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Lyso-Glycosphingolipids and Leukemia in Children: A Case Report

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Abstract **Case Report**

Sphingolipidosis is epidemiologically associated with an increased risk of cancer. This disease is accompanied by a storage of sphingolipids, glucosylceramide and glucosylsphingosine [1], mainly in hematopoietic organs. Sphingolipids are bioactive effectors involved in many cellular functions including proliferation and apoptosis. We hypothesize that the increase in glucosylceramide and/or the ceramide/glucosylceramide imbalance produced by GCase deficiency may contribute to tumor development. The mechanisms responsible for the overrepresentation of cancers in these diseases are currently unknown. It is not known whether it is excess glucosylceramide in the cancer cell that is involved in the pathophysiology or whether it is changes in the tumor microenvironment [2]. ***Observation:*** We report a case of a 3-year-old child admitted for bone marrow failure syndrome associated with a tumor syndrome and in whom a workup confirmed acute lymphoblastic leukemia. A concomitant blood and urine amino acid chromatography revealed the presence of sphingolipidosis. ***Conclusion:*** Several sphingolipids, play crucial roles in various stages of oncogenesis, so the determination of these markers in leukemia patients should be considered.

Keywords: sphingolipidosis, cancer, hematopoietic organs, pathophysiology, patients.

INTRODUCTION

The association between sphingolipidosis and cancer has been reported for about thirty years. Indeed, the appearance of hematological diseases, in particular B lymphopathies and plasma cell cancers such as multiple myeloma (MM), acute or chronic leukemia, or Hodgkin's disease, has been described during these pathologies. In 1982, a causal link between glucosylceramide accumulation and cancers was postulated [3, 4].

OBSERVATION

The patient was 3 years old, from a first-degree consanguineous marriage, the youngest of three siblings, admitted for bone marrow failure syndrome with normocytic normochromic anemia, thrombocytopenia and neutropenia associated with a tumor syndrome with splenomegaly, hepatomegaly and multiple adenopathies; evolving for 1 month.A myelogram was performed showing a marrow with a lymphoid aspect of 17%, medullary eosinophilia and overload cells completed with a bone marrow biopsy confirming the diagnosis of acute lymphoblastic leukemia. A chromatography of the blood and urinary amino acids was carried out in parallel and objectified lysoglucosylceramides and sphyngomyelines confirming the diagnosis of sphingolipidosis.

A brain MRI looking for white matter infiltration by these markers was normal. Patient was transferred to the pediatric hematology oncology department for specialized management.

DISCUSSION

Sphingolipidosis is epidemiologically associated with an increased risk of cancer. It is accompanied by a storage of sphingolipids, glucosylceramide and glucosylsphingosine, mainly in hematopoietic organs. Sphingolipids are bioactive effectors involved in many cellular functions including proliferation and apoptosis. We hypothesize that the increase in glucosylceramide and/or the ceramide/glucosylceramide imbalance produced by G Case deficiency may contribute to tumor development. At present, the mechanisms responsible for the

overrepresentation of cancers in sphingolipidosis remain unknown. It is not known whether it is the excess of glucosylceramide in the cancer cell that is involved in the pathophysiology or whether it is changes in the tumor microenvironment that are responsible.

Carcinogenesis could be directly related to the accumulation of sphingolipids such as glucosylceramide and/or to a decrease in ceramide levels, resulting in an imbalance in favour of cell proliferation [5, 6]. Indeed, as described above, elevated glucosylceramide is observed in various resistant lines.

Lyso-glycosphingolipids are generated in excess in glycosphingolipid storage disorders. In these disorders, glycosylated sphingolipids accumulate in lysosomes due to defects in lipid degradation mechanisms. Deacylation of the accumulated glycosphingolipids results in the formation of lyso-glycosphingolipids [7]. In lysosomal storage diseases such as Gaucher disease, Fabry disease, Krabbe disease, GM1 and GM2 gangliosidoses, Niemann disease type C, and metachromatic leukodystrophy, a massive accumulation of intra-lysosomal glycosphingolipids occurs. The lysosomal enzyme ceramidase generates deacylated lyso-glycosphingolipid species. This accumulation predisposes to neoplastic pathologies [8-11].

CONCLUSION

The association between lyso-glycosphingolipids and leukemia in children has rarely been elucidated, which opens the debate on the usefulness of the determination of these markers in a leukemic patient.

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