INTRODUCTION

The first case of CEP (Congenital erythropoietic Porphyria) was described by Schultz in 1874 and later described in detail by Gunther in 1911. It is the most mutilating type of the porphyrias presenting with severe cutaneous photosensitivity and hemolytic anemia. It occurs due to deficient activity of enzyme uroporphyrinogen III synthetase. Photosensitivity develops as a result of accumulation of porphyrins in the skin and red blood cells. Generation of reactive oxygen species and inflammatory mediators lead to tissue damage. Cutaneous findings include marked fragility, eroded or intact vesicles and bullae that may contain pink fluorescent fluid, hypertrichosis of lanugo-type hair in sun-exposed areas, dyspigmentation, diffuse scarring and atrophy, which may result in deformity of the ears, nose, fingers and face, scarring alopecia and sclerodermoid changes. Associated complications include keratoconjunctivitis, corneal scarring, scleral ulceration, cataracts, hepatosplenomegaly, thrombo-cytopenia and osteolysis. Erythrodontia, owing to deposition of porphyrins, is a common finding of CEP. It is a rare disorder and to date only about 130 cases have been described.

Most cases start in early infancy. A very rare and milder form may have its onset in later years of life, called late onset EP (erythropoietic porphyria) of which 14 cases have been reported to date.1-10 We report the 15th case of late onset EP with associated findings of haemolysis and thrombocytopenia.

CASE REPORT

In April 2009, a 40 years old unmarried businessman from Lahore, Pakistan, presented with just 2 months history of recurrent blistering on dorsal surfaces of hands without any obvious trauma. The blisters were initially clear, while some of them used to become hemorrhagic later on. These episodes were more pronounced on exposure to sun with associated tingling and pain in hands. Examination revealed tense clear blisters on dorsum of hands, few of them hemorrhagic on dyschromic background of hyper and hypopigmentation. The skin of hands and face also showed sclerosis, tightening and areas of atrophy without any milia. Hypertrichosis on cheeks and neck was also noticed (Figure 1). He was markedly pale and also had firm non-tender massively enlarged spleen measuring 12 cm from left costal margin. Rest of the systemic examination did not reveal any abnormality.

There were no complains of abdominal pain, paresthesias or nerve paralysis with no history of alcohol abuse, past hepatitis, renal failure or any chemical and drug intake. None of the family members were affected.

Based on this clinical scenario, a differential diagnosis of porphyria cutanea tarda, late onset erythropoietic porphyria and variegate porphyria were considered. Further evaluation revealed teeth to be stained brownish-red. Urine was also stained dark red on naked eye examination. Wood's lamp examination showed pink fluorescence of teeth, urine and a sample of faeces (Figure 2).

Blood analysis revealed normocytic normochromic anaemia (Hb 5.9g/dL, range 13-16g/dL), thrombocyto-
penia (95x10^9/dL, range 150-450x10^9/dL) with raised reticulocyte count (4.4%, range 0.5-2%) and LDH (1278 u/L, range 230-460 u/L). ALT and AST were within normal limits, while serum bilirubin (6.20 mg/dL, range 0.00-1.20 mg/dL) was moderately raised. USG of the abdomen showed normal liver and massive splenomegaly. A bone marrow aspirate analysis revealed hypercellular marrow without any myelodysplastic changes or abnormal cells. A biopsy of the bullous skin revealed subepidermal separation with deposition of PAS positive material in the dermis. Urinary uroporphyrin and coproporphyrin were raised. Plasma fluorescence, cytogenetics and assays of enzyme activity were not done due local unavailability and economic constraints. Altogether, these clinical and laboratory findings were consistent with late onset erythropoietic porphyria associated with hemolytic anemia and thrombocytopenia secondary to hyper-splenism (Table I).

Preventive and symptomatic measures make the patients current treatment with photoprotection, anti anaemics and blood transfusion that has resulted in a moderate decrease in symptomatology. He is being followed-up and considered for splenectomy.

**DISCUSSION**

Late onset EP was first described by Kramer et al. from Bantu in 1965.1 There have been a total of only 14 cases of late onset EP reported worldwide. This patient is the fifteenth case. Analysis of all the reported cases revealed that the age of onset ranged from 21 to 74 years.1-10 Onset of disease at the age of 40 in this patient makes almost middle of the age spectrum. It seems to be a disease of male population as only one of all 14 reported patients was female.8

A higher association of late onset EP is noted with myelodysplasia, present in 8 out of 14 cases. It is interesting to note that all of the patients showing association with myelodysplasia were having age more than 48 years, while patients having no evidence of myelodysplasia (including the present case) have an age range below 38 years. This seems to display two distinct forms of disease, early age late onset EP (21 to 38 years) without myelodysplasia and late age late onset EP (48 to 74 years) with myelodysplasia.11 Interestingly this patient did not show myelodysplasia even at the age of 40 years.

As also evident in this patient, late onset disease tend to have less severe manifestations as compared to CEP presumably due to a less severe deficiency of the uroporphyrinogen III cosynthetase activity.

What delays the onset of the disease remains purely speculative at this time. It is possible that the two types of late onset EP, first, not associated with bone marrow dysplasia (as in this case) have germ line UROS gene mutations with mild phenotypic expression, while the other is caused by myelodysplasia with acquired mutation of the UROS gene. At least 35 mutations responsible for CEP have been identified in the uroporphyrinogen III synthase gene located on chromosome 10. These include 18 point deletion and insertion mutations and 04 promoter mutations. The heterogeneity of these mutations may provide a better understanding of predicting the severity of CEP.

Although cytogenetics and enzyme assays could not be done in the case presented here, it has previously been suggested that late onset EP may represent a heterozygous state for their gene defect. However, based on the observations of markedly suppressed uroporphyrinogen III synthase activity in 2 patients with late onset EP, it has been suggested to be a homozygous disease and the nature of the metabolic abnormality is a primary defect of the cosynthetase activity.4

Treatment of erythropoietic porphyria is supportive and symptomatic with photo protection usually making the bulk.

In conclusion, we report a very rare and milder presentation of photo mutilating CEP. This entity should be borne in mind, while diagnosing other late onset porohyrias like porphyria cutanea tarda (Table I). Misdiagnosis can have devastating results as the treatment of both is opposite i.e. hyper transfusion for late onset EP and venesection for PCT. The limitation in this case was the unavailability of plasma fluorescence, plasma fluorescence, cytogenetics and enzyme assays but this case is very rare.

**Table I:** Differential diagnosis of EP, PCT and VP.

<table>
<thead>
<tr>
<th>Type</th>
<th>Enzyme deficient</th>
<th>Age</th>
<th>Manifestation</th>
<th>Staining</th>
<th>Porphyrins Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>EP</td>
<td>Uroporphyrin</td>
<td>Infancy</td>
<td>Mutilating photosensitivity</td>
<td>Teeth</td>
<td>Uroporphyrin 1</td>
</tr>
<tr>
<td></td>
<td>cosynthetase</td>
<td>Late</td>
<td>haemolysis</td>
<td>Coproporphrin1</td>
<td>Coproporphrin 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>splenomegaly</td>
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<td></td>
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<tr>
<td>PCT</td>
<td>Uroporphyrin</td>
<td>Late</td>
<td>Photosensitivity</td>
<td>–</td>
<td>Uroporphyrin 3</td>
</tr>
<tr>
<td></td>
<td>deacarboxylase</td>
<td></td>
<td>liver disease risk factors</td>
<td></td>
<td>Hecta and penta</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>carboxy porphyrin</td>
</tr>
<tr>
<td>VP</td>
<td>Protoporphyrin</td>
<td>Rarely before</td>
<td>Photosensitivity</td>
<td>–</td>
<td>Uroporphyrin</td>
</tr>
<tr>
<td></td>
<td>oxidase</td>
<td>puberty</td>
<td>acute attack</td>
<td></td>
<td>(may be)</td>
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<td></td>
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<td>Copro and</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Protoporphyrin</td>
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</tbody>
</table>

EP (Erythropoietic Porphyria); PCT (Porphyria Cutanea Tarda); VP (Variegate Porphyria).
cytogenetic studies and assays of enzyme activity which would have further substantiated the findings presented here.

REFERENCES


A discrepancy has occurred in the name of first author of the article titled: “Glycaemic indices and non-traditional biochemical cardiovascular Disease markers in a Diabetic population in Nigeria” published in JCPSP 2011, Vol 21 (8): 455-459. The name of first author was incorrectly published as Ogbera Anthonia Okeoghene instead of Okeoghene Anthonia Ogbera, which may be corrected in the article and read as Okeoghene Anthonia Ogbera.