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Analysis of a Case of Infant Growth Retardation Caused by a Lactating Mother's Use of Motherwort

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Abstract

This paper describes a male infant in whom linear growth slowed after taking *Leonurus artemisia* motherwort tablets during his mother's breastfeeding period. Examination ruled out common endocrine, nutritional, and genetic causes, and the case was therefore classified as idiopathic short stature. It is concluded that bioactive compounds through milk may have disrupted signalling pathways related to growth. It advocates minimizing the use of drugs during breastfeeding.

Subject Areas

Pediatrics, Pharmacology

Keywords

Delayed Physical Development, Infancy, Traditional Chinese Medicine, Motherwort, Lactation Period

1. Introduction

Short stature in childhood and even adulthood mostly originated from infancy and early childhood. Studies reported that 30.7% of children began to experience short stature before 6 months of age, 32.3% developed short stature between 6 and 24 months of age, and 88.3% showed signs of short stature before 3 years of age [1]. Among children visiting outpatient clinics for short stature, idiopathic short stature (ISS) accounted for as high as 41% of cases [2]. This article discussed and analyzed cases where commonly used medications during postpartum lactation might have contributed to delayed growth and development in infants and young children. The aim was to identify potential causes of growth retardation during

this critical stage and to improve prevention and intervention strategies for growth delays in infants and young children.

2. Case Presentation

A male infant of Han ethnicity was born with a length of 51 cm and a weight of 3.85 kg. He was delivered via cesarean section without intrauterine growth retardation and had an Apgar score of 10. He was breastfed 24 hours after birth. Due to maternal reasons, he received motherwort granules from the 3rd day after delivery until the 21st day (15 g/dose, twice daily). During this period, he continued to breastfeed with sufficient milk. At one month old, he measured 54 cm in length and weighed 4.85 kg. At 3 months, his length was 60 cm, and his weight was 6.5 kg. At 6 months, he measured 66 cm and weighed 8.1 kg. At 9 months, his length was 69 cm, and his weight was 8.9 kg. At 12 months, he measured 72 cm and weighed 9.5 kg. At 15 months, his length was 75 cm, and his weight was 9.9 kg. At 18 months, he measured 78 cm and weighed 10.5 kg. At 21 months, his length was 80 cm, and his weight was 11.0 kg. By 24 months, he measured 82 cm and weighed 11.5 kg. His mother was 158 cm tall, and his father was 169 cm tall. After birth, all laboratory tests (including blood routine, urine routine, liver and kidney function, blood glucose, trace elements, and thyroid function) were within normal ranges, and no milk protein allergy was detected. At 12 months of age, his insulin-like growth factor (IGF-1) level was 64.1 ng/mL (reference range: 15 - 129 ng/mL). Imaging examinations showed no significant pituitary abnormalities, and the peak growth hormone level during the stimulation test was 10 ng/dL.

3. Method

Used the CAREreporting guidelines [3].

4. Discuss

In this case, the patient's postnatal body mass index and various laboratory indicators were within the normal range. Therefore, congenital intrauterine factors, malnutrition, chromosomal abnormalities, and chronic systemic disease factors were excluded. The patient's growth rate slowed down, and the growth curve gradually deviated from the median by about −2SD (refer to **Table 1**). The peak secretion of the growth hormone stimulation test met the standard, and the concentration of IGF-1 was within the normal range. The patient took 5-vitamin lysine granules (5g once, orally once a day) from 12 months to 24 months of age, but there was no significant improvement in growth rate. The clinical diagnosis was idiopathic physical retardation.

5. Conclusions

Motherwort (*Leonurus japonicus* Houtt.) was a kind of herbal plant in the family Lamiaceae, which had effects of promoting blood circulation, resolving stasis, regulating menstruation, and relieving pain. The stem, leaves, and flowers of the mother-

wort are shown in Figure 1. It was clinically used mainly for postpartum vaginal bleeding and postpartum abdominal pain [4]-[7]. By searching the chemical components of motherwort collected in the Traditional Chinese Medicine Systems Pharmacology Analysis Platform (TCMSP), Li Conglin *et al.* [8] found that motherwort had 14 main components, and more than 120 compounds had been identified and classified (the chemical formula of the compounds was shown in Table 2 [9]), corresponding to 216 targets (including 5 key targets AKT1, TP53, IL-6, CALM2, JUN), involving 59 biological processes, revealing the material basis and multi-dimensional pharmacological effects of motherwort. Many studies also showed that motherwort alkaloids could inhibit the JAK2/STAT3 signaling pathway [10], inhibit the Akt/MDM2/p53 signaling [11], kill cancer cells, induce their apoptosis, and ultimately inhibit the progression of malignant tumors.

It was well known that newborn children grew and developed rapidly, and GH and IGF-1 were important regulatory factors for longitudinal growth. Glucocorticoids, paracrine growth factors including various FGF, BMP, Wnt signaling pathways, parathyroid hormone-related peptides, Indian hedgehog factor, and C-type natriuretic peptide could all affect the growth and development of infants and young children. It was confirmed that an increasing number of genes were associated with dwarfism, and mutations in the paracrine signaling system could seriously damage bone growth [12]. Growth hormone mainly promoted bone growth by stimulating the division of chondrocytes in the growth plate. If the growth plate was involved in the proliferation, hypertrophy, and secretion of extracellular matrix of chondrocytes, genetic abnormalities could also lead to a slower growth rate in young children [13].

