Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 09, pp.58170-58172, September, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

CASE STUDY

PORPHYRIA-A RARE ASSOCIATION IN PREGNANCY

[1]Dr. Ragini Mehrotra, [*,1]Dr. Jaya Patel and [2]Dr. Nirendra Rai

[1]Department of Obst & Gynae, AIIMS Bhopal, India
[2]Department of Neurology, AIIMS Bhopal, India

ARTICLE INFO

Article History:
Received 24th June, 2017
Received in revised form
08th July, 2017
Accepted 16th August, 2017
Published online 30th September, 2017

Key words:

Acute intermittent porphyria,
porphobilinogen deaminase, Paraparesis,
Haem biosynthetic pathway,
Hyponatremia,
Neurological manifestations.

ABSTRACT

Acute intermittent porphyria is an unusual pathology with potentially severe consequences when not detectedearly. The porphyrias are a heterogeneous group of rare, primarily hereditary, metabolic diseases caused by a partial deficiency in one of the eight enzymes involved in the hemebiosynthesis, that can lead to severe disease that requires early diagnosis to avoid complications. The frequency of the disease is low and its association with pregnancy unusual, but it is a good time for patients carrying develop the disease or suffer an exacerbation of the same, hence the vital importance of prophylaxis of the risk factors. Despite the fact that pregnancy in women suffering from AIP has to higher rates of morbidity and complications, close management throughout the pregnancy could ensure a good outcome. Since practitioners rarely encounter this disease process, it is commonly not considered in the differential diagnoses. AIP can be confused with other causes of acute abdominal disorders such as appendicitis with peritonitis or nephrolithiasis. Here we are discussing the case of a 24 years old pregnant women with Acute intermittent porphyria its consequences and poor obstetrics outcome.

Citation: Dr. Ragini Mehrotra, Dr. Jaya Patel and Dr. Nirendra Rai. 2017. "Porphyria-A rare association in pregnancy", *International Journal of Current Research*, 9, (09), 58170-58172.

INTRODUCTION

Porphyria is a hematological disorder; the word derives from the Greek word *porphuros,* which means red or purple (Crimlisk, 1997). Acute intermittent porphyria (AIP) is an autosomal dominant metabolic disorder in which there is an abnormality in the haem biosynthetic pathway due to the deficiency of uroporphobilinogen I synthetase (porphobilinogen deaminase), which leads to excessive production of porphyrin precursors. (Ackner *et al.,* 1962) The classic triad of an acute attack includes abdominal pain, peripheral neuropathy, and changes in mental status. (Regan *et al.,* 1999) Abdominal pain is the most common cause of frequent hospital admission. (Laiwah *et al.,* 1985) Although all subtypes are rare, acute intermittent porphyria is the most common. (Crimlisk, 1997; Thadani *et al.,* 2000; Hift *et al.,* 1997; Scarlett and Brenner, 1998; Petrides, 1998; Moore, 1993; Sassa and Kappas, 2000; Burgovne *et al.,* 1995; Santosh and Malhotra, 1994; Deacon and Peters, 1998)

Case History

A 24 years old female patient presented in the OPD of Obstetrics and Gynaecology department of AIIMS Bhopal on 5th January 2017, with complaint of acute lower abdomen pain and positive pregnancy test. At the time of admission patient had fair general condition, paraparesis and fullness in her left fornix on vaginal examination. Ultrasonography showed triple line endometrium with suspicion of early ectopic pregnancy Patient and her attendants did not reveal the history of psychiatric illness, which was evident on detailed interrogation and she herself had stopped antipsychotic drugs 10 days back. She had laparoscopic apendisectomy, six month back. Patient was haemodynamically stable. Medical treatment with Methotrexate was planned for unruptured ectopic pregnancy (GS <3.5 cm diameter) but could not be given as her liver function and kidney functions were deranged and she was kept under observation. Next morning she developed tachycardia (PR>150/m), acute abdominal pain, abdominal distension and retention of urine, for which catheterization was done and Emergency laparotomy was performed. Uterus was soft and bulky, ovaries, tubes and pouch of Douglas were normal and there was no hemoperitoneum. After 12 hr of laparotomy patient developed abnormal behavior, disorientation and unresponsiveness to verbal commands and tachycardia. On investigation, she had hyponatremia (Na-115 mmol/L), Hypomagnesinemia (Mg-1.30 mg/dL), decreased levels of Chloride and Potassium. Patient was shifted to ICU immediately and was kept on continuous monitoring and serial ABG analysis. After medical and Neurological opinion and on

