

Endocrine Profile of Microcephaly patients from central Punjab

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ABSTRACT

Microcephaly is the reduction in occipito-frontal circumference i.e., <2 SD of normal. In this condition there is a smaller brain size and neurodeficiency is usually present. A lot of research has been done to find the genetic causes of microcephaly, scarce literature is present to show any association between microcephaly, BMI and endocrine profile. The main aim of this study was to compare the BMI and endocrine profile (including leptin, cortisol, GH and TSH) of patients having microcephaly with age matched normal siblings served as controls. BMI of microcephaly patients was 17.9±1.0 and of controls it was 25.4±2.3, significant association (P=0.03) was found between BMI and microcephaly. Although mean cortisol levels were above normal range in subjects with microcephaly as compared to age matched controls (29.5±3.3 vs 23.7±6.8), the difference between cortisol concentrations in microcephaly patients and normal siblings was not found statistically significant. The study showed that no association is present between BMI and microcephaly but no significant association was seen between leptin, cortisol, GH and TSH and microcephaly.

Keywords: Microcephaly, Cortisol, Growth Hormone, Thyroid Stimulating Hormone and Leptin

INTRODUCTION

Microcephaly in humans is a genetic disorder caused by failure in brain development. Genes that cause microcephaly are involved in neural development. Rapid advancement in the use of genetic mapping techniques had helped to identify genetic loci of this condition. Several loci have been traced but the condition is clearly genetic and heterogeneous in clinical presentation¹. Literature supports the fact that microcephaly is autosomal recessive disorder with genetic heterogeneity^{2,3,4,5} and other causes of microcephaly can be genetic or environmental⁶.

Putative etiology for microcephaly was found in 59% of the patients and in the rest 41% no definite diagnosis could be made. In the cohort consisting of pathogenic cases of microcephaly, genetic causes were the reason in 50% of the patients, in 45% perinatal brain damage was the reason whereas in 3% of the cases postnatal brain damage was the cause. It was seen that in 65% of the selected individuals had intellectual impairment, in 43% epilepsy was diagnosed and in 30% ophthalmological disorders were found. Brain MRI of the participants revealed abnormalities in 76% of the participants⁷. Scarce literature is present regarding the endocrine profile of patients with microcephaly therefore, the

objective of the present study was to compare the BMI and endocrine profile (including leptin, cortisol, GH and TSH) of patients with microcephaly with normal controls.

METHODOLOGY

This is a descriptive case series based on 10 individuals. On the basis of microcephaly, the subjects were divided into the two groups: Group I: Subjects with microcephaly (n=7), Group II: Normal siblings as controls (n=3). Four families including total of 10 subjects was selected. Seven individuals with microcephaly (cases) and three normal siblings (without microcephaly) were taken as controls. Participation of the subjects in this study was recruited voluntarily and written informed consent to participate in the study was obtained from each subject and/or their parents. The subject and/or their parents were informed about the potential benefits and risks of this study. A structured questionnaire was filled by the primary investigator. Body weight (BW) and height of all participants was recorded and Body mass index (BMI) was calculated as (BMI = BW (kg) / height (m)²).

Five ml of venous blood of all participants was drawn from the cubital vein through aseptic measures. The blood samples were centrifuged at 4,000 rpm for 10 min and the serum sample was quoted and stored at -80° C until used. All biochemical parameters were determined in duplicate using standard procedures. Serum leptin, cortisol,

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growth hormone (hGH) and thyroid stimulating hormone (TSH) concentrations were determined by enzyme linked immunosorbent assay (ELISA) using commercial kits (leptin Labor Diagnostika Nord GmbH, Nordhorn, Germany; cortisol, hGH and TSH: MonobindInc, Lake Forest, CA, USA) with an automated EIA analyzer (Bio-Rad Laboratories, Hercules, CA, USA).

The significance of differences between two groups was analyzed by Independent Samples Mann–Whitney U test. P -value ≤ 0.05 was considered statistically significant. Data was entered and all calculations were carried out with the SPSS)version 20.

RESULTS

There was no difference in the mean age of microcephaly patient compared to healthy siblings. BMI of microcephaly patients was 17.9 ± 1.0 and of controls it was 25.4 ± 2.3 , significant association was found between BMI and microcephaly. Mean serum leptin concentrations in microcephaly patients was 4.7 ± 1.0 vs 20.7 ± 12.7 compared with controls but the association was non-significant. Whereas, mean cortisol levels in microcephaly patients was high as compared with normal siblings (29.5 ± 3.3 vs 23.7 ± 6.8) but the difference is not significant. No significant association was found in serum growth hormone and TSH levels in microcephaly patients as compared with controls. P -value was non-significant for leptin, cortisol, GH and TSH.

Table 1: Comparison of Age, BMI, Leptin, Cortisol, GH and TSH between patients with microcephaly and normal controls.

	Microcephaly patients (cases) (n=7)	Normal siblings (controls) (n=3)	p- value
Age	25.8 ± 3.4	25.0 ± 2.7	0.83
BMI	17.9 ± 1.0	25.4 ± 2.3	0.03*
Leptin (ng/ml)	4.7 ± 1.0	20.7 ± 12.7	0.12
Cortisol (μ g/dl)	29.5 ± 3.3	23.7 ± 6.8	0.83
GH (uIU/ml)	1.1 ± 0.2	1.8 ± 0.3	0.12
TSH (uIU/ml)	2.1 ± 0.4	2.2 ± 0.5	1.0

*Independent samples Mann-Whitney U Test

P value ≤ 0.05 is significant.

DISCUSSION

Present study highlights a significant association between BMI and microcephaly. Our results are supported by another study on microcephaly infants and children which reported lower weight and height in addition to abnormally small brain size⁸. Peptides secreted by the adipose tissue i.e., leptin and adiponectin, play a crucial role in expenditure of energy and body weight regulation. Rett syndrome, a neurological abnormality, is characterized by microcephaly, growth failure and behavioral disorders. So an association can be suggested between leptin levels and microcephaly⁹. But in our study no significant association could be found.

Another study on four microcephalic siblings (3 males and 1 female) showed that they were short heighted and had hypergonadotropic hypogonadism along with multiple congenital abnormalities. This family also had 5 healthy siblings. The affected siblings also had impaired growth and sexual developmental. Testresults showed normal growth, adrenocortical hormones and abnormal levels of sex hormones¹⁰. Our study also showed no significant association between microcephaly and GH. A research on patients with low glucocorticoid levels revealed neurological deficit in them¹¹. But in our study no significant association was seen between cortisol and microcephaly.

A case report done in 1991 included 2 cases of microcephaly, which showed GH deficiency with abnormal arginine and insulin provocation tests¹². A rare case was reported, who had a combination of short stature, impaired sexual development, microcephaly, hypothyroidism and altered pancreatic functions. His chromosomal analysis showed 47 XXY¹³. These results might also indicate some relationship of microcephaly and hypothyroidism. A research study on 3 female suffering from a syndrome highlighted short stature, deafness, mental retardation, tooth abnormality, microcephaly and thyroid dysfunction¹⁴. But this study showed no such association.

CONCLUSION

In light of this study it can be suggested that there is a significant association of BMI and microcephaly but the association of Leptin, Cortisol, GH and TSH with microcephaly could not be found as suggested by non-significant results. This may also emphasize on heredity aspect of this condition. Limitations included fewer subjects therefore study results cannot be generalized. Further studies should be done to determine the cause-effect relationship between endocrine profile and microcephaly.

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