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Case Report

Acute intermittent porphyria exacerbation following *in vitro* fertilization treatment

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ABSTRACT

Objectives: Assisted reproductive technology is commonly used for women with infertility. We report a case of acute intermittent porphyria associated with *in vitro* fertilization treatment.

Case Report: A 35-year-old woman with tubal factor infertility presented to our clinic with persistent low abdominal pain and hyponatremia after transvaginal oocyte retrieval. During admission, she experienced a generalized tonic–clonic seizure attacked following by dark brown color urine. Urinary tests showed elevated porphobilinogen, 5-aminolevulinic acid, uroporphyrin, and coproporphyrin, confirming the diagnosis of acute intermittent porphyria. The patient's condition continued to improve after hemin treatment and rehabilitation.

Conclusion: Newly onset acute intermittent porphyria during the course of controlled ovarian hyperstimulation for *in vitro* fertilization is a rare but possible complication. Acute intermittent porphyria should be taken into consideration for persisted unexplained abdominal pain and seriously alerted if accompanied with neurological symptoms. Special tests for acute intermittent porphyria should be taken into consideration for the differential diagnosis of lower abdominal pain after oocyte retrieval.

Introduction

Acute intermittent porphyria (AIP) is an autosomal dominant disorder with low penetrance resulting from a partial deficiency of the heme biosynthetic enzyme porphobilinogen deaminase [1]. Alterations in the enzymes of heme biosynthesis cause a variety of neurovisceral symptoms. The diagnosis of AIP should be considered in many patients with otherwise unexplained abdominal pain, severe constipation, systemic arterial hypertension, or other characteristic symptoms. It is a rare disease which affects reproductive age women more commonly than men. Development of symptoms is affected by a variety of exacerbating factors including sex hormones.

Oocyte retrieval in assisted reproductive technology is nowadays achieved almost exclusively by the transvaginal ultrasound-guided follicle aspiration method. Hormonal level fluctuations before and after oocytes retrieval could potentially induce exacerbations of AIP. We present a case of AIP exacerbations manifested as a rare complication which may be associated with hormonal fluctuation during *in vitro* fertilization (IVF) treatment.

Case Report

A 35-year-old nulliparous woman with a history of ectopic pregnancy came to our infertility department in hopes of pregnancy. Bilateral tubal occlusion was suspected under hysterosalpingography and IVF treatment was advised. The flare up protocol with gonadotropin-releasing hormone agonist (Leuprolide Acetate; FAMR L'AiGLE, France) 1.0 mg per day was administered subcutaneously until the day of human chorionic gonadotropin (HCG). Controlled ovarian hyperstimulation was achieved by a total of 1200 IU recombinant follicle stimulating hormone (Puregon; Organon, Oss, the Netherlands) and 75 IU recombinant luteinizing hormone (Luveris; Merck-Serono, Darmstadt, Germany). HCG was given to trigger ovulation. The patient's estrogen level was 3650 pg/mL and progesterone level was 1.86 ng/mL on the day of HCG administration. Transvaginal oocyte retrieval (TVOR) was done smoothly 36 hours after the administration of HCG, with a total of

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15 oocytes retrieved. Due to premature elevated progesterone level on the day of HCG, all fertilized embryos were cryopreserved.

The woman presented to the emergency department (ED) on the next day after the surgery with acute onset lower abdominal pain. Physical examinations showed lower abdominal tenderness and rebound tenderness. Small amount of ascites was noted under ultrasonography and post-TVOR peritonitis was suspected. Her symptoms improved gradually after the administration of intravenous fluid, oral antibiotics, and analgesics. She was then discharged from the ED after 57 hours of stay.

The patient presented to the ED again 4 days after TVOR. This time, she complained of right upper quadrant and lower abdominal pain. Nausea and vomiting were also found. Laboratory work-up was unremarkable except for hyponatremia (Na 127 mmol/L). Imaging studies with abdominal ultrasonography and computed tomography (CT) revealed enlarged bilateral adnexae with small amount of ascites. Early onset of ovarian hyperstimulation syndrome was suspected. Conservative management was taken. Her symptoms improved on the next day, and the patient was discharged again from the ED.

The patient visited our out-patient clinic 9 days after TVOR, complaining of persisted intermittent abdominal pain. She also asked for menstrual manipulation. Intramuscular injection with 50 mg progesterone was given in hopes of reducing the patient's anxiety and discomfort. However, her symptoms persisted and reported again to our ED for the third time on the 11th day after TVOR. Right lower quadrant pain with abdominal fullness aggravated and no bowel movement for 4 days were complaints. Follow-up lab work-ups revealed persisted hyponatremia (Na 127 mg/dL). Plain abdominal film (Figure 1) showed distended colon and fecal impaction. Due to persisted abdominal pain, the patient was hospitalized on the 13th day after TVOR.

