

Multidisciplinary Team (MDT) Approach Is Key to Optimizing Care of Acute Intermittent Porphyria (AIP) In Pregnancy

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Abstract

Acute Intermittent Porphyria (AIP) is a rare autosomal dominant metabolic disorder affecting the production of heme, due to deficiency of enzyme porphobilinogen deaminase. AIP is the most common inherited acute porphyria. Pregnancies complicated by AIP can be associated with poor maternal and perinatal outcomes. AIP affects autonomic and central nervous systems presenting in pregnancy with clinical symptoms similar to obstetric emergencies that may cause delay with diagnosis and management. Advances in disease condition have enabled better understanding of AIP with the commissioning of three UK porphyria centres; in Cardiff, Cambridge and London (Kings College Hospital) and additional outreach centres in Salford and Leeds since 2012. The value of using MDT to optimize care of AIP in pregnancy resulting in good outcomes is shown and discussed.

Keywords: Acute intermittent porphyria (AIP); Acute obstetric emergencies; Commissioning; Gastrointestinal tract (GIT); Multidisciplinary care (MDT); Out-reach centres

Case Report

A 35-year year old Caucasian Para1+1 woman with known Acute Intermittent Porphyria (AIP) in pregnancy was admitted on medical wing of our hospital at 19 weeks' gestation'. Ultrasound examination showed a single active foetus consistent with gestation with no abnormalities. Her first pregnancy at of 27 years of age was uncomplicated, resulting in a healthy female child. Her second pregnancy two year's prior, was complicated with acute intermittent porphyria, and terminated at 10 weeks' gestation for maternal health. There was history of Porphyria in her family. In current pregnancy, she was admitted under the Physician, usually responsible for her and family of disease condition. Clinical symptoms on admission were acute abdominal pain radiating to her back and thighs, bloating, nausea and vomiting. She complained of migraines, was weepy and depressed.

She exhibited neuropsychological disorders of verbal aggression, anxiety, panic attacks with psychiatric and psychological behaviours. She smoked 10 cigarettes a day

(commenced after first pregnancy). Baseline clinical parameters were: B/P 100/50 mm Hg; Pulse 78 bp m, height 1.63; weight 77.8, BMI 29.3. "Blood chemistry results were sodium 133 mmol/L, potassium 4.7 mmol/L, alkaline phosphatase 81 u/L. Spot test for porphobilinogen on a freshly produced urine was 24 mg. Diagnosis of AIH in pregnancy was based on detailed history, clinical presentation, and biochemistry results". Following the diagnosis of AIP in pregnancy and initiation of treatment, she was referred to obstetric team for care. Transfer to obstetric suite was anticipated. Treatment commenced were morphine 5 - 10 mg 6 hourly for pain relief, antiemetic prochlorperazine 50 mg 4-6hly (As required); haeme arginate 225 g for AIP, administered intravenously daily for four consecutive days through PICC line over 15 - 20 minutes and fluid hydration.

Her condition was uploaded to National Acute Porphyria Service (NAPS-UK), Wales, where she was already registered. Results of antenatal, intrapartum and postpartum management from sought from personal, RCOG, NICE, literature, and National Acute Porphyria Service (NAPS-UK) were suboptimal. A Multidisciplinary Team (MDT) consisting of the lead obstetrician, a physician, neonatologist, anaesthetist, specialist medical nurses and midwives was formed for management. Best optimal location of patient for care was uncertain however, with recurrent acute

flare-ups of AIP crisis, planned antenatal reviews at 24, 28, and 30-week's gestations were carried out on the medical ward. She was commenced on subcutaneous Clexane (40mg) daily to reduce risk of thromboembolism.

Despite optimal AIP treatment, recurrent AIP crisis continued, allowing patient very short-term pain free intervals. Her psychological state became very unpredictable. She requested more morphine than recommended for pain relief and refused fetal monitoring. She asked for delivery. Based on request, MDT meeting was held (now 30 weeks' gestation) with patient present (invited) to discuss delivery. Risks of premature birth were explained. Patient agreed to suggestion of delivery after 34 weeks that was fixed. Patient's psyche improved. She agreed to assessments of fetal wellbeing was given intramuscular steroids following which delivery by caesarean section took place at 34 + 2 days resulting in a healthy female infant weighing 2.52 kg with Apgar scores of 7/10. Maternal AIH symptoms improved spontaneously and resolved within 48 hours of delivery. No physical abnormalities were observed on the neonate. Mother and baby were discharged from hospital one week after delivery.