Corresponding author: **Dr. Jaya Patel,**
Department of Obst & Gynae, AIIMS Bhopal, India.

further investigations she showed positive urine porphobilinogen (PBG) test. She had normal thyroid profile. EEG and MRI Brain, Her BHCG was repeated after 48 hours of the initial test and was found to be almost double the initial value confirming a viable intrauterine pregnancy. After 24 hours patient became conscious and oriented, was treated with MgSO4, Ca gluconate, fludrocortisone and Ivabradin along with symptomatic and supportive treatment. Her Para paresis progressed to quadriplegia, she was now kept in medical ward for supportive treatment. After 1 week ultrasonography showed intrauterine gestational sac of 6 weeks with no fetal pole and after 3 weeks it showed empty intrauterine gestational sac of 5 week 2 days. Patient was anxious to conceive since 5 years of her marriage. She underwent good amount of emotional trauma for not concieving and she went in to depression, started antipsychotic drugs after consultation with some local doctor. After giving specific & supporting treatment her general condition and quadriparesis improved gradually, she also showed improvement in quadriperasis and in her general condition. After a week she herself took LAMA from the hospital due to her personal reasons and came for follow up after 1 week that time she was well oriented to time place and persons and able to walk with support. She had complaint of bleeding per vaginum since 3 days, her sonography report showed empty intrauterine gestational sac of 5 week 2 days. She was advised medical management along with necessary investigations. After taking MTP Pills she bleed for 7 days. After 15 days repeat USG was done that showed empty uterine cavity and her investigations were within normal limits.

(Crimlisk, 1997; Thadani *et al.,* 2000; Hift *et al.,* 1997; Ashley, 1996; Jensen *et al.,* 1995). Clinical features of AIP consist of heterogeneous manifestations of acute neurovisceral attacks; there is no cutaneous involvement. The most common signs and symptoms of AIP are abdominal pain (80%), constipation (50%), nausea and vomiting (50%), Tachycardia (40%), hypertension (31%), urine discoloration (25%), and fever (16%). (Suarez *et al.,* 1997) The most common physical sign of AIP is tachycardia, which occurs in as many as 80% of patients with acute attacks. (Stein and Tschudy, 1970) Tachycardia results, in part, from the release of catecholamine during an acute attack and has been implicated in the sudden death attributed to cardiac arrhythmias. (Gross *et al.,* 2000) Hyponatremia is often associated with acute attacks of AIP and may result, in part, from the inappropriate secretion of antidiuretic hormone. Hyponatremia in AIP can occur with or without clinical volume loss (De Block *et al.,* 1999) The neuropsychiatric signs and symptoms of AIP are diverse and nonspecific. The most common presenting symptom of an acute attack is abdominal pain. (Bustamante *et al.,* 1999) Neurological manifestations comprise of flaccid paralysis, neuropsychiatric disturbances and rarely generalised epileptic fits. (Becker and Kramer, 1977; Goldberg, 1959) Paralysis may be confined to lower or upper extremities or may affect all the four limbs. It may be more marked proximally or distally or may be generalised and is due to predominant motor neuropathy. Sensory symptoms may also occur but objective sensory loss is unusual. (Goldberg, 1959)