After admission, gastroenterologists were consulted and they suspected Ogilvie's syndrome. Supportive care was suggested. For persistent hyponatremia, nephrologists suggested it might be related to syndrome of inappropriate antidiuretic hormone. However, on the 2nd day of her admission, generalized tonic–clonic seizure occurred twice. Her seizures lasted for several minutes which ceased spontaneously before any intervention. Neurologists were consulted. Brain CT showed a hypodense lesion at the right parieto-occipital lobe. Abdominal CT revealed bilateral ovarian cysts and markedly dilated colon. Dilantin was given for 6 consecutive days as suggested by the neurologist, but another seizure episode occurred. Brain magnetic resonance imaging was performed and revealed amorphous lesions with hyperintensity on T2 weighted fluid-attenuated inversion recovery (T2 FLAIR) imaging (Figure 2) and hypointensity on diffuse weighted imaging in the bilateral parieto-occipital and right frontal lobes, suggesting posterior reversible encephalopathy syndrome. Also, dark brown color urine was found during hospitalization. Urinary tests showed

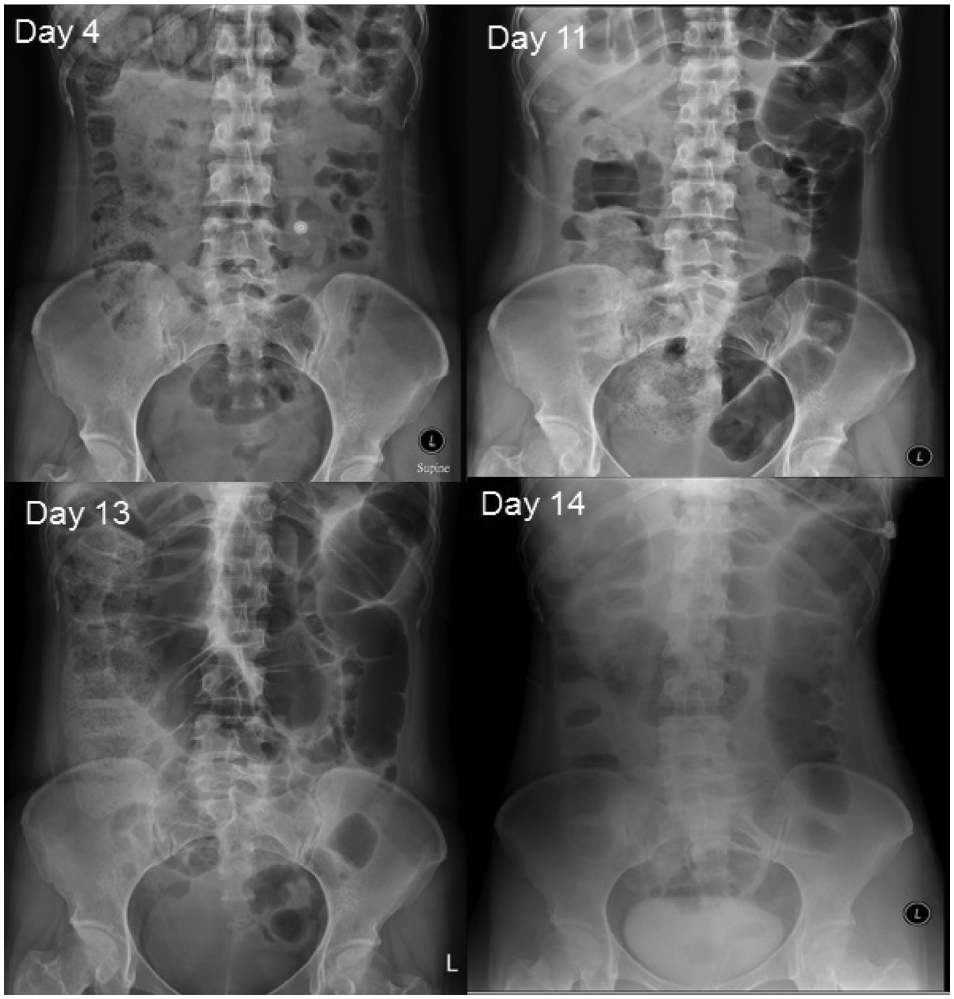

Figure 1. Plain abdominal films showed progressive distended colon.