6. Adjust

Figure 1. jpg Stem, leaves and flowers of motherwort. (a) Motherwort herbal pieces: irregular segments. Stem square, concave on all sides into longitudinal grooves, gray green or yellow green. There is white pulp in the middle of the section. The leaves are gray green, often wrinkled and broken. The air is faint and the taste is slightly bitter. (b) Fresh motherwort: During the seedling stage, there is no stem. In the early flowering stage, the stem is square and columnar, with many branches on the upper part and longitudinal grooves on all sides. It is 30 - 60 cm long and 0.2 - 0.5 cm in diameter. Leaves interact with each other, with stems. The leaves are green in color, fresh and tender, and when kneaded, they produce juice. The lower stem has palm shaped leaves with three lobes, while the upper leaves have feather like deep or shallow lobes that are divided into three pieces. The lobes are entire or have a few serrations. Cymbidium inflorescence axillary, small flowers light purple, calyx tube shaped, corolla two lip shaped. (c) Dried motherwort: The stem surface is gray green or yellow green, the body is light and tough, and there is a pulp in the middle of the section. The leaves are gray green, wrinkled, and prone to falling off.

The DrugBank database consisted of approximately 800 genes that were well-characterized drug targets, and rare mutations in drug target genes could lead to complex diseases and were widespread [14]. During the neonatal period, the mother absorbed the components of *Leonurus japonicus* through her breast milk, and the exposure was prolonged. The rapid growth and development of the infant required many factors and signaling pathways to participate, and the chemical composition of *Leonurus heterophyllus* and its influence on signaling pathways could lead to corresponding gene variations during growth, such as in paracrine growth factors, growth plate-related cartilage extracellular matrix, and other processes. The author advocated avoiding or minimizing medication during breastfeeding whenever possible. If drug use was necessary due to medical conditions, infant formula was recommended as an alternative.

Table 1. Standard deviation of infant height and weight (male).

(month/year)	−3 SD		−2 SD		−1 SD		Median		−1 SD		−2 SD		−3 SD	
	Height (cm)	Weight (kg)	Height (cm)	Weight (kg)	Height (cm)	Weight (kg)	Height (cm)	Weight (kg)	Height (cm)	Weight (kg)	Height (cm)	Weight (kg)	Height (cm)	Weight (kg)
Born	45.2	2.26	46.9	2.58	48.6	2.93	50.4	3.32	52.2	3.73	54.0	4.18	55.8	4.66
2 m	52.2	3.94	54.3	4.47	56.5	5.05	58.7	5.68	61.0	6.38	63.3	7.14	65.7	7.97
4 m	57.9	5.25	60.1	5.91	62.3	6.64	64.6	7.45	66.9	8.34	69.3	9.32	71.7	10.39
6 m	61.4	5.97	63.7	6.70	66.0	7.51	68.4	8.41	70.8	9.41	73.3	10.50	75.8	11.72
9 m	65.2	6.67	67.6	7.46	70.1	8.35	72.6	9.33	75.2	10.42	77.8	11.64	80.5	12.99
12 m	68.6	7.21	71.2	8.06	73.8	9.00	76.5	10.05	79.3	11.23	82.1	12.54	85.0	14.00
15 m	71.2	7.68	74.0	8.57	76.9	9.57	79.8	10.68	82.8	11.93	85.8	13.32	88.9	14.88
18 m	73.6	8.13	76.6	9.07	79.6	10.12	82.7	11.29	85.8	12.61	89.1	14.09	92.4	15.75
21 m	76.0	8.61	79.1	9.59	82.3	10.69	85.6	11.93	89.0	13.33	92.4	14.90	95.9	16.66
24 m	78.3	9.06	81.6	10.09	85.1	11.24	88.5	12.54	92.1	14.01	95.8	15.67	99.5	17.54
2.5 y	82.4	9.86	85.9	10.97	89.6	12.22	93.3	13.64	97.1	15.24	101.0	17.06	105.0	19.13
3 y	85.6	10.61	89.3	11.79	93.0	13.13	96.8	14.65	100.7	16.39	104.6	18.37	108.7	20.64
3.5 y	89.3	11.31	93.0	12.57	96.7	14.00	100.6	15.63	104.5	17.50	108.6	19.65	112.7	22.13
4 y	92.5	12.01	96.3	13.35	100.2	14.88	104.1	16.64	108.2	18.67	112.3	21.01	116.5	23.73
4.5 y	95.6	12.74	99.5	14.18	103.6	15.84	107.7	17.75	111.9	19.98	116.4	22.57	120.6	25.61
5 y	98.7	13.50	102.8	15.06	107.0	16.87	111.3	18.98	115.7	21.46	120.1	24.38	124.7	27.85
5.5 y	101.6	14.18	105.9	15.87	110.2	17.85	114.7	20.18	119.2	22.94	123.8	26.24	128.6	30.22
6 y	104.1	14.74	108.6	16.56	113.1	18.71	117.7	21.26	122.4	24.32	127.2	28.03	132.1	32.57

A study on data of physical growth and development of children in China (before the age of 3 for the length).