Table 1. Features of acute porphyrias

Feature	Plumboporphyria	Acute intermittent porphyria	Variegate porphyria	Hereditary coproporphyria
Other name	Doss porphyria; aminolevulinic acid dehydrase deficiency	Type ii-a; swedish porphyria; the little imitator	Type ii-b;south african genetic porphyria;mixed acute intermittent porphyria	
Organ or system	Liver	Liver	Liver	Liver
Category	Neuroporphyria	Neuroporphyria	Neurocutaneous	Neuro-cutaneous
Enzyme deficiency	A- aminolevulinic acid dehydrases(also called porphobilinogen synthase)	Porphobilinogen deaminase (also called hydroxymethylbilane synthase and uroporphyrinogen i synthase)	Porphobilinogen oxidase	Coproporphyrinogen oxidase
Genetic expression	Autosomal recessive	Autosomal dominant	Autosomal dominant	Autosomal dominant
Age at onset	Any age	Adulthood	Adulthood	Adulthood
Higher incidence in women than in men	Yes	Yes	Yes	Yes

DISCUSSION

Acute intermittent porphyria (AIP) pertains to a group of at least eight distinct genetic diseases, the acquired forms is called porphyrias. It is most commonly seen in England, Ireland and Sweden (where it reaches 1:10,000) with estimated occurrence is 1 to 2 in every 100,000 persons. (Jorge, 2007) In bearers of psychiatric disease, literature cites a prevalence of up to 1:500. (Tishler *et al.,* 1985) Females are more commonly affected than males.[15] Revision of the literature concludes that the illness can worsen because of symptomatic exacerbations, estimated in 50% of cases. Mothers' mortality rates range from 27% to 42.5%. (Soriano *et al.,* 1996) During pregnancy for symptomatic exacerbations exposing the patients to certain drugs resulting in abortion, preterm births, and other pregnancy complications. Up to 60% of pregnancy complications happen at the beginning, in early gestational ages. (González *et al.,* 2006) Initial suspicion of a possible diagnosis is based on a myriad of clinical manifestations (Table 1 and are confirmed by laboratory testing where available.

The reason for neurological involvement in acute porphyrias remains poorly understood. Direct neurotoxicity of delta-ALA by interaction with GABA receptor, altered tryptophan metabolism, or a neural respiratory haem-dependent enzymatic deficiency in nerve cells has been hypothesized. (Ref-Meyer *et al.,* 1998) Nevertheless, axonal degeneration of peripheral and autonomic nerve fibres rather than demyelination seems to be responsible. The neurological effects of acute porphyria are generally reversible, though incomplete recovery and residual paresis have also been reported. The reported mortality in porphyric polyneuropathy varies from 20-50%. (Oomman and Gurtoo, 2002)

Conclusion

Acute intermittent porphyria should be included in the differential diagnosis of neurological, psychiatric and gastroenterological alterations when results of all other exams are normal. Porphyria can be a negative influence in pregnancy so it is important to highlight the possibility of diagnosing this

illness during pregnancy and puerperium in fertile women who are carriers of the defect, as this period is of special risk. Women who carry the deficiency should be well informed about risks and receive health information about the symptoms and precipitating factors so they can have healthier pregnancies and healthier children. Diagnosis should be performed by measuring excretion of porphyrins or, better still, by running genetic tests. Thus, we will be able to avoid precipitating factors.

REFERENCES

Ackner, B., Cooper, J.E., Gray, C.H. Cooper, et al. 1962. Acute porphyria a neuropsychiatric and biochemical study. *J Psychosom Res.,* 6:1,1–2

Ashley, E.M. 1996. Anaesthesia for porphyria. Br J Hosp Med 56:37–42

Becker, D.M. and Kramer, S. 1977. The neurological manifestations of porphyria A review. Medicine, 56: 411-423.

Burgovne, K., Swartz, R. and Ananth, J. 1995. Porphyria: reexamination of psychiatric implications. *Psychother Psychosom,* 64:121–130

Bustamante, M., Moll, J.L., Sarrion, J.V. and Berenguer, J. 1999. Acute intermittent porphyria: a possible cause of abdominal pain [in Spanish]. *Gastroenterol Hepatol,* 22:497–500.

Crimlisk, H.L. 1997. The little imitator—porphyria: a neuropsychiatric disorder. J NeurolNeurosurg Psychiatry 62:319–328.

De Block, C.E., Leeuw, I.H. and Gaal, L.F. 1999. Premenstrual attacks of acute intermittent porphyria: hormonal and metabolic aspects—a case report. *Eur J Endrocrinol,* 141:50–4.

