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Case Report

A CASE OF ACUTE INTERMITTENT PORPHYRIA CORRELATING CLINICAL AND BIOCHEMICAL FINDINGS

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ABSTRACT

Acute intermittent porphyria is an autosomal dominant disorder resulting from a deficiency in PBG deaminase activity. The cardinal pathophysiology of the disease is a neurologic dysfunction of indeterminate etiology which may affect peripheral, autonomic or central nervous system. The disorder is expressed clinically almost invariably after puberty and more commonly in women than in men. Abdominal pain is almost invariably present and is often the initial symptom of an acute attack. Neuropathy is also invariably present . The Watson –Schwartz Screening test uses pH adjustment and solvent extractions to separate PBG chromogen from other interfering substances. It is a simple biochemical test for diagnostic purpose having compatible outcome with clinical findings
Key words: Acute intermittent porphyria, Watson –Schwartz test, porphobilinogen

INTRODUCTION

Acute intermittent porphyria is an autosomal dominant disorder resulting from a deficiency in PBG deaminase activity. The deficient enzyme activity is almost always 50% of normal ,consistent with heterozygous state of affected individual .However, the majority (≈90%) of people with this genetic enzyme deficiency remain otherwise biochemically and clinically normal (latent) throughout their lives. Clinical expression of disease is usually linked to environmental or acquired factors (nutritional status, steroid hormones or their metabolites and drugs) which may intermittently induce acute exacerbations. The cardinal pathophysiology of the disease is a neurologic dysfunction of indeterminate etiology which may affect peripheral, autonomic or central nervous system. [(1)]The disorder is expressed clinically almost invariably after puberty and more commonly in women than in men

Abdominal pain is almost invariably present and is often the initial symptom of an acute attack. It may be generalized or localized and in severe cases may mimic acute surgical abdomen[(2,3)]. Neuropathy is a common feature of AIP. Motor neuropathy may also involve cranial nerves. Autonomic neuropathy may manifest as tachycardia, hypotension, vomiting, diarrhoea or sweating. Acute attacks are frequently accompanied by seizures especially in patients with hyponatremia due to vomiting, inappropriate fluid therapy or syndrome of inappropriate ADH release.

CASE REPORT

One female patient of 23 years age presented to casuality with history of loss of consciousness and disorientation. The patient had presented 1 week back on casuality with complaints of abdominal pain and vomiting. No history of any other complaints. Ultrasonographic scan of abdomen was done and it was normal study and later the abdominal pain subsided .Later patient was on a trip and suddenly abdominal pain and vomiting started .Patient again presented to casuality. Was not willing for admission and so she was sent back home against medical advise. After reaching home there was no relief in symptoms , lost her consciousness . She was brought to casuality and was admitted to ICU After she regained consciousness she was disoriented. There was no history of fever , headache or fall. No history of similar symptoms in the past. Patients mother narrated the history that she was diagnosed as having acute intermittent porphyria 20 years back when she had problems like abdominal pain and dysuria. Patient was not on any medication.

Physical examination

Patient was disoriented to time, place and person. Plantar reflex was bilateral extensor reflex. Other deep tendon reflexes normal. Sensory system was within normal limits. There was no neck stiffness. No signs of meningeal irritation. Other systems cardiovascular and respiratory system are within normal limits. On examination abdomen was soft and tender.

Biochemical finding

Biochemical tests done on blood showed hyponatremia (serum sodium levelwas107mmol/L),hypocalcemia (serum calcium level was 7.7mg/dl) and a slight increase in serum total bilirubin (total bilirubin level was 2.6 mg/dl)and increase in AST and ALT(AST 98 IU/L and ALT 111 IU/L).Other blood biochemistry tests were normal.
The patient was given the provisional clinical diagnosis of Acute intermittent porphyria and urine sample was sent for screening for AIP. The Watson –Schwartz Screening test was done.

The Watson –Schwartz Screening test

This test uses pH adjustment and solvent extractions to separate PBG chromogen from other interfering substances. Equal voumes of urine and ‘‘modified ’’ Ehrlich’s reagent (0.7g DMAB,150ml of concentrated HCl and 100ml of water were mixed and two volumes of saturated sodium acetate added [5,6,7].There was immediate development of pink colour.The solution is checked for pH. It was in the pH range of 4 to5 .An equal volume of chloroform is added and solution was shaken vigorously for 2minutes.The colour persisted in the aqueous (upper layer).The aqueous layer is separated and extracted with equal volume of butanol. With butanol also rose red colour was in the aqueous(lower) layer.This suggests a concentration of porphobilinogen that is several times upper limit of reference interval

DISCUSSION

In this patient there is typical presentation of acute abdominal pain and neurologic manifestations like coma and disorientation. Patient's mother was also diagnosed as having Acute intermittent Porphyria. So the pattern of inheritance is vertical transmission which is seen in Autosomal dominant disorders. The simple biochemical test for diagnostic purpose (Watson –Schwartz Screening test) having compatible outcome with clinical findings. In this patient the acute attack is accompanied by hyponatremia which may be due to vomiting or SIADH secretion. Abdominal pain is almost invariably present and is often the initial symptom of an acute attack. Characteristically such pains are intermittent .Other gastroenterology features are common and may include nausea ,vomiting and constipation [(4)]. Urinary incontinence ,dysuria and frequency may occur ; in severe cases the urine may be of port wine colour due to high content of porphobilin .Apart from abdominal pain and vomiting , neuropathy is a common feature of acute intermittent porphyria. Although motor neuropathies predominate ,virtually any type of neuropathy may occur. Motor neuropathy may also involve cranial nerves most commonly 7^{th} or 10^{th} or lead to bulbar paralysis, respiratory impairment and death. Autonomic neuropathy is also frequently present and may manifest as tachycardia ,hypertension ,peripheral hypotension, vomiting, diarrhea and sweating.

The course of an acute attack of AIP is highly variable within and among patients with attacks lasting from a few days to several months. One of central unexplained mysteries in AIP has been the relatively recent awareness that 90% of people with documented defeciencies of PBG deaminase remain asymptomatic throughout their life time. Patients with both latent and clinically expressed AIP may be precipitated into AIP attack by exogenous and endogenous environmental factors. Endocrine factors play a major role in precipitating the attack. Clinically expressed AIP is rare before menarche and after menopause. Subset of female patients experiences regular cyclical perimenstrual exacerabations. Progesterone has been implicated in increased heme catabolism. Synthetic estrogens and progesterone induce porphyria. Another under emphasized precipitating factor is inadequate nutrition. Reducing diets aimed at sudden precipituous loss of weight lead to acute exacerabation of AIP. Barbiturates are the best known and most injurious group of agents among drugs which

induce porphyria[1]. Diagnosis is by natural history of disease, increased urinary excretion of ALA and PBG and demonstration of reduced PBG deaminase activity in erythrocytes.

Treatment

Treatment between attacks are by adequate nutritional intake, avoidance of drugs known to exacerbate porphyria and prompt treatment of intercurrent illnesses. In some patients onset of acute attack can be aborted by increasing carbohydrate intake. Use of intravenous haematin is the treatment of choice in reducing ALA and PBG excretion.

Pitfalls of Watson –Schwartz Screening test

Interpretation of some results may be ambiguous, particularly for the inexperienced. In the Watson –Schwartz test PBG and the chromogen that it forms always remain in the aqueous phase[7].The extractions with chloroform and butanol remove frequently occurring substances that interfere with the test. The most common interfering substance is urobilinogen which is choloroform soluble and which produces a red colour with Ehrlich's reagent similar to porphobilinogen.Substances are sometimes present in urine can produce a variety of colours when combined with Ehrlich's reagent(green ,yellow and orange),all of which tend to make positive identification of PBG difficult. Substances such as phenothiazines and methyldopa produce colours similar to those for PBG ,leading to production of false positive results[8].Indole and related compounds interfere by reacting with chromophore to produce colorless derivatives ,reducing the concentration of DMAB and giving potentially false negative results[8]

CONCLUSION

In conclusion, we have described a rare case of acute intermittent porphyria. In this patient there is typical presentation of acute abdominal pain and neurologic manifestations like coma and disorientation. The simple biochemical test for diagnostic purpose (Watson –Schwartz Screening test) having compatible outcome with clinical findings. The Watson –Schwartz test can be opted for the screening of patients of Indian rural community having clinical suspicion of AIP ,so that they can diagnose early and PBG deaminase activity in erythrocytes can be done to confirm the diagnosis.

REFERENCES

1.The metabolic and molecular basis of inherited disease volume II Charles R Scriver ,Arthur L Beudet ,William.S.Sly ,David Valle Seventh Edition Volume 2 Chapter 66 page 2117-2126
2. Waldenstrom J: The porphyrias as inborn errors of metabolism.Am J Med 22:758 1957
3. Goldberg A:Acute intermittent porphyria : A study of 50 cases.QJ Med :28 183 ,1959
4. SteinJA ,Tschudy DP Acute intermittent porphyria : A clinical and biochemical study of 46 patients Medicine (Baltimore)49;1970
5.Tietz textbook of clinical chemistry Third EditionChapter 47page no 1723 -24
6.Watson CJ,SchwartzS:A simple test for urinary porphobilinogen.Proc.Soc.Exp.Biol.Med.,47:393,1941
7. Watson CJ ,Taddeini .L,Bossenmaier ,I:Present status of the Ehrlich aldehyde reaction for urinary porphobilinogen JAMA190: 501,1964
8.PierachC.A. ,CardinalR, BossenmaierI ,Watson CJ Comparison of Hoesch and Watson –Schwartz test for urinary porphobilinogen. Clin Chem,23 :1666-1668,1977