Chinese Journal of Evidence-Based Medicine

A CHILD WITH GROWTH HORMONE INSENSITIVITY- LARON SYNDROME - CASE REPORT

[1] Dr G Aneesh Kumar Reddy , [2] Dr Vidhusree Dhakshnamoorthy , [3 *] Dr Krithika A.P

[1] Post graduate, Sree Balaji Medical college and Hospital

[2] Post graduate, Sree Balaji Medical college and Hospital

[3] * Professor, Sree Balaji Medical college and Hospital

Abstract

Laron syndrome(LS) is one of the rare genetic causes of short stature that occurs due to growth hormone resistance. It is caused by mutations in growth hormone receptor gene causing growth retardation, craniofacial defects, high serum Growth hormone and low insulin-like growth factor-I (IGF-I) levels. In this article we report a 18 month old girl child, brought to the hospital with an alleged history of trivial injury by falling from bed about 1 to 2 feet high. There were no signs of head injury. Physical examination revealed short stature and underweight. Her length was 65cm, less than -3SD and weight was 5.8Kg, less than -3SD. Basal serum GH level was elevated (22.83 ng/mL), whereas serum IGF-I levels are significantly low. Clinical and laboratory parameters were matching with that of Laron syndrome. This condition is managed by Recombinant IGF-I therapy.

Keywords : Growth hormone, Recombinant IGF-1 therapy, Short stature

INTRODUCTION

Laron syndrome (LS) is a rare genetic cause of short stature with growth hormone insensitivity caused due to growth hormone receptor (GHR) defect[1]. It is inherited in autosomal recessive manner. In this condition child presents with growth failure as a main feature whereas obesity, micro genitalia and severe hypoglycemia are the other features. Children with laron syndrome will have a saddle nose due to protruding forehead and small face. They have high pitched voices and their hair is sparse[2,3,4]. In this condition the normal insulin-like growth factor-I (IGF-I) secretion in response to exogenous and endogenous GH is absent and serum IGF-I value remains very low whereas the serum GH value is high. The prevalence of this condition is 1 to 9 in 10,00,000 children[4]. Clinically, these children are similar to those who have isolated GH deficiency[5]. Here we discuss a rare case of short stature due Growth hormone resistance.

CASE REPORT

13 month old girl child was brought to the hospital with the alleged history of trivial injury by falling from bed about 1 to 2 feet high. There were no signs of head injury. Physical examination

revealed short stature and underweight. So we probed the parents for any abnormal history regarding the endocrine system. Child had no H/O hypoglycaemia, constipation, forehead sweating, feeding difficulty, breathing difficulty, decreased urine output or polyuria, chronic diarrhoea, greasy stools, yellow coloured eyes, high coloured urine, bony abnormality and any other chronic systemic illness. Birth history of the baby is uneventful with a birth weight of 2.64 kg. Birth length was not measured. Anthropometry was interpreted using WHO growth charts. Weight of the baby was 5.8Kg less than -3SD (expected weight is 10kg), the length of the baby was 65cm less than -3SD (expected length is 75cm). Weight for length was -2 to -3 SD. Head circumference was 42cm which is between -2 to -3 SD. Upper segment to lower segment ratio is 1.2:1. Mid parental height was 149 cm(between 3rd and 10th centile). On examination anterior fontanelle was open admitting tip of the finger, posterior fontanelle was closed. Hair was sparse with features of facial dysmorphism like frontal bossing and depressed nasal bridge. Delayed dentition was noted. External genitalia appeared to be normal. Systemic examination is normal. Routine investigations like complete blood count, liver function test, thyroid function test, fasting blood sugar, serum electrolytes and cortisol were done, showing normal levels. Arterial blood gas values were normal. Basal GH levels were 22.83 ng/ml (normally less than 13.6ng/ml). GH stimulation test was done by arkhamine-clonidine revealed increased levels of GH consecutively. The basal IGF levels are low 6.5ng/ml (normal range 38-190ng/ml). Hence we came to a conclusion that this is due to growth hormone resistance. Genetic studies could not be done.

