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Case Report

Treatment dilemma in an adolescent girl with idiopathic intracranial hypertension presenting with abnormal uterine bleeding and severe anemia

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ABSTRACT

Abnormal uterine bleeding (AUB), specifically heavy menstrual bleeding (HMB) is a frequent complaint for adolescents. Idiopathic intracranial hypertension (IIH) is a syndrome of raised intracranial pressure, in the absence of any evidence of an intracranial space occupying lesion. Female sex, obesity and polycystic ovarian disease are known risk factors associated with IIH. This case report depicts the unusual case of an 18-year-old girl with IIH who presented with HMB for 28 days with severe anemia with Hb of 5.5 gm%. Urgent ophthalmic and neurological review was taken in view of IIH. Prompt treatment of AUB was done with blood transfusion, hemostatics, and orally administered iron supplements. Despite medical treatment for AUB, patient continued to bleed and hence after multidisciplinary discussion and informed consent she was started on low dose progesterone. Symptoms improved rapidly and she was discharged in a stable condition with tapering doses of medication and regular follow- up advice. Treatment of AUB in adolescents with IIH is a dilemma for physicians. To date, there is no direct evidence suggesting either implantable or oral contraceptives as a cause for IIH but few studies have closely linked oestrogen containing oral contraceptive pills and some levonorgestrel implants in IIH and hence these should be avoided.

Keywords: Abnormal uterine bleeding, Adolescents, Idiopathic intracranial hypertension, Progesterone

INTRODUCTION

Approximately 10 to 35 percent of women are affected by abnormal uterine bleeding (AUB).[1] Anovulatory heavy menstrual bleeding (HMB) is the most common presentation of AUB.[2] All adolescents with HMB should be evaluated for endocrine and bleeding disorders. Idiopathic intracranial hypertension (IIH), or pseudotumor cerebri, is a disorder of elevated intracranial pressure (ICP) resulting in visual loss, headaches, and papilledema in absence of an identifiable clinical, laboratory, or radiologic cause. The incidence of IIH in the general population is 1:100,000, whereas in obese women aged 15–44 it is increased to 10–20:100,000.[3] Much needs to be learned about etiopathogenesis and role of neuroendocrine factors in IIH and establishing a relationship between obesity, polycystic ovary syndrome (PCOS), age and pubertal status in adolescent population. The treatment of AUB in IIH patients should aim to provide hemodynamic stability, anemia correction, preserving vision and relief of symptoms.

CASE REPORT

We report a case of an 18- year-old female with history of IIH, who presented with heavy menstrual bleeding with clots for 4 weeks. She was initially investigated elsewhere and was undergoing treatment with tablet tranexamic acid 500 mg twice daily and oral iron supplements for 7 days. She was diagnosed as IIH 2 years back in view of

throbbing headache, photophobia with blurring of vision in both eyes. Her ophthalmologic examination then showed bilateral grade 2 papilloedema (Figure 1) with visual acuity of 6/9 in both right and left eye. No relative afferent pupillary defect was demonstrated. Intraocular pressure and anterior segment were unremarkable. The visual field showed an enlarged blind spot with moderate constriction of visual fields in both eyes. Her CSF opening pressure was 21 mmHg and her MRI brain with MR venogram showed no significant abnormalities. She was on tab acetazolamide 250 mg once and tab topiramate 25 mg twice daily.

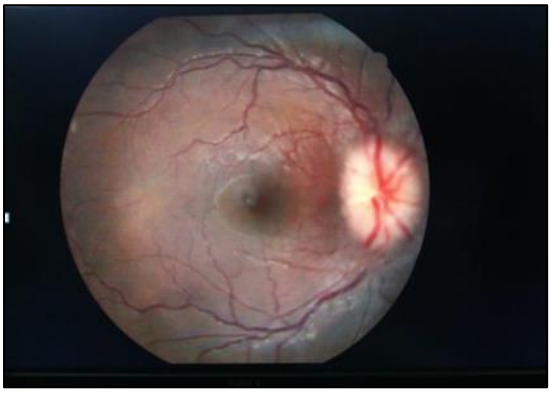

Figure 1: Retinal examination showing right eye grade 2 papilloedema.

On admission, her temperature was 98.4°F with a heart rate of 100 beats per minute, blood pressure of 100/70 mm Hg, respiratory rate of 22 breaths per minute and SpO2 of 97%. On examination, she had a normal body mass index of 24, severe pallor, glossitis, with normal central nervous system, respiratory system, and cardiovascular system findings. Initial lab results revealed hemoglobin (HGB) of 5.5 gm/dl, and platelet count of 484×10*9/l. Peripheral blood smear, ferritin level, prothrombin time, activated partial thromboplastin time and fibrinogen were within normal limits with negative pregnancy test. ECG, 2 D Echo, thyroid profile, renal profile were within the normal range. Ultrasound abdomen showed normal sized uterus and ovaries with endometrium thickness of 5 mm. She underwent an urgent ophthalmic examination, which revealed visual acuity of 6/6 in both right and left eye. No relative afferent pupillary defect was demonstrated. Intraocular pressure and anterior segment were unremarkable. Fundus evaluation showed no evidence of papilloedema in either eyes. The peripheral retina, vessels and other cranial nerves were normal. Visual field testing revealed few focal visual field defects with mild constriction of peripheral fields in both eyes. She also underwent an urgent inpatient neurological review, which was normal.

