CONGENITAL GENERALIZED LIPODYSTROPHY

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Clinical features of congenital generalized lipodystrophy, a rare disorder, first described by Zeigler[1] include loss of subcutaneous fat, hepatomegaly, increased bone growth, hyperlipaemia and, later, diabetes. The inheritance is probably autosomal recessive[2]. Generalized lipodystrophy may involve the diencephalon. A probable defect in the hypothalamus may lead to increased levels of hypothalamic releasing factors in the peripheral blood[2].

CASE REPORT

A two year four month old girl of consanguineous parents, was seen at the Jinnah Postgraduate Medical Centre, Karachi. She weighed 2.8 kg after normal full term gestation, but lacked demonstratable subcutaneous fat at birth. Her miles stones were normal, but her rate of growth was more than other children of her age and appetite was voracious. Her height was 90 cm, weight 19 kg. On examination there was apparent loss of subcutaneous fat (Figure 1)

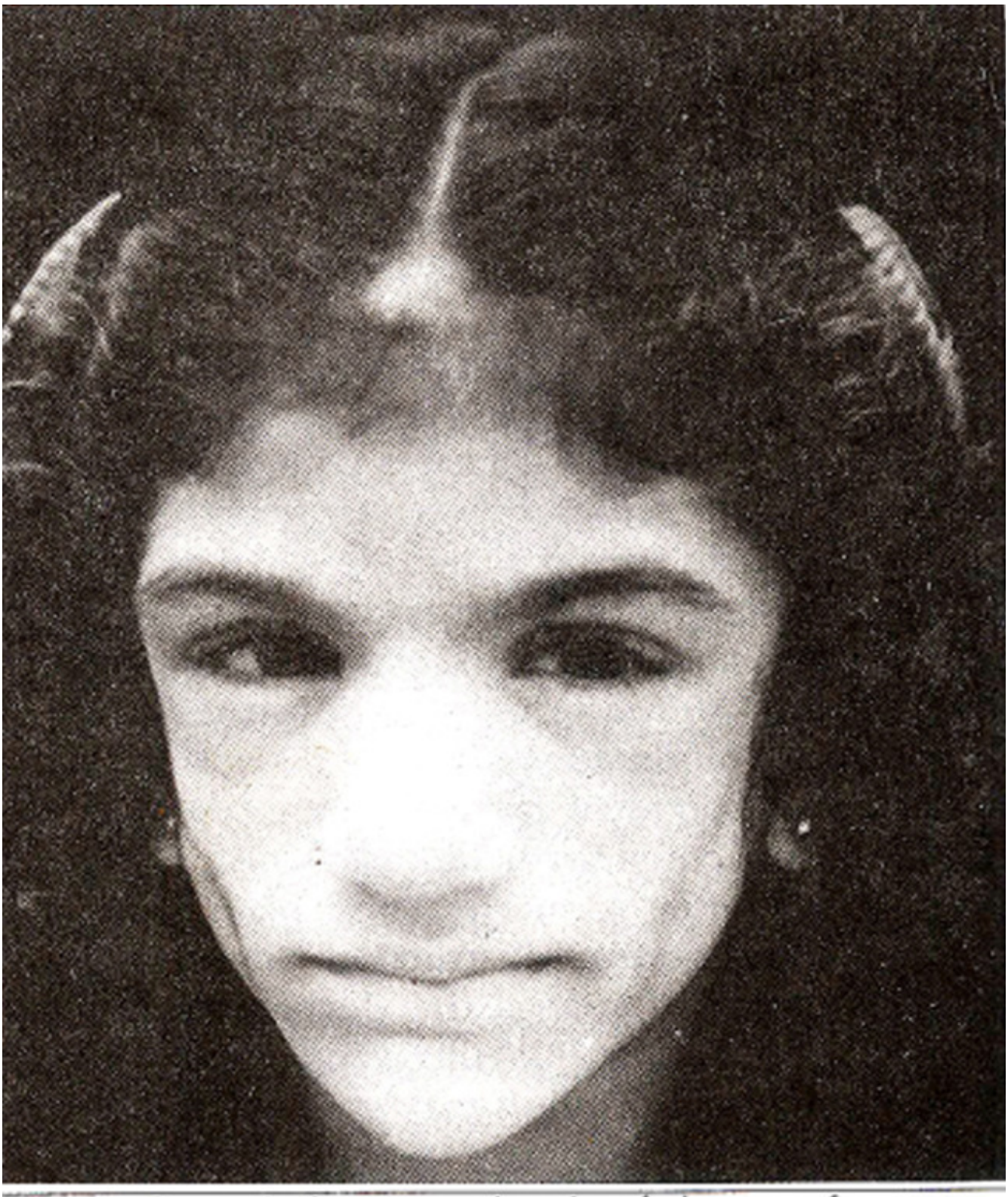

Figure 1. Senile appearance due to loss of subcutaneous fat.

generalized hypertrichosis, but scalp hair was abundant and curly (Figure 2).