DISCUSSION

Laron syndrome can be caused by homozygous point mutations in the growth hormone receptor gene on the short arm of the 5th chromosome. These mutations prevent the interaction between Growth hormone and its receptor resulting in Growth hormone resistance[6]. Molecular studies

play an important role in the diagnosis. Children with Laron syndrome have a standard birth weight and length [7]. Short stature and obesity will be seen in the later stages. Craniofacial defects like frontal bossing and a saddle nose, mild mental retardation, blue sclera, crowded teeth, sparse hair growth, microgenitalia, small gonads, small hands and feet, obesity, improper skeletal maturation, delayed puberty and hypoglycemia are the early symptoms. In the later stages, child will have severe short stature, severe obesity, muscle weakness, osteoporosis, hypercholesterolemia, hyperinsulinemia, differential glucose intolerance [8,9,10]. Inspite of absence of pubertal spurt and delayed puberty, the fertility is not affected [11]. Hypoglycemic seizure and fractures due to osteopenia are long term complications[12]. Recombinant human IGF-1 replacement therapy is the effective treatment for Laron syndrome which is started from early childhood, for the rest of the life. Even though normal adult height is not reached, there is improvement in the height when compared to the patients who are not treated [13]. High cost and limited availability are the disadvantages of the treatment. Edema, electrolyte imbalance and increased urine calcium are the side effects of the treatment. Obesity should be managed with diet containing high protein and low fat.

Conclusion

Diagnosis of Laron syndrome is mainly by clinical approach and early initiation of the IGF-1 therapy helps in considerable improvement in height.

Ethics

Informed Consent: A consent form was completed by all participants.

References

1.Guleria S, Sharma J, Kaushik SL. Laron syndrome. J Postgrad Med. 2014;60(3):322-3.
2.Kornreich L, Konen O, Lilos P, Laron Z. The globe and orbit in Laron syndrome. AJNR Am J Neuroradiol. 2011;32(8):1560-2.
3.Ranke MB, Savage MO, Chatelain PG, Preece MA, Rosenfeld RG, Wilton P. Long-term treatment of growth hormone insensitivity syndrome with IGF-I.
Results of the European Multicentre Study. Horm Res. 1999;51(3):128-34.
4.Phanse GSR, Khadilkar VV, Khadilkar AV. Clinical features and endocrine profile of Laron syndrome in Indian children. Indian J Endocrinol Metab.
2014;18(6):863-7.
5.Lopez BA, Buckway CK, Rosenfeld RG. Genetic defects of the growth hormone-insulin-like growth factor axis. Trends Endocrinol Metab.
2000;11(2):39-49.
6.Kliegman RM, Behrman RE, Jenson HB, Stanton BF. Growth hormone insensitivity. Nelson's Textbook of Pediatrics. 18th ed. USA: Salinder;

2007: 2296-2297.
7.Laron Z, Lilos P, Klinger B. Growth curves for Laron syndrome. Arch Dis Child 1993;68:768-70.
8.Laron Z, Laron syndrome (primary growth hormone resistance or insensitivity): the personal experience 1958-2003. J Clin Endocrinol Metab 2004;89:1031-44.
9.Rosenbloom AL, Guevara Aguirre J, Rosenfeld RG, Fiedler PJ. The little women of Loja--growth hormone-receptor deficiency in an inbred population of southern Ecuador. N Engl J Med 1990;323:1367-74.
10.Ayling RM, Ross R, Towner P, Von Laue S, Finidori J, Moutoussamy S et al. A dominant-negative mutation of the growth hormone receptor causes familial short stature. Nat Genet 1997;16:13-4.
11.Laron Z, Sarel R, Pertzelan A. Puberty in Laron type dwarfism. Eur J Pediatr. 1980;134(1):79-83.
12.Savage MO, Blum WF, Ranke MB, Postel VMC,Cotterill AM, Hall K, et al. Clinical features and endocrine status in patients with growth hormone
insensitivity (Laron syndrome). J Clin Endocrinol Metab. 1993;77:1465-71.

13.Chernausek SD, Backeljauw PF, Frane J, Kuntze J, Underwood LE, GH Insensitivity Syndrome Collaborative Group: Long-term treatment with recombinant insulin-like growth factor (IGF)-Iin children with severe IGF-I deficiency due to growth hormone insensitivity. J Clin Endocrinol Metab 2007;3:902-10.