Table 2. Compounds isolated and identified from *L. japonicas* (chemical formulas).

1. $C_7H_{14}ClNO_2$	2. $C_{14}H_{21}O_5N_3{\cdot}HCl{\cdot}H_2O$	3. $C_{20}H_{32}O_5$	4. $C_{22}H_{34}O_6$	5. $C_{23}H_{36}O_6$	6. $C_{20}H_{32}O_4$	7. $C_{20}H_{30}O_4$
8. $C_{20}H_{30}O_3$ (5 sorts)	9. $C_{23}H_{36}O_7$	10. $C_{24}H_{38}O_7$	11. $C_{22}H_{36}O_6$	12. $C_{22}H_{36}O_5$	13. $C_{21}H_{34}O_5$ (3 sorts)	14. $C_{23}H_{36}O_7$
15. $C_{21}H_{32}O_6$	16. $C_{20}H_{30}O_{40}$	17. $C_{20}H_{28}O_3$	18. $C_{20}H_{28}O_4$ (2 sorts)	19. $C_{20}H_{29}O_4$	20. $C_{25}H_{38}O_8$	21. $C_{20}H_{28}O_2$

Continued

22. $C_{20}H_{30}O_3$	23. $C_{22}H_{32}O_5$	24. $C_{20}H_{26}O_3$	25. $C_{20}H_{36}O_2$	26. $C_{20}H_{34}O_3$	27. $C_{22}H_{34}O_7$	28. $C_{20}H_{28}O_4$
29. $H_{30}O_{16}$	30. $C_{15}H_{10}O_7$ (3 sorts)	31. $C_{21}H_{20}O_{12}$	32. $C_{15}H_{10}O_5$	33. $C_{36}H_{39}O_{19}$	34. $C_{36}H_{38}O_{19}$	35. $C_{36}H_{38}O_{20}$
36. $C_{30}H_{26}O_{13}$	37. $C_{27}H_{30}O_{16}$	38. $C_{21}H_{20}O_{11}$	39. $C_{27}H_{30}O_{15}$	40. $C_{30}H_{26}O_{13}$	41. $C_{21}H_{20}O_{11}$	42. $C_{20}H_{20}O_7$
43. $C_{15}H_{10}O_4$	44. $C_{36}H_{38}O_{20}$	45. $C_{34}H_{44}O_{19}$	46. $C_{34}H_{44}O_{20}$ (2 sorts)	47. $C_{29}H_{36}O_{15}$	48. $C_{43}H_{62}O_{19}$	49. $C_{26}H_{40}O_{16}$
50. $C_{20}H_{32}O_{16}$	51. $C_{27}H_{42}O_{17}$	52. $C_{14}H_{20}O_7$	53. $C_{19}H_{28}O_9$	54. $C_8H_{10}O_2$	55. $C_{10}H_{12}O_4$	56. $C_{17}H_{26}O_{10}$
57. $C_{16}H_{22}O_{10}$	58. $C_{12}H_8O_4$	59. $C_{13}H_{11}O_5$	60. $C_{16}H_{15}O_5$	61. $C_{16}H_{14}O_4$	62. $C_{15}H_{16}O_5$	63. $C_{15}H_{16}O_4$
64. $C_{15}H_{14}O_4$	65. $C_{15}H_{16}O_3$	66. $C_{23}H_{32}O_6$	67. $C_{24}H_{32}O_6$	68. $C_{20}H_{18}O_6$	69. $C_{20}H_{20}O_7$	70. $C_{29}H_{48}O_2$
71. $C_{29}H_{48}O_3$	72. $C_{30}H_{50}O$	73. $C_{30}H_{48}O_3$	74. $C_{29}H_{48}O_2$	75. $C_{30}H_{44}O_3$	76. $C_{30}H_{52}O_2$	77. $C_{30}H_{48}O_4$
78. $C_{30}H_{46}O$	79. $C_{44}H_{78}O_4$	80. $C_{30}H_{50}O$	81. $C_{30}H_{48}O_3$	82. $C_{11}H_{14}O5$	83. $C_8H_8O_4$	84. $C_9H_{10}O_5$
85. $C_9H_8O_4$	86. $C_{14}H_{20}O_9$	87. $C_7H_8O_2$	88. $C_{10}H_{12}O_3$	89. $C_8H_{10}O_3$	90. $C_{10}H_{10}O_5$	91. $C_{10}H_{10}O_4$
92. $C_{13}H_{20}O_3$	93. $C_7H_6O_2$	94. $C_{29}H_{48}O$ (3 sorts)	95. $C_7H_6O_3$	96. $C_{31}H_{40}O_{15}$		

Statement

This study was approved by the Medical Ethics Review Committee of Shijiazhuang Traditional Chinese Medicine Hospital; and written informed consent was obtained from the participants in the and their guardians.

Conflicts of Interest

The author declares no conflicts of interest.

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