Deacon, A.C. and Peters, T.J. 1998. Identification of acute porphyria: evaluation of a commercial screening test for urinary porphobilinogen. *Ann Clin Biochem,* 35:726–732

Goldberg, A. 1959. Acute intermittent porphyria. A study of 50 cases. Quart. J. Med., 28: 183-209.

González, C.J., López, R.E., Herrera, A.B.P., Alfaro, A.J., Navarro, M.C. and Chávez, S.G. 2006. PorfiriaagudaIntermitenteen el embarazo. *Am Med Assoc Med Hosp ABC. 51:* 134-7

Gross, U., Hoffmann, G.F. and Doss, M.O. 2000. Erythropoietic and hepatic porphyrias. *J Inherit Metab Dis* 23:641–61.

Hift, R.J., Meissner, P.N. and Kirsch, R.E. 1997. The clinical diagnosis, prevention and management of the hepatic porphyrias. *Trop Gastroenterol,* 18:41–44

Jensen, N.F., Fiddler, D.S. and Striepe, V. 1995. Anesthetic considerations in porphyrias. *Anesth Analg,* 80:591–599

Jorge, S.G. 2007. Porfiriashepáticas [Internet]. Hepcentro; [citado 2008 Abr 20]. Disponívelem:http://www.hepcentro.com.br/porfiria.htm

Laiwah, A. C. Y., MacPhee, G. J. A., Boyle, P., Moore, M. R. and Goldberg, A. 1985. "Autonomic neuropathy in acute intermittent porphyria," *Journal of Neurology Neurosurgery and Psychiatry*, vol. 48, no. 10, pp. 1025–1030, 1985.

Moore, M.R. 1993. Biochemistry of porphyria. *Int J Biochem.,* 25:1353–1368

Oomman, A. and Gurtoo, A. 2002. Acute intermittent porphyria as a cause of respiratory failure. *J Indian Med Assoc,* 100:44-6.

Petrides, P.E. 1998. Acute intermittent porphyria: mutation analysis and identification of gene carriers in a German kindred by PCRDGGE analysis. *Skin PharmacolAppl Skin Physiol,* 11: 374–380

Ref-Meyer, U.A., Schuurmans, M.M. and Lindberg, R.L. 1998. Acute porphyrias: pathogenesis of neurological manifestations. *Semin Liver Dis,* 18:43-52.

Regan, L., Gonsalves, L. and Tesar, G. 1999. Acute intermittent porphyria. Psychosomatics, 40:521–523

Santosh, P.J. and Malhotra, S. 1994. Varied psychiatric manifestations of acute intermittent porphyria. *Biol Psychiatry,* 36:744–747

Sassa, S. and Kappas, A. 2000. Molecular aspects of the inherited porphyrias. *J Intern Med,* 247:169–178

Scarlett, Y.V. and Brenner, D.A. 1998. Porphyrias. *J Clin Gastroenterol,* 27:192–198

Soriano, D., Seidman, D., Mashiach, S., Sela, B. and Blonder, J. 1996. Acute intermittent porphyria first diagnosed in the trimester of pregnancy. Case report. *J Perinat Med. 24:* 185-9.

Stein, J. A. and Tschudy, D. P. 1970. Acute intermittent porphyria. A clinical and biochemical study of 46 cases. Medicine, 49: 1-16.

Stein, J.A. and Tschudy, D.P. 1970. Acute intermittent porphyria. A clinical and biochemical study of 46 patients. Medicine (Baltimore) 49:1–16.

Suarez, J.I., Cohen, M.L., Larkin, J., et al. 1997. Acute intermittent porphyria: clinicopathologic correlation. Report of a case and review of the literature. *Neurology* 48:1678–84.

Thadani, H., Deacon, A. and Peters, T. 2000. Diagnosis and management of porphyria. *Br Med J,* 320:1647–1651

Tishler, P.V., Woodward, B., O'Connor, J., Holbrook, D.A., Seidman, L.J., Hallett, M. and Knighton, D.J. 1985. High prevalence of intermittent acute porphyria in a psychiatric patient population. *Am J Psychiatry,* 142(12):1430-6

****