Evaluation of lipid-bound sialic acid tumor marker in sera of acute lymphocytic (ALL) patients

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ABSTRACT

Background: Lipid-bound sialic acid (LSA) concentration was determined in the sera of 90 patients with acute lymphocytic leukemia (ALL) and 50 controls (30 normal subjects and 20 chronic non-malignant diseases). The aim of this work is to determine the reference values for serum sialic acid in healthy subjects and in patients with acute lymphocytic leukemia.

Materials and Method: All of serum sample were collected by venepuncture and kept frozen (-20 °C) until analyzed, then a spectrophotometric technique is used for the estimation of the concentration of sialic acid marker in sera.

Results: The mean sialic concentration in healthy individual s was 132 mg/ml and that in chronic non-malignant disease was 171.1 mg/ml, where as, the concentration of (LSA) in 90 cancer patients with (ALL) was 270.3 mg/ml.

Conclusion: Both cancer patients with (ALL) and patients with chronic non-tumor disease can cause an elevation in the concentration of sialic acid values in serum as compared to healthy individuals.

Keywords: Sialic acid, tumor marker, acute lymphocytic leukemia. (J Bagh Coll Dentistry 2008; 20(1)28-30)

INTRODUCTION

Sialic acid is an acetylated derivation of neuraminic acid. (1) It is attached to non-conducting residue of carbohydrate chains of glycoprotein and glycolipids. Glycoproteins and glycolipids are cell surface constituents containing N-acetylnuraminic acid (Sialic acid) as a common terminal saccharide. Aneoplasm often has an increased concentration of sialic acid on the tumor cell surface and this may be due to the fact that aberrant glycosylation process in tumor cells may contribute to the biosynthesis of the carbohydrate structures so that malignant or transformed cells contain increased levels of sialic acid on their surface. Cell shape, anchorage and growth rate have been shown to influence the sialic acid content of the cell (2).

The suggested biological functions of sialic acid include: Stabilizing the concentration of glycoproteins and cellular membrane, assisting in cell to cell recognition and interaction, contributing to membrane transport, affecting the function of membrane receptors providing binding sites of ligands, influencing the function stability and survival of blood glycoprotein’s, regulating the permeability of the basement membrane of glomerul (3).

The serum LSA concentration has been reported to be potentially useful as a complementary Tumor marker (4). Elevated concentration of sialic acid has been observed in several types of cancer include breast cancer, gynecological cancer, prostate cancer, colorectal cancer, neuroendocrine tumors, myeloma, and lung cancer (5), in addition to myocardial infarction, diabetes and inflammatory disorder (6-7).

However, Kalela (8) reported the association of the elevation of serum sialic acid and metalloproteinase-9 with lipid profile and inflammatory marker in heart disease, while Ponnio (9) suggested that the concentration of sialic acid was a potential marker for alcohol abuse. Nikkar (10) reported a significant change in lipid profile associated with LSA, which can be used for the follow up risk factors and monitoring coronary heart disease prevention activity.

Cancer patients have an increased LSA concentration, which coordinate positively with the degree of metastasis and are useful in monitoring and treatment (6). In another study conducted by Croke et.al (11) they showed that the increase in serum sialic acid in patients with multiple myeloma were highly significant compared with control group.

The aim of the work is to determine the reference value for the concentration of serum sialic acid in healthy subjects and in patients with ALL.

MATERIALS AND METHODS

Serum LSA was measured using the method that was developed by Katopoids et. al (12).

The experiments were conducted using unhemolzyed sera obtained from 90 patients with

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acute lymphocytic leukemia (ALL) with age range from 20-60 years. All patients were diagnosed in college of medicine Al.Nahrain university though the year 2001, and the blood sera were also collected from 30 age matched healthy volunteers and 20 patients with disease other than tumors (Rheumatoid, arthritis and joint disease).

The sera samples were studied immediately after collection or otherwise frozen at -20 °C until used.

**Procedure**

One ml of serum was mixed with 3 ml of distilled water and extracted with 30 ml of 50% chloroform: 50% methanol mixture. The sample was centrifuged, and the aqueous layer containing LSA was precipitated with phosphotungstic acid. After centrifugation the supernatant was discarded and the precipitate suspended in distilled water. One ml of resorcinol reagent was added and the sialic acids determination was done by the spectrophotometric procedure at 580 nm.

**RESULTS**

Data for LSA concentration in the sera of chronic non-malignant patients, normal subjects and cancer patients are presented in table 1.

**Table 1: Measurements of LSA (μg/ml) in the sera of patients with ALL, chronic non-malignant and control groups**

<table>
<thead>
<tr>
<th>Mean + SD</th>
<th>No.</th>
<th>Mean ± SD</th>
<th>Age (years)</th>
<th>No.</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>262.6 ±14.9</td>
<td>38</td>
<td>20-30</td>
<td>270.1 ± 14.8</td>
<td>19</td>
<td>30-40</td>
</tr>
<tr>
<td>261.8 ± 15.8</td>
<td>25</td>
<td>40-50</td>
<td>275.0 ± 11.7</td>
<td>9</td>
<td>50-60</td>
</tr>
<tr>
<td>90</td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>171.1 ± 15.6</td>
<td>6</td>
<td>20-30</td>
<td>166.6 ± 13.3</td>
<td>8</td>
<td>30-40</td>
</tr>
<tr>
<td>174.8 ± 10.9</td>
<td>6</td>
<td>40-50</td>
<td>20</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Normal</td>
<td>control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>135.5 ± 11.9</td>
<td>10</td>
<td>20-30</td>
<td>136 ± 10.38</td>
<td>10</td>
<td>30-40</td>
</tr>
<tr>
<td>132 ± 6.7</td>
<td>10</td>
<td>40-50</td>
<td>30</td>
<td>Total</td>
<td></td>
</tr>
</tbody>
</table>

The results shown in the table 1 demonstrate non significant different among age groups examined so data were pooled together for the 4 age groups with:-

- Mean and S.D. (270.3 ± 6.306) for ALL.
- Mean and S.D. (170.84 ± 4.121) for chronic non malignant, (Figure 2). It is evident from the results in table 1 that the LSA concentration in all the 90 patients with ALL were significantly higher when compared with normal control group and they were in the range of 240-290 μg/ml with the mean value of 270.3 μg/ml.

**DISCUSSION**

Lipid bound sialic acid concentrations in healthy subjects have been determined with several methods in a number of studies. There are many methodological and other factors that can influence the measured LSA concentrations in reference individuals. Age, sex, smoking and use of contraceptive pills may affect serum LSA concentration (9).

Sialic acid is of major importance in cell biology because of the external position of LSA on glycoproteins and glycolipids, and on the outer cell membranes. Sialic acid participates in the stabilization of the conformation of glycoproteins and cellular membrane (13).

Furthermore, the negative charge present in sialic acid means that the compound takes part on binding and transports of positively charged molecules and in the attraction and repulsion of the cells and molecules (14). It also contributes to the regulation of the permeability of the basement membrane on glomeruli (13).

An elevation of LSA has been reported in majority of children with leukemias (15) in adults with acute myeloid leukemia, chronic myeloid leukemia (16), acute lymphoblastic leukemia (17), chronic lymphocytic leukemia (18) and lymphomas (19) (20). The results of this work are in agreement with those obtained by katopodis (4) who found that the average level of LSA in sera of leukemic patients was 305 μg/ml, lymphoma 287 μg/ml, Hodgkin’s disease 342 μg/ml and melanoma 269 μg/ml. These results allowed him to conclude that the LSA levels in these diseases are significantly higher when compared with normal control group 160 μg/ml.

Further analysis of LSA was done by Bhargava et.al (21) on