She was started on tranexamic acid injections, 500 mg intravenous thrice daily. The patient was transfused with 2 units of red blood cells and commenced on oral acetazolamide 250 mg twice a day. After 2 days of hemostatics in view of continued bleeding, she was started on low dose progesterone, tab norethisterone 5 mg once daily after counseling and informed consent. Bleeding drastically reduced following this and was stopped in 2 days. Her HGB level returned to 8.5 gm/dl at day 5. Following tapering of acetazolamide treatment over 3 days, to once daily dose, the patient remained asymptomatic. She was discharged on day 5 with a 21 day course of progesterone with oral iron supplements and is under regular follow-up in our gynaecology and neuro-ophthalmology clinic with no deterioration of symptoms after 6 months.

DISCUSSION

In 1897, Quincke reported the first case of IIH after introducing lumbar puncture into medicine.[4] Headache is the most common symptom and is seen in approximately 85% to 90% of patients.[5] Papilledema ranging from mild blurring of the disc margins to gross disc swelling with hemorrhages and exudates, is the hallmark of the disorder.[5]

According to criteria updated by Friedman et al. IIH is a diagnosis of exclusion which requires the following: papilledema; normal neurologic examination except for cranial nerve abnormalities; neuroimaging that finds normal brain parenchyma without evidence of hydrocephalus, mass, structural or vascular lesions, or meningeal abnormalities; normal CSF composition; and elevated ICP (opening pressure > 25 cm H2O in adults).[6]

The etiology and pathogenic mechanisms of this debilitating condition still remain undetermined. Many conditions have been proposed as causative for IIH, like growth hormone, levonorgestrel implants, desmospressin nasal spray, tetracyclines, retinoids, nalidixic acid, nitrofurantoin, chemotherapies, vitamin A or D deficiencies or toxicity, thyroxine replacement therapy, corticosteroid withdrawal, viral infections and some systemic diseases.[7] As the disease is more commonly associated with obesity, weight gain, and PCOS in young females, the possibility of a role of female steroid hormones, adipose tissue, androgens, and gut peptides in modulating intra cranial pressure in IIH is under evaluation.[8]

Increased levels of estrone in the CSF, obesity-driven low-grade inflammation and a prothrombotic state have been noted in IIH patients, but a causal relation was not established.[9] A study by Markey KA, showed raised levels of androgens, including testosterone and androstenedione, in young onset female patients with IIH, of whom 39- 57% also had PCOS.[9] Combined oral contraceptives (COC's), emergency contraceptive pills, levonorgestrel- intrauterine systems [LNG- IUS] and depot medroxy-progesterone acetate [DMPA] injections have been linked with IIH and as such should be avoided. Only one report by Chan J, describes a 29-year-old woman who developed IIH 8 weeks after an injection of DMPA.[10] Wysowski and Green found 39 cases of IIH in patients with LNG-IUS.[3] In 1995,

Alder et al. described 8 women with IIH who had received LNG contraceptive implants (Norplant).[11] They suggested LNG as an effective form of contraception, in a woman with IIH or at risk for IIH as the contraceptive benefits were more than the risks.[11] Possibility of already raised intracranial pressures in these patients before prescription of steroid hormones was not ruled out. Oral tetracycline following LNG insertion could also be a risk factor for IIH. It was not clear why exogenous LNG would cause IIH, but endogenous progestins (as in pregnancy) would not.[11]

Medical therapy for IIH includes weight loss, lumbar punctures, salt and fluid restriction, carbonic anhydrase inhibitors, diuretics, and nonsteroidal anti-inflammatory drugs (NSAIDS). Treatment options of AUB include iron supplementation, COC's, progesterone, NSAIDS, antifibrinolytics, desmopressin and Gonadotropin-releasing hormones (GnRH).[2] In patients having contraindications to estrogen-containing regimens, progestin-only therapy may be an option with oral medroxyprogesterone acetate or norethindrone acetate in tapering doses.[2] Compared to oestrogen, progesterone has been found to be safer for women with IIH. If conservative management fails to decrease bleeding within 24-36 hours, examination under anesthesia, intrauterine balloon insertion or endometrial curettage may be required.[2] Procedures such as uterine artery embolization, endometrial ablation, and hysterectomy should not be performed unless there is a life threatening bleed.[2]

CONCLUSION

Adolescent girls with HMB should be evaluated with care and a wide differential diagnosis should be borne in mind. Treatment of AUB in adolescents with IIH is a dilemma for the physician as many medicines are contraindicated in IIH and fertility preservation is a priority. Ophthalmology, neurology consultation is mandatory before starting any hormones in IIH patients. Given the dangers of the use of oestrogen hormones in women diagnosed with IIH it really is best avoided. To date, there is no evidence implicating either implantable or oral progesterones as a cause for IIH but caution should be exercised when prescribing progesterones to IIH patients. Surgical intervention should be considered only in life- threatening conditions.

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