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HARTNUP DISEASE

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A rare case of Hartnup disease is presented - the patient being an 11-year-old schoolgirl suffering from a typically pellagroid rash in the absence of any other signs of malnutrition. No accompanying neurological or psychiatric features are seen, but electro-encephalography revealed abnormal baseline activity. Investigations and management are detailed, and the literature on Hartnup disease reviewed.

Key Words : Pellagroid rash, Aminoaciduria, Hartnup disease

Introduction

Hartnup disease is a rare autosomal recessive inborn error of neutral amino-acid transport. It was first reported by Baron et al in 1956[1] and so named after the surname of the initial family identified. Since then only 53 cases have been diagnosed all over the world, of which 4 have been from India.[2]

Of all the amino-acids affected, it is the abnormal membrane transport of the essential amino-acid, tryptophan, which results in a secondary niacin deficiency; this gives rise to the pellagra-like manifestations, both cutaneous and neuropsychiatric.

Case Report

A 11-year-old schoolgirl presented with red, scaly, mildly itchy pellagrous lesions on exposed parts of the face and extremities of 4 months duration. There was no history of blistering, mucosal lesions, sun sensitivity or drug intake. In the last 7 days, she had also developed high grade intermittent fever without chills.

She had been a full-term normal delivery born of a non-consanguineous marriage. Her milestones had been normal and she was scholastically bright, well behaved and well oriented. There was no abnormal gait or movement, and she was not irritable, moody or apathic.

The patient was a vegetarian eating a balanced diet not containing maize. Over the past 4 years, she had a few transient episodes of similar skin rashes, but restricted to both forearms .She had also suffered thrice from urinary tract infection and once from hepatitis.

No family member was similarly affected. For the present complaint, she had been treated with systemic steroids and other medications with no benefit.

On examination, the patient was febrile but well oriented and of adequate built and nutrition. The cutaneous lesions were classically pellagroid, being sharply demarcated erythematous plaques with peripheral scaling, crusting and hyperpigmentation. They were located on the face, neck, extensor aspects of both forearms from hands to elbows and on both legs extending from feet to knees. The tongue was swollen and beefy red, and the alae nasi and lips showed adherent crusts. The vulva and groins were macerated. No systemic abnormality was detected.

This uncommon presentation of a recurrent pellagroid rash in a young girl with no obvious nutritional deficiency indicated a search for disorders of amino-acid metabolism, viz. Hartnup disease and congenital

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tryptophanuria. On investigation, routine blood, urine and stool studies, X-ray chest and ECG were all normal except for evidence of a urinary tract infection.

A urinary amino-acidogram, performed first by high pressure liquid chromatography, and later by paper chromatography, revealed a constant generalised amino-aciduria of the neutral amino-acid group. The amino-acids excreted were glutamine, serine, alanine, tyrosine, valine, methionine, phenylalanine, leucine, isoleucine and tryptophan, conforming to the Hartnup pattern. Urinary indoles, initially negative, tested positive on increasing the sensitivity of the test, thus reieterating the diagnosis. Plasma tryptophan levels were markedly low.

Porphyrin studies and protein electrophoresis were negative. EEG showed a pattern of baseline activity suggestive of a seizure disorder. A lesional skin biopsy revealed subacute eczematous changes compatible with a pellagroid rash.

The patient was treated with oral Nicotinamide, 300 mg per day and Pyridoxine, 30 mg per day. She improved dramatically; all the cutaneous lesions healed leaving behind post-inflammatory hyperpigmentation. She has in addition. been advised a balanced diet and photoprotection.

Her urine analysis done at regular intervals continues to show the amino-aciduria. Urine samples of her family members tested similarly however have detected no abnormality.

Comments

The point in favour of the diagnosis of Hartnup disease in our patient are the pellagroid rash, constant generalised amino-aciduria of the neutral (mono-amino mono-carboxylic) group, increased urinary excretion of indoles and response to nicotinamid therapy.

Hartnup disease typically presen between 3-9 years of age, and most often wi cutaneous manifestations. Neurological sign the commonest of which is cerebellar ataxi appear later, may or may not accompany th rash and are usually transient and complete reversible. Psychiatric abnormalities are les common and may range from minima emotional disturbances to depression delusions and suicidal tendencies. The disease follows a course of remissions and relapses may improve with age, and is noted to commonly exacerbate in spring or earl summer with sulfa therapy, or following febril illnesses,[3] as witnessed in our patient.

The primary defect is monogenic and results in impairment of membrane transport mechanisms selectively for amino-acids of the mono-amino mono-carboxylic (neutral) group; this impairment can be localised to the intestine or the kidney, or involve both together;[5] pure intestinal defect results in marked growth and developmental delay, pure renal, in urinary findings only. It is the combined defect in both organs that gives rise to cutaneous, systemic and urinary manifestations classical of Hartnup disease and the present case fits into this category.

The clinical polymorphism seen in this disease may be due to difference in severity of the primary defect, especially in the intestine, in different patients; thus even minor periods of nutritional imbalance, as seen in diarrhoea or acute febrile illnesses, may set off a relapse. Biochemical changes however remain constant in all patients regardless of clinical features or treatment and in fact, routine urine screening has detected many asymptomatic cases.

In the present case, therefore, absence of neurological and psychiatric manifestations

does not in any way contradict the diagnosis of Hartnup disease; the abnormal EEG pattern noted may be an indicator of future such developments.

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