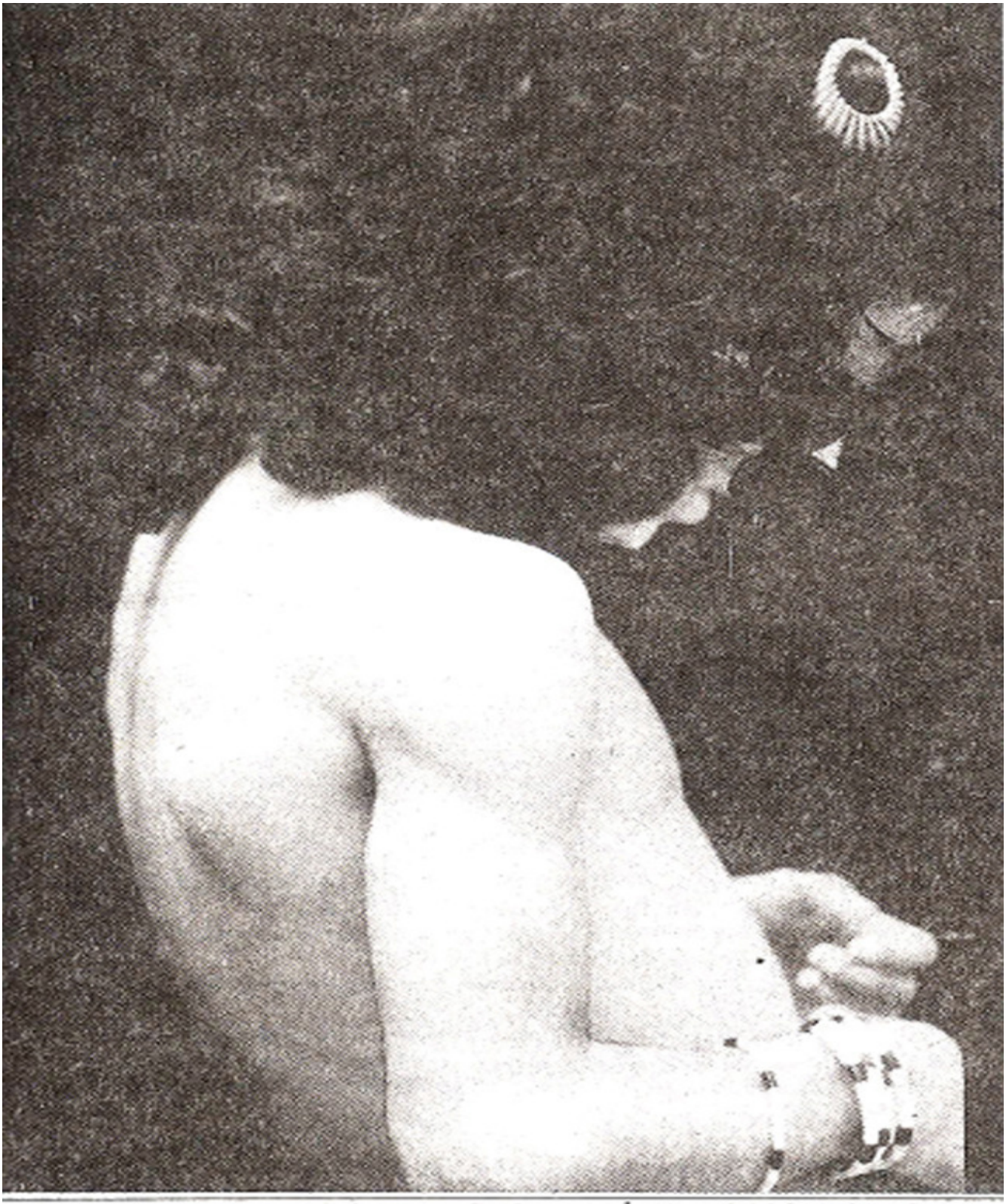

Figure 2. Apparent muscle hypertrophy, hypertrichosis and thick curly scalp hair.

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Mild acanthosis nigricans was present in the axillae (Figure 3).

Figure 3. Acanthosis nigricans of the axilla.

She had prominent muscles, veins and teeth and had a pointed chin. Abdomen was protuberant, liver was 8 cms enlarged and no splenomegaly. Clitoris was slightly enlarged (Figure 4).