Discussion

Acute intermittent porphyria (Often known as Swedish porphyria) is the most common of the disease condition. It is an inherited dominant metabolic disorder caused by abnormal functioning of hem biosynthesis enzyme Hydroxymethylbilane Synthase (HMBS), also known as porphobilinogen deaminase and characterised by excessive accumulation of porphyrins and their precursors in the body [1]. AIP affects all races. Recent population based genetic studies indicate 1 in 2000 of the population, inherit the pathogenic mutation causing disease condition [2-6]. Majority (90%) of gene carriers of disease however will not show signs of illness in their lifetime. However, 5-10 % of carriers will suffer acute attacks with 3-5 % of these suffering recurrent attacks (> 4 per year). AIP attacks rarely occur before puberty and after menopause. Men and women suffer acute attacks, with attacks commencing in twenties in women and thirties in men. Attacks occur more frequently in women than men due mostly to menstrual hormones [1,7-9]. Attacks are precipitated by risk factors known as triggers. Pregnancy is a known trigger of acute attacks.

Clinical features of AIP are variable and nonspecific. Acute attacks can be life threatening with combined effects on autonomic and central nervous systems. The most common symptoms are severe unremitting abdominal pain, that may be associated with nausea and vomiting, constipation or diarrhoea some of which patient presented on admission [2,3,5,7,10,11]. Neurological symptoms include, anxiety, depression, insomnia, hallucinations with psychosis presented by patient [6,7,10]. Affected individuals may experience tachycardia, high blood pressure and cardiac

arrhythmias not present in this patient. When severe blood pressure is present, urgent appropriate assessment and management is necessary due to associated maternal and perinatal morbidity and mortality from eclampsia that is an obstetric emergency. AIP is rare in pregnancy and if complicating pregnancy, acts as trigger of more acute attacks, with worse protracted clinical features, hence increased risks of spontaneous miscarriages, terminations, obstetric interventions, prematurity, low birthweight and increased perinatal mortality and maternal morbidity [12-14]. Other triggers of attacks include weight loss common in hyperemesis gravidarum, smoking, alcohol (Especially bingeing) and drugs such as barbiturates, hydantoins, rifampicin, sulphonamides [14,15].

Experience of managing AIP in pregnancy is limited as shown in this case. Issues identified from case reports of AIP include diagnosis (delayed/misdiagnosed); treatment (safety) and counselling [9-17]. In this case, prompt diagnosis was made by the Medical Team (MDT), previously aware of patient and family history of disease condition. With prompt diagnosis drug treatment (Heme arginate) was commenced. Had diagnosis been made by obstetric team, treatment may have required transfer either to a tertiary unit or certified centre for treatment, unless a medical unit as in this case was available. With obstetrics, heme arginate administration might possibly not have been given due to anxieties with drug safety [18,19]. Furthermore, prolonged use of morphine (Narcotics) for maternal pain relief may have been difficult. Anxieties regarding effects on fetus raised at MDT and at personal levels did not materialise. Personal communications with individuals at the porphyric centre, Wales were reassuringly helpful on several issues during management of pregnancy and delivery.

Conclusion

We have published this paper to bring difficulties encountered in management to attention of clinicians and; how to recruit appropriate MDT early for the management of rare/difficult cases as well as involving patients in their management. Obstetrician should always leave lines of communication open with the regional centres. We feel appropriate MDT was instrumental in successful outcome of this case. We wish to emphasize major roles of regional porphyria centres in registering cases, research, data collection, patient counselling, providing support and educating sufferers on risk factors that trigger acute attacks such as smoking, alcohol, dieting and anaemia.

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We confirm all authors made appropriate contribution towards producing this manuscript.

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