrow).

than 14 follicles on each ovary (Figure 2) and modified Ferriman-Gallway (mFG) score was eight. On laboratory tests, testosterone, 17α-OH progesterone, free cortisol, DHEA-sulfate, and HbA1c, random glucose level were in normal range. Prolactin was slightly increased to 28.54 ng/ml. LH was 14.7 mIU/ml and FSH was 3.42 mIU/ml; LH/FSH ratio was increased to 4.29 and estradiol was 7.40 pg/ml on the second day of menstruation. Androstenedione was increased to 3.05 pg/ml. Under diagnosis of polycystic ovary syndrome (PCOS), metformin (1,500 mg a day) was used for improving hormonal imbalance, but there was no improvement in her symptoms, so the authors performed laparoscopic ovarian drilling. After general anesthesia, electrosurgical needle puncture was made on each ovary about ten times (Figure 3).

After 1 month of operation, her symptoms were improved with reduced medication (metformin one gram a day) and slit-lamp biomicroscopy test showed no papilledema. LH was 1.05 mIU/ml and FSH was 2.69 mIU/ml on the second day of menstruation. Finally all medication was stopped at 12 months after surgery. At 24 months after surgery, she had regular menstrual cycle and no recurrence sign of IIH.

Discussion

IIH is uncommon disorder in normal population, however, in young overweight women, the annual incidence is 20 per 100,000 persons [4]. The IIH has several clinical findings as follows: 1) increased intracranial pressure or papilledema, 2) normal CSF composition, 3) no imaging evidence of ventriculomegaly or mass lesion, and 4) no other cause was identified such as medication [4].

For a decade, several authors had mentioned that IIH might be a thrombotic disorder, because its findings were closely related with certain sites of intracranial thrombosis, and this thrombosis can cause impairing of CSF resorption.

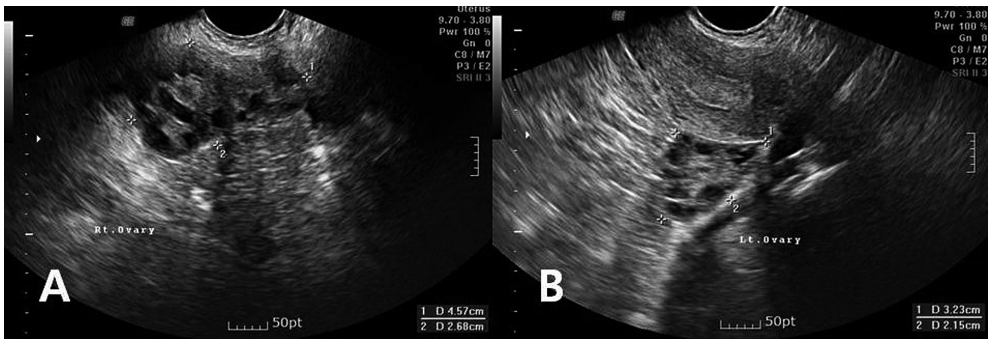

Figure 2. — Transrectal sonographic finding (A: right ovary; B: left ovary).

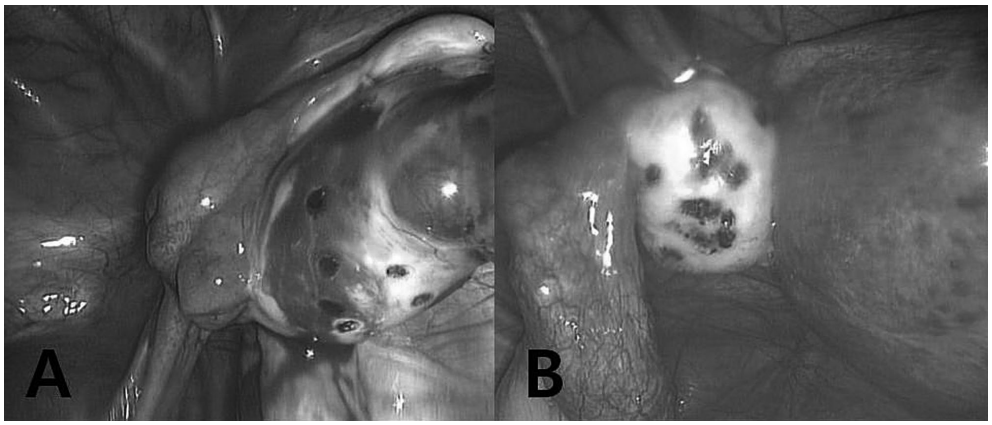

Figure 3. — Laparoscopic ovarian drilling (A: right ovary; B: left ovary).

PCOS is the most common endocrinopathy which incidence is 4%~10% of reproductive age women [7]. There is statistical association of PCOS and increased risk of deep venous thrombosis [5]. Increased aromatization of testosterone to estradiol could induce estrogen-mediated thrombophilia [7].

Glueck *et al.* studied 65 (consecutive) women referred due to IIH [6]. In this study, 37 of the 65 women had polycystic ovaries. All of the 37 were obese: 16 had a BMI between 30 and 40 and 19 had a BMI >40. There were also some findings related to more conventional predictors of thrombotic risk. Thirty-eight percent of the women with IIH were homozygous for the thrombophilic C677T mutation in the methylene tetrahydrofolate reductase gene: a finding present in 14% of 102 controls. Nine of the patients also had baseline Factor VIII levels greater than 150% percent, 29 had elevations of lipoprotein, and roughly half had symptoms appear during a high-estrogen state (oral contraceptive use, estrogen replacement therapy, or pregnancy) [6]. This study shows the possibility that PCOS can cause thrombophilia and hypofibrinolysis and may facilitate development of IIH.

Diagnosis of PCOS in adolescents demands more attentions because characteristics of menstruation in adolescent are very similar with symptoms of PCOS [8]. However, in this case the patient's menarche occurred at three years and six months before the diagnosis of IIH. Also, ultrasound finding of polycystic ovaries, increased LH/FSH ratio, increased mFG score, and irregular menstruation suggest that she had PCOS. Acetazolamide medication and lumbar puncture for decreasing of intracranial pressure are standard IIH treatment and metformin is widely used to ameliorate hormonal imbalance in PCOS patients. However, her neuro-ophthalmologic symptoms were not improved by these treatments. After laparoscopic ovarian drilling, her symptoms were improved. Laparoscopic ovarian drilling in adolescent girls has a risk for diminishing ovarian reserve so it demands utmost attention. However, in this case, medical treatment was not effective and the patient could not live daily life due to the symptoms of IIH.

From this case, the authors can make a conclusion that PCOS might be associated with development of IIH and treatment of PCOS might stabilize or reverse IIH. If initial medical treatment of IIH and PCOS is not effective, surgery such as ovarian drilling may become an optional treatment. Understanding of the contributions of PCOS to the development of IIH should facilitate development of new approaches to treat this disabling neuro-ophthalmologic disorder.

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