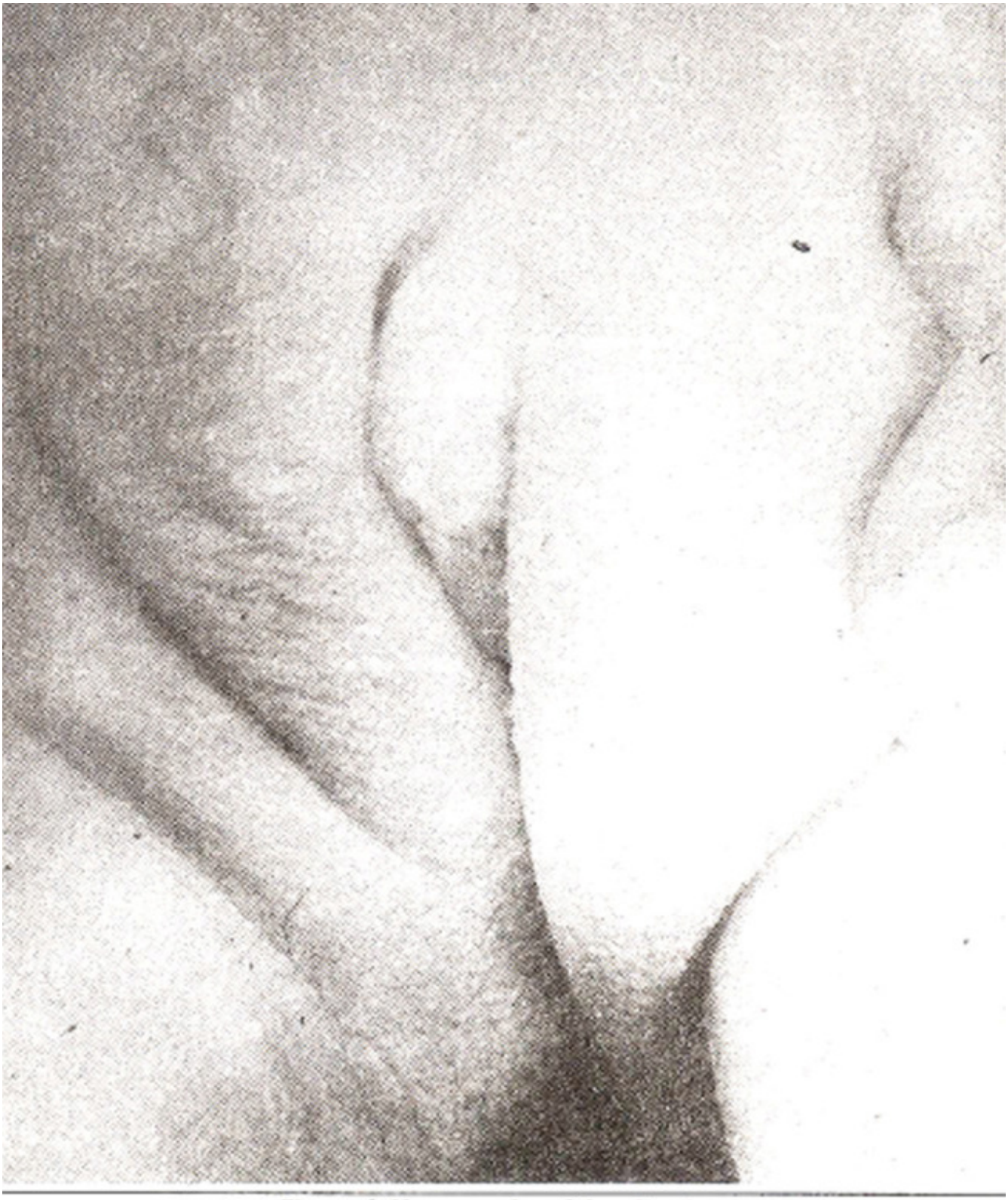

Figure 4. Hypertrophy of the clitoris.

The patient appeared mentally retarded. Parents were normal and no other siblings affected. There was no history of fat atrophy in the family. Investigations showed normal blood count and urine analysis. Fasting blood sugar was 87 mg%, liver functions showed no abnormality. Total lipids were 724 mg%, cholesterol 151 mg%, triglycerides were elevated 253 mg% (normal 70-150 mg%). Blood urea 22 mg

%, T3 and T4 were 1.6 ng/ml and 10.6 meg/dl respectively. Urinary 17 ketosteroids level was 7.6 ng/24 hrs and urine creatinine 109 mg%, x-ray skull was normal. Ultrasound of the abdomen showed enlarged homogenous liver with normal echopattern and normal spleen. Both kidneys were enlarged, right kidney was 9. lx 3.8 cm, left kidney 8.1x3.4 cm, E.C.G. was normal, l.Q. was 62. Biopsy of the skin showed an absence of subcutaneous fat. Hyper-insulinaemia was noted 148.2 IU/ml (normal 3-35 IU/ml). She was treated with pimozide 2 rug once daily for about a year. During this period, her appetite decreased, fat started to appear on the face and buttocks. Serum triglyceride levels decreased from 253 mg% to 168 mg%. On withdrawal of the drug, there was a return of many characteristics of the disease, There was a loss of subcutaneous fat, triglyceride level increased to 353 mg%, total lipids to 1430 mg%. These findings indicate that a prolonged treatment is required for continued clinical suppression of the disease.

DISCUSSION

