A possible genetic component of obesity in childhood. Observations on acid phosphatase polymorphism

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Summary. Phenotypes of acid phosphatase with low enzymatic activity (ACP_1 A and BA) are correlated with the highest degree of body mass increase observed in a sample of obese children. Since acid phosphatase probably functions as a flavin-mononucleotide phosphatase, differential modulation of flavo-enzyme activity and energy metabolism due to acid phosphatase genetic variability may explain the observed association.
Key words. Acid phosphatase; genetics of obesity.

Obesity in childhood is a relatively common situation which is associated with a significant risk of severe complications during later stages of life. It is likely that besides cultural, nutritional and relational factors, the individual genetic background contributes significantly to this heterogeneous condition[1-3].

We have recently observed that intrauterine growth is related to acid phosphatase locus 1 (ACP_1) phenotype[4]. The highest proportion of macrosomic infants was observed among those with the ACP_1 phenotypes with the lowest enzymatic activity (A and BA) and the lowest proportion among those with phenotypes with the highest activity (CA and CB). These observations prompted us to investigate a possible role of ACP_1 in childhood obesity.

Methods and patients

A series of 75 children (both sexes, age between 3 and 14 years), referred for 'obesity' to the out-patient department of our Pediatric Clinic, have been studied. Children were considered obese if their weight exceeded the mean weight for their age, height and sex by more than 20%. All the children were above median height. Severity of 'obesity' was evaluated as the standard deviation above the mean value. Cases considered in this paper were not associated with known diseases and did not show abnormalities of the following parameters: glycemia, triglyceridemia, cholesterolemia, urinalysis with determination of free cortisol in the urine. The ACP_1 phenotype was determined in all subjects using starch gel electrophoresis[5].

Results and discussion

The table analyzes the degree of obesity in relation to ACP_1 phenotype. Degree of obesity depends on ACP_1, as shown by the highly significant association between the two variables. The proportion of A and BA subjects increases – and the proportion of B decreases – with the severity of body mass deviation, suggesting a negative correlation between ACP_1 enzymatic activity and degree of 'obesity'.

Erythrocyte acid phosphatase (ACP_1) is an enzyme found in the cytoplasm of many tissues besides red blood cells. It is genetically distinct from acid phosphatases found in lysosomes and is polymorphic, with three codominant alleles (P^a, P^b and P^c) at an autosomal locus. ACP_1 genotypes show a strong quantitative variation of enzyme activity; the contribution of the allozymes decreases in the order $P^c > P^b > P^a$ [6,7].

ACP_1 probably functions as a flavin-mononucleotide phosphatase[8-11]. Since A and BA phenotypes are associated with the lowest enzymatic activity, one would expect in these phenotypes a higher level of flavo-enzyme activity and energy output as compared to other ACP_1 types. Also the negative correlation found between P^a allele frequency and the mean annual temperature of the

The relation between body weight (W) and ACP_1 phenotypes. Severity of 'obesity' has been expressed in standard deviations (SD) above the mean weight for age, height and sex.

		A + BA (low activity) %	B (medium activity) %	C + CA + CB (high activity) %	Total No.	Association of ACP_1 with severity of obesity (p)
Subdivision in two classes of severity	W ≤ 4 SD	27.3	54.5	18.2	55	0.0070
	W > 4 SD	60.0	15.0	25.0	20	
Subdivision in three classes of severity	W < 4 SD	23.3	63.3	13.3	30	0.0208
	4 SD ≤ W < 6 SD	37.8	35.1	27.0	37	
	W ≥ 6 SD	75.0	12.5	12.5	8	
Controls		40.97	45.37	13.66	1025	

place where the populations sampled are living[12] supports the conjecture of a relation between ACP_1 and metabolism. It is possible that in A and BA subjects the pattern of flavo-enzyme activities may allow a full response to stimuli (environmental and/or genetic) aimed to maximize body mass.

It is interesting to note that considering the whole sample of obese children, no significant difference is observed in the distribution of ACP_1 phenotypes with respect to the general population. On the other hand, when the sample of obese children is subdivided according to severity of disease a highly significant pattern of association with the ACP_1 phenotype emerges. The data suggest that genetically determined variability of ACP_1 activity influences the degree of obesity, but only when departure from 'normality' has already been triggered.

The pattern of association described here in obese children is in line with that observed in newborns[4], and encourages[5] further investigations on the role of ACP_1 in obesity and especially in the predisposition to extreme body mass deviations.

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Plasma lipid-bound sialic acid alterations in neoplastic diseases

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Summary. Plasma lipid-bound sialic acid (LSA) was assayed in normal volunteers, patients with non-malignant diseases, and a variety of cancer patients. Mean plasma LSA in 50 normal volunteers, 16 patients with non-malignant diseases, 54 breast cancer, 17 lung cancer, 15 colon cancer, 7 ovarian cancer, 5 prostate cancer, 4 leukemia, 4 gastrointestinal, 3 thyroid cancer, 3 pancreas cancer and 2 adrenal cancer patients were 17.7, 23.2, 58, 85, 56.7, 46.2, 56.7, 53.3, 31.1, 33.2 and119.5 mg/dl, respectively. None of the normal volunteers had elevated plasma LSA values. Plasma LSA level was not significantly different in male and female volunteers. Two patients with rheumatic arthritis had LSA values slightly elevated over the mean + 2 SD for the normal volunteers. Two out of 114 different cancer patients had plasma LSA levels within normal range exhibiting 98.2% sensitivity of the assay. Plasma LSA, which is relatively simple to assay, may be used as a tumor marker in wide variety of neoplastic diseases.
Key words Lipid-bound sialic acid; cancer patients; tumor marker; non-malignant diseases.

The surface of cancer cells differs in many respects from normal cells[1]. Neoplastic transformations of a variety of cell types are associated with changes in the composition of membrance glycoproteins[2,3], a major structural component of the cell surface. One such change is in the level of sialic acid on the cell surface[4,5]. Sialic acid levels are higher in cancer patients than normal controls[6-9]. Studies have indicated that assay of lipid-bound sialic acid (LSA) may be more useful and discriminating than the assay of total sialic acid[10,11]. Dnistrian and Schwartz evaluated[12] the LSA and carcino-embryonic antigen (CEA) in cancer patients and concluded that LSA was increased in more patients with leukemias, lymphomas, Hodgkin's disease and melanomas in comparison to the CEA. The purpose of the present investigations is to extend our knowledge of LSA in a wide variety of neoplastic patients.

Materials and methods

Blood samples were obtained in citrate tubes from normal volunteers (age 25–35 years), patients with non-malignant diseases (2 sickle cell anemia, 1 hepatitis and 13 rheumatoid arthritis), and a variety of cancer patients