Polyglandular Endocrinopathy in Myotonic Dystrophy: Letter to Editor

Myotonic dystrophy (MD) has an autosomal dominant inheritance with a high penetrance. The disease is characterized by a unique topography of muscle atrophy, myotonia and dystrophic changes in non-muscular tissues like lens of eye, testes, cerebrum, esophagus and other endocrine glands. A patient of myotonic dystrophy, who had polyglandular failure in the form of hypergonadotrophic hypogonadism, primary hypothyroidism and Addison’s disease is described.

A 27 year old unmarried male, first in birth order, presented to the endocrine clinic of our Institute with the complaints of anorexia, weight loss and darkening of facial features of five years duration. He also complained of weakness and stiffness of both hands and neck muscles. He could not lift his neck when in supine position. There was no history of pain abdomen, vomiting, syncope, dysphagia, or nasal regurgitation. There was no history of cold intolerance or constipation. Other sibs were normal. None of the parents had similar sickness. Clinical examination revealed a young asthenic male with buccal mucosal pigmentation and diffuse pigmentation of exposed parts of body. He had pulse of 70/minute, blood pressure of 90/70 mmHg (sitting), 80/60 mmHg (standing) and body mass index of 17.41 kg/m². His secondary sexual characters were normal and both testes were small and atrophic. He had frontal baldness, hatchet facies, swan neck, high arched palate, low set ears, pectus excavatum and scoliosis of dorsal spine (Fig. 1). Central nervous system examination revealed normal intelligence, power grade 2-3 in neck muscles, shoulder muscles and jaw muscles. He had myotonia of the tongue and the muscles of hand. Both optic fundi were normal.

Detailed investigations revealed hemoglobin of 11 gm/dl; total leucocytic count of 7500/ml (neutrophils 70%, lymphocytes 28% and eosinophils 2%). Biochemical investigations revealed normal fasting and postprandial blood sugar, normal renal and hepatic functions. Serum lactic dehydrogenase was 418 U/L (normal value 100-120); and creatine kinase, 3781 U/L (normal value 25-90). X-ray of chest, skull, hands and 12 lead electrocardiogram were normal. Semen analysis revealed azoospermia. Electromyography of deltoid showed myopathic pattern. Endocrine evaluation included estimation of tri-iodothyronine, tetra-iodothyronine, thyroid stimulating hormone, prolactin, growth hormone, and gonadotropins. ACTH stimulation test was performed with 40 units of Aethergel (a long acting preparation of ACTH) and serum cortisol levels estimated at 0h, 4h, 8h and 24h. A stimulated cortisol level of >18 µg/dl was considered normal. Details of hormone estimation are given in Table I.

This patient had classical features of MD and Addison’s disease. Low basal cortisol level and sub-optimal elevation of cortisol after ACTH stimulation, in presence of pigmentation, hypotension and low blood glucose confirm the diagnosis of Addison’s disease. Presence of small atrophic testes, elevated levels of gonadotropins and thyroid stimulating hormone confirm the diagnoses of hypergonadotropic hypogonadism and primary hypothyroidism. In patients with MD associated endocrinopathy, particularly testicular atrophy, is well documented; however, polyglandular failure is a rare phenomenon.

Pizzi et al studied 12 patients with MD for any endocrine abnormalities. They documented decreased thyroid hormones in one patient. Three out of 8 patients showed no response to ACTH stimulation. Rioperez et al described two patients of MD, one with primary hypothyroidism and the other had non-toxic multinodular goiter. Pagliara et al reported hyperthyroidism and Addison’s disease in a case of MD. An instance of isolated prolactin deficiency in association with MD has also been documented. Rosenberg et al published data on four patients with hyperparathyroidism associated with MD. Their data also suggests the possibility of this disorder being associated with neurofibromatosis and multiple endocrine adenomatosis type 2A. All were females aged between 2 and 45 years. They were from three separate families, with two related patients being mother and daughter. A recent study has documented.
that the total endocrine cells area in the duodenum, as demonstrated by chromogranin-A immunoreactivity, was significantly increased in MD as compared to controls. The increase included all types of endocrine cells studied, namely those positive for serotonin, cholecystokinin, gastrin, secretin, gastric inhibitory polypeptide and somatostatin. This indicates disturbed endocrine regulation of the gastrointestinal tract.\textsuperscript{9}

The endocrine disturbances in MD seem to be quite varied and diverse. Our patient primarily presented with clinical features of Addison's disease. After evaluation, the concomitant presence of hypergonadotropic hypogonadism and primary hypothyroidism were confirmed. The presence of polyglanular failure, though known is rare. The high association of endocrinopathy and MD suggests possible cause and effect relationship between the two.

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Preliminary Observations on Valproate and Cystic Ovaries : Letter to Editor

Women with epilepsy continue to pose special therapeutic problems and dilemmas to their physicians. The latest is the scare about development of polycystic ovarian disease (PCOD) with valproate.\textsuperscript{1} The clinical features of PCOD include oligoamenorrhea, infertility, centripetal obesity, hirsutism and raised plasma testosterone level along with bilateral ovarian enlargement and multiple cysts. Recent reports suggested on increased incidence of PCOD amongst women on valproate for epilepsy.\textsuperscript{2-9} The author’s personal experience with this condition and a critical analysis of the problems at hand is presented.

Between January and February 2000, 20 consecutive young women with epilepsy, attending the author’s clinic, who had been on valproate monotherapy for more than two years were advised to have pelvic ultrasound examination. Of these, 14 patients complied. The USG examinations were performed by two experienced ultrasonologists and the results were cross checked. Clinical and EEG diagnoses of patients included : typical absence seizure (1), juvenile
myoclonic epilepsy (JME) (7) and idiopathic
generalised tonic clonic seizures (IGTCS) (6). All
patients were on valproate monotherapy (dosage 600-
1200 mg) for over two years with nearly 100% seizure
control. 13 patients were in the age range 16-20 years.
Only one young girl was aged 5.5 years.
The USG findings in the 14 patients showed normal
ovaries in six patients. Three patients had enlarged
ovaries with bilateral 6-8 mm cysts (PCOD). Mild
ovarian enlargement (< 6 mm) cysts was seen in 2
cases (probable PCOD). Three patients had normal
size ovaries with tiny cysts (<4 mm) bilaterally
(possible early PCOD).
The present report is of a preliminary nature based on
observations on a relatively small number of patients.
It was felt that the pros and cons of such serial
screening need to be discussed and views exchanged
with professional colleagues across the country,
before pursuing further work in this field. Hence the
need for this early communication.
Five out of 14 subjects studied had definite/probable
PCOD (about 35%) and a further 3 had USG evidence
of polycystic changes without any clinical stigmata of
PCOD. The latter group may include some follicular
ovarian cysts but these are usually unilateral and
would be highly unlikely in a pre-pubertal girl aged
only 5.5 years. Conversely, these may well represent
early PCOD changes in ovaries before overt clinical
disease manifests. Including all, more than 50% of
subjects had cystic changes in ovaries while
continuing on valproate therapy. As mentioned earlier,
the results must be interpreted with extreme caution
and implications carefully judged.
PCOD is not a very uncommon disease but we are
unaware of its exact incidence in our population; nor
are we aware how often cystic changes in ovaries may
be detected in young women in the population in
routine USG screen (preferably by vaginal USG) is
undertaken. In the west, the incidence of PCOD has
been quoted to be around 19% amongst healthy
women.10 PCOD is now thought to be a primary
hypothalamic disease with dysregulated LH secretion.
Such type of abnormal LH pulse frequencies, of
course, has been described in drug free women with
epilepsy and may cause anovulatory cycles. Hormonal
effects of valproate have recently been discussed and
may be implicated in the pathogenesis of PCOD.4
Dysregulated insulin release may cause obesity and
lipid abnormalities in some such individuals. Judging
simply by the frequency of occurrence (64% PCOD in
the series of Isojarvi et al,3 over 50% abnormal USG
in the present series), the issue of association of
valproate and cystic ovaries, seems to be a real one
and would call for reviews of management strategies
in women with epilepsy.

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Editor’s note : The answer to the problem lies in
follow up of patients, regular ultrasound scans,
before and after start of valproate in women,
along with hormonal studies and ultrasound of
epileptic females on other anti convulsants. The
editor is aware of two such detailed planned
studies being carried out in India at present.

Leber’s Idiopathic Stellate Neuroretinitis : Letter to Editor

Leber’s idiopathic stellate neuroretinitis is a disorder
with unilateral vision loss associated with optic disc
edema and macular star formation. It is different from
other forms of stellate, retinopathy by being a benign,
self limiting condition.1

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A 51 year old female patient presented with complaints of diminution of vision in the right eye of 4 weeks duration, unassociated with any other ocular or systemic symptoms. She was a known hypertensive on treatment for the past 10 years. Examination revealed visual acuity of 6/36 in the right eye and 6/6 in the left eye. The funduscopy of the right eye revealed a clear media. The optic disc was hyperemic with blurred disc margins and peripapillary exudates. The macula was studded with a macular star of exudates. Rest of the fundus was within normal limits (Fig. 1). Left eye and fundus induding the periphery, was within normal limits. The ophthalmic picture was that of optic disc edema with a macular star. Neurological examination by a neurologist did not reveal any other deficit. CT scan was within normal limits. Visually evoked potentials showed P100 latency of 136 msec in the right eye compared to 100 msec in the left eye. Blood sugar levels were within normal limits. Fundus fluorescein angiography revealed a sectorial hyperfluorescence with an intact macula (Fig. 2). Bjerrum’s campimetry at 2 m revealed a cecocentral scotoma in the right eye with 10/2000 white. The patient was followed up with non-steroidal anti-inflammatory agents. By the end of the third month, the macular star had broken up and the hyperemia had resolved. Visual acuity however was only 6/24 unimprovable.

The unilateral macular star with disc edema corroborated by characteristic angiographic picture in the absence of a neurological deficit and a normal CT scan study completes a diagnosis of Leber’s idiopathic stellate neuroretinitis. This patient however, did suffer from hypertension, albeit, with no features of affection of hypertension in the eyes, which is at variance with the report of Dreyer et al.2

References

Rare Shunt Complication : Letter to Editor

We report a rare case of ventriculo peritoneal shunt, in which shunt tip perforated a bowel loop and protruded out of anal opening. An 11 month old male child had been operated for post meningetic hydrocephalus at an age of two months and standard right ventriculo peritoneal shunt was placed. Patient was on regular follow-up. He started having recurrent fever nine months after surgery. One morning, patient’s mother noted a white tube protruding out from anal opening (Fig. 1). He was brought to emergency department and removal of shunt was carried over. His abdomen remained soft and there was normal passage of feces in post operative period. However patient developed signs and symptoms of raised intracranial pressure and contrast CT brain revealed multiple abscesses and ventriculitis. Prognosis was explained to attendants who refused further treatment.
Shunt complications are very commonly seen in the form of blockage, broken or disengaged shunts. Rare complications have been noted by various authors in the form of obstruction, perforation of bowel, vagina or perforation through umbilicus or entry into scrotum. Rectal perforation has been reported, but is a rare complication, hence this report.

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References

Acyclovir Induced Extrapyramidal Symptoms: Letter to Editor

Acyclovir is usually a well tolerated antiviral agent. Vomiting and hypotension after intravenous administration and, occasionally, non-oliguric renal failure in dehydrated patients, are well known side effects. Confusion, hallucinations, seizures and coma are much rarer and have been reported in immunocompromised patients. Since there is a wide overlap of serum concentrations in patients with and without neurologic side effects, the relation between central nervous system effects and acyclovir serum concentrations remains unclear. Most of the cases of neurotoxicity with acyclovir have been described either with intravenous formulation, with or without preexisting renal disease, or with oral acyclovir formulation with end stage renal disease. A case of neurotoxicity following orally administered acyclovir in a young healthy girl with herpes labialis is described here.

A 18 year old female developed rash over left angle of mouth. Tzanck smear was positive for giant cells and suggested herpes virus infection. Acyclovir (oral) was started on the next day in a dose of 200 mg, five times per day. She developed dystonia of tongue within 24 hours. Dystonia was reported to have developed after two hours of last dose. She was given another dose again under supervision in the hospital on the same day. 50 minutes later she developed dystonic posturing of tongue. Other drugs given before acyclovir were amoxycillin and paracetamol. She had rash over left angle of mouth, upper lip and tip of nose on examination (Fig. 1). Systemic and neurologic examination was normal. Her blood urea (30 mg %), serum creatinine (0.7 mg %), serum sodium (137 meq/L), serum potassium (3.8 meq/L), urine and hemogram were normal. Acyclovir was stopped, and she was put on phenergan and diazepam for three days. She had no recurrence of extrapyramidal symptoms.

Frequency of reported CNS side effects in 24 patients with acyclovir toxicity according to Haefeli et al is given in the Table I. The common symptoms of acyclovir toxicity include mental status disorders and involuntary movements. All patients usually recover. In serious cases, hemodialysis hastens the rate of recovery. Patients with end stage renal disease may not recover with peritoneal dialysis. There are case reports of death due to acyclovir toxicity treated with peritoneal dialysis. With the exception of renal
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Table I

Frequency of CNS Side Effects with Acyclovir Toxicity

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremor, Myoclonus</td>
<td>58%</td>
</tr>
<tr>
<td>Confusion</td>
<td>50%</td>
</tr>
<tr>
<td>Agitation</td>
<td>38%</td>
</tr>
<tr>
<td>Lethargy</td>
<td>25%</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>25%</td>
</tr>
<tr>
<td>Extrapyramidal symptoms</td>
<td>21%</td>
</tr>
<tr>
<td>Clouding of consciousness</td>
<td>17%</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>17%</td>
</tr>
<tr>
<td>Unilateral focal symptoms</td>
<td>13%</td>
</tr>
</tbody>
</table>


References

Fig 1: Showing herpetic vesicles over upper lip and left angle of mouth.

failure, no definite predisposing factors for neurotoxicity have been defined. Since the prevalence of severe infection is higher in immunocompromised patients, it is not surprising that most of the patients reported until now were transplant recipients or patients with tumors. The present case appears to be first of its kind in a otherwise healthy patient.

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