Various etiologies for the syndrome include excess of hypothalamic releasing factors, an inherited or acquired anomaly in the peripheral insulin response, increased levels of fat mobilising factors and others[3]. Pimozide was given in this case on the basis that due to deranged hypothalamic catecholamine mechanism dopamine accumulates in the brain, which may result in an excess of hypothalamic releasing factors in the peripheral blood. Treatment with pimozide eliminated the releasing factors, corrected most of the abnormal blood chemistry and led to a return of subcutaneous fat. On withdrawal of the drug most of the symptoms reappeared. Prolonged treatment is apparently required for the continued clinical suppresion of the disease[4]. Other drugs used in the treatment of congenital generalised lipodystrophy arc chlorpromazine, fenfluramine, prolonged subcutaneous infusion of in sulin and plasmaphoresis[1-5]. Involvement of the nervous system is manifested by diffuse gliosis of the cerebrum and dilatation of the ventricles[6] and increase of growth hormone[7]. Although growth hormone levels have been normal in most of the cases[3,8], presence of acanthosis nigricans may also point to a neuroendocrinal disorder. The other important features of the disease are hepatomegaly and hyperlipaemia. Hepatomegaly is due to fatty infiltration which may lead to portal cirrhosis[2]. The increase in lipids seems to be confined to neutral fats. In some cases fatty acids and cholesterol were also raised[7]. Most cases of congenital generalised lipodystrophy develop insulin resistant nonketotic diabetes at puberty[1-10]. The disease should be differentiated from progeria, metageria, congenital muscular hypertrophy and then cephalic syndrome of infancy. Combination of biochemical and clinical pictures makes the diagnosis easier to differentiate.

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