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Erythropoietic protoporphyria in first pregnancy

Abstract: Erythropoietic protoporphyria is a rare, inherited disorder, mainly characterised by photosensitivity. Its accompanying vitamin D and iron deficiencies, as well as potential effects on the liver, make it an important condition to monitor in pregnancy. However, as discovered in our subject case, pregnancy and delivery appear to pose little additional burden to the woman or baby, and in fact, may lead to an improvement of symptoms.

Keywords: Erythropoietic protoporphyria; photosensitivity; porphyrin; pregnancy.

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Introduction

Erythropoietic protoporphyria (EPP) is a rare, inherited disorder of haemoglobin biosynthesis. Traditionally considered autosomal recessive, this may be open to challenge, as <10% of carriers express clinical symptoms of disease [7]. Ferrochelatase (FECH) is the terminal enzyme in the haem synthesis pathway to haemoglobin production. A deficiency of FECH results in an accumulation of excess protoporphyrin IX, depositing in erythrocytes, plasma, skin and liver [2]. This then causes acute photosensitivity upon exposure to ultraviolet (UV) light [4]. Usually, photosensitivity only manifests in those who inherit a low expression FECH gene polymorphism (FECH concentrations below 30%), as the non-mutant allele has insufficient expression to compensate [1, 7]. Most affected with EPP report photosensitivity as the only major manifestation, with neurovisceral symptoms (such as abdominal pain) in some sufferers [7, 9]. Complications that are more serious may result from excess protoporphyrin IX deposition and cholestasis, such as gallstones, and rarely, hepatotoxicity (liver failure is fatal in a small percentage of cases) [2, 5–7]. Other consequences include vitamin D deficiency and iron deficiency anaemia [3]. It is free porphyrin concentration in erythrocytes that supports a diagnosis of EPP, together with the clinical picture; being lipophilic, porphyrin levels in urine do not increase [9].

Case presentation

This case reviews a 26-year-old primipara who was referred by her general practitioner at 7 weeks gestation of a planned pregnancy, by last menstrual period. The conception was spontaneous. The patient was a non-smoker with a body mass index of 25.1 and no significant medical history other than EPP.

The patient was diagnosed at 10 years of age with EPP. Her primary presenting symptom at that time was severe abdominal pain and she has suffered similar episodes on a semi-annual basis since. Her history elicited a brief period of phototherapy at birth for neonatal jaundice. She actively avoids exposure to direct sunlight and other UV lights, which cause erythema to her face and extremities. Her dermatologist recommended sunscreens containing titanium dioxide and protective clothing. Two previous surgeries to her back and knee proceeded without any problem caused by operating theatre lights. At the time of her initial antenatal visit, the patient had not recently suffered any symptoms and had never required a blood transfusion. Her annual liver function tests (LFTs) have remained largely unremarkable. The patient had two female siblings and one was diagnosed with a slightly milder form of EPP than the patient. No other family members are affected.

LFTs throughout the pregnancy were normal, with the exception of a mild rise in alanine aminotransferase (ALT) to 36 u/L (normal range 5–30 u/L) in the first trimester. At that time, a mild deficiency in vitamin D of 43 nmol/L (mild deficiency range 25–50 nmol/L; normal range 51–140 nmol/L) was detected. This was at a low-normal concentration of 51 nmol/L by the third trimester, without supplementation. Vitamin D after delivery was borderline normal at 50 nmol/L. The routine glucose challenge test was within normal limits. Antenatal serum screening was negative (including hepatitis B and
elevated at 4.5 g/L (normal range 2.0–3.6 g/L), but was (normal range 5–20 µmol/L). Transferrin was briefly from low normal (11.4 µmol/L) to deficiency at 5.0 µmol/L trimester and the day after delivery. Iron levels dropped limits. Iron studies were then compared between the third zin and varicella.

Discussion

EPP belongs to a group of disorders known as the porphyrinas, where synthesis of haemoglobin is disrupted by a deficiency in FECH, leading to excess deposition of protoporphyrin IX, particularly in bone marrow [2]. Photosensitivity to UV light may cause skin changes, such as urticaria, burn, plaque, oedema, pruritis and scarring [7]. Vitamin D deficiency is common and most likely secondary to poor exposure to sunlight (in an attempt to avoid symptoms). Supplementation should be considered [3]. β-carotene (a precursor of vitamin A) is a widely used prophylactic treatment for EPP, believed to partially counteract free radical cell damage produced by porphyrin as the skin reacts to light and, therefore, improving tolerance to sun exposure in some [8]. The effectiveness is questionable and is contraindicated in smokers [2, 3, 9]. As there is insufficient evidence related to its use in pregnancy and breastfeeding, high doses of β-carotene should be used cautiously, or indeed avoided, in these patients.

Iron deficiency anaemia is not reflective of iron loss [2, 3]. Rather, it most likely due to FECH deficiency, resulting in a lack of haemoglobin production [3]. It acknowledged that pregnancy itself is a cause of iron deficiency anaemia and may therefore compound the problem in EPP patients. Difficulties exist with iron supplementation, as worsening of photosensitivity has been known to occur [6]. ALT is reportedly the most often elevated of the LFTs [3].

Our case supports previous reports that pregnancy poses little challenge to the EPP patient or baby [1, 7]. Interestingly, this condition often improves from a symptomatic perspective during pregnancy [3, 7]. Monitoring of vitamin D levels and LFTs are the most important aspects of antenatal care in relation to EPP management. It is also necessary to have an understanding of the difficulties associated with managing iron deficiency anaemia, which is a common finding, compounded by the pregnant state, but not necessarily responsive to exogenous supplementation (and risking enhanced photosensitivity). The potential for operating theatre lights to exacerbate symptoms and cause phototoxicity of intra-abdominal organs is a relevant consideration when making decisions regarding mode of delivery and other perinatal procedures [9]. For patients suffering episodes of abdominal pain, treatment with simple analgesia such as paracetamol, or codeine and opioids for more severe pain, is recommended [9]. Non-steroidal anti-inflammatory agents should be avoided in the pregnant state due to potential adverse effects on the foetal ductus.

Received January 24, 2013. Accepted July 31, 2013. Previously published online September 5, 2013.
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The authors stated that there are no conflicts of interest regarding the publication of this article.