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Serum sphingomyelin species profile is altered in hematologic malignancies

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ABSTRACT

Sphingomyelin (SM) plays key roles in regulating cell membrane fluidity and in intracellular signal transduction. However, little is known as to whether alterations in SM concentration or SM species distribution are linked pathological conditions. The present study examined SM concentrations and species profiles in serum taken from patients with hematologic malignancies.

Serum was collected from normal subjects and from patients with B-cell lymphoma, myelodysplastic syndrome (MDS), acute myeloid leukemia (AML) and acute lymphatic leukemia/ lymphoblastic lymphoma (ALL/LBL). Serum SM species distribution was analyzed using electrospray ionization mass spectrometry/ mass spectrometry (ESI MS/MS). Serum lipids concentration were measured using enzymatic assays.

Normal and hematologic malignancy sera were similar in terms of total serum SM and phosphatidylcholine (PC) concentrations and SM/PC ratio. However, all hematologic malignancy sera had lower levels of SM species containing saturated odd chain fatty acids (OCFAs) in the side chain compared to normal serum. In addition, the proportion of SM species with saturated (C20 and C22) and mono unsaturated fatty acids (C18, C20, C22) were lower in MDS patient serum compared to normal serum.

The present study revealed that the serum SM species profile in patients with hematologic malignancies differed from that of normal subjects despite total serum SM and PC concentrations and SM/PC ratios being similar between the various cancer groups and the normal group.

1. Introduction

Sphingomyelin (SM) is composed of ceramide and phosphorylcholine, and ceramide itself is composed of a sphingoid base and a fatty acid. SM accounts for 85% of all sphingolipids, and is a major component of cell membranes, lipoproteins and nerve cell myelin sheaths. SM contains very-long-chain fatty acids (VLCFAs) which are either saturated or mono-unsaturated. SM species differ with respect to their fatty acid moiety. Odd chain fatty acids (OCFAs) are more common in SM compared to glycerophospholipids [1]. OCFAs are derived from both exogenic (e.g., dietary intake) and endogenic (e.g., biosynthesis and metabolism) sources. A recent study indicated that enteric bacteria played a role in OCFA biosynthesis [2]. A role of OCFA for disease etiology has yet to be established. The type and concentration of SM in cell membranes can affect membrane fluidity [3]. Reduced cell membrane fluidity is correlated with increased blood SM concentration in atherosclerosis patients [4].

SM is an important component of lipid microdomains. Sphingomyelinase (SMase) can catabolize SM into ceramide and phosphorylcholine. Ceramide acts in intracellular signaling pathways that regulate processes such as apoptosis, differentiation and proliferation [5]. Shingolipids are involved in cancer cell metabolism and drug resistance through bioactive lipids such as ceramide. Sphingomyelin and ceramide are closely linked between synthesis and metabolism. There

Abbreviations: ESI MS/MS, electrospray ionization mass spectrometry/ mass spectrometry; MDS, myelodysplastic syndrome; AML, acute myeloid leukemia; ALL/LBL, acute lymphatic leukemia/ lymphoblastic lymphoma; OCFA, odd chain fatty acids.

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