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CASE REPORT

GENETIC SUSCEPTIBILITY TO LEAD POISONING – A CASE REPORT

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ABSTRACT

Lead poisoning is well documented in persons occupationally exposed to lead. What is less known is, that even in persons working in lead based industries, the effect of lead and the appearance of signs and symptoms of lead poisoning is genetically determined. Three genes related to lead metabolism, exhibiting polymorphism have already been demonstrated -δALA-dehydratase, Vitamin D receptor gene and Hemochromatosis gene. These alleles determine the susceptibility of the individuals to lead. We present here a case of a lead acid battery worker, who presented without any signs and symptoms of lead poisoning except for a very high level of blood lead (82.8μg/dl and 47.5μg/dl 9 months later)

KEY WORDS

Lead poisoning, Gene polymorphism, Alleles

INTRODUCTION

Lead is the 5th most abundant metal in the world. Human exposure to lead occurs primarily through diet, air, drinking water, dust, and paint chips. Lead is absorbed into the body following ingestion and inhalation exposure. The toxic effects of lead in humans have been well documented. Nonspecific signs and symptoms of lead intoxication include loss of appetite, metallic taste, constipation, pallor, malaise, weakness, insomnia, headache, irritability and pain in muscles and joints. Specific effects occur in target organs and systems: nervous system, hematopoietic system, cardiovascular system, kidneys and reproductive systems. In the recent times there is a lot of interest in the concept that genetic polymorphism plays a role in the presentation of symptoms in lead exposed individuals. Three very important genes have already been recognized to exhibit polymorphism, which influences susceptibility to lead exposure.

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CASE REPORT

A 30-year old male working in a lead acid battery factory for over 6 years came to our laboratory, at the National Referral Centre for lead poisoning in India, Bangalore, wanting to check out his blood lead levels after his friend, who had abdominal pain and weakness of the right arm was detected to have high blood lead levels. He was totally asymptomatic. On examination, he was found to be a middle aged male, well built and well nourished. There was no pallor, icterus or cyanosis. His pulse, blood pressure and other vital signs were normal. Systemic examination including that of the central nervous system did not reveal any abnormality.

Blood investigations were done and the findings were as follows (Values in parenthesis indicate normal range) : Haemoglobin = 14.3gms/dl (13-18gms/dl), Total count = 9900 (4000-11000), Differential count - Neutrophils = 49% (40-75%), Lymphocytes = 37% (20-45%), Eosinophils = 11%(1-6%), Myelocytes =2%(<1%), Metamyelocytes =1%(<1%), Platelets = 2.25 lacs/ml (1.5-4.1 lacs/ml) and Blood lead = 82.8μg/dl (<10μg/dl)

On further enquiry, he was found to be on an average diet and was not taking any special precautions like changing his clothes after work or before going home or taking iron/calcium/ vitamin supplementation. He was referred to a hematologist and was given the regular advice regarding environmental

intervention and asked to come for follow up 3 months later. He returned after a period of 9 months, without having any interventional therapy, still asymptomatic.

Follow-up investigations showed the following findings: Haemoglobin = 16.8gms/dl, Total count = 10,800, Differential count – Neutrophils = 57%, Lymphocytes = 31%, Eosinophils = 1%, Monocytes = 2%(N=2-10%), Basophil = 10%(N=<1%), Platelets = 3.28 lakhs/ml and Blood lead = 47.5μg/dl.

DISCUSSION

Major studies have been done on the sources, effect of lead, both on humans and on animals. There have not been many studies done on genetic markers of susceptibility to environmental toxins such as lead.

It has been found that there are at least three polymorphic genes that potentially can influence the bioaccumulation and toxokinetics of lead in humans. (1). We are aware that one of the most important enzymes affected by lead is the δALA-dehydratase (2) and thus considered as sensitive indicator of lead exposure (3,4,5). Inhibition of erythrocyte δ-ALAD has been noted at very low blood levels. The threshold blood lead level for δ-ALAD activity is less than 10 μg/dL in adults and children. (6). There are eight variants of this gene described in literature but one polymorphism that yields two polymorphic alleles -ALAD-1 and ALAD-2, have been implicated in susceptibility to lead toxicity (7). These two alleles determine three isoenzymes, designated 1-1, 1-2 and 2-2, all of which display similar activities but have different charges (8). ALAD-1-2 heterozygotes produce an enzyme that is more electronegative than that of ALAD-1 homozygotes.(7) Genotype frequencies vary by geography and race. ALAD-2 is the rarer of the two alleles and has been associated with high blood lead levels. In comparison, African and Asian populations have a low ALAD-2 allele frequency with few or no ALAD-2 homozygotes found in such populations (9). It has been thought to increase the risk of lead toxicity by generating a protein that binds lead more tightly than the ALAD-1 protein. Other evidence suggests that ALAD-2 may confer resistance to the harmful effects of lead by sequestering lead and making it unavailable for pathophysiologic participation. (7) Recent studies have however, showed that individuals who are homozygous for the ALAD-1 allele have a higher cortical bone lead level. This implies that these individuals may have greater body burden of lead and may be at a higher risk of the long-term effects of lead.

The second gene is the Vitamin D receptor (VDR) gene (7). VDR is involved in calcium absorption through the intestines and the bone. The polymorphism of this gene may influence the accumulation of lead in the bone. Finally the third gene which may influence the absorption of lead is the Hemochromatosis gene, which codes for the HFE protein. The presence of mutations in the HFE gene leads to hemochromatosis in homozygotic individuals.(1). Due to the strong association between iron and lead transport, the polymorphism of the Hemochromatosis gene, may also influence the absorption of lead. (1)

In the above case, we see that despite very high levels of blood lead (82.8μg/dl and 47.5μg/dl), the patient is asymptomatic and the blood picture remains unaffected by the high blood lead levels. This may be explained by the polymorphism exhibited by the genes like the ALAD. Studies involving PCR-based genotyping followed by an electrophoretic technique to distinguish ALAD protein variants need to be done to demonstrate the polymorphism. More studies will be needed to define the role of genes in lead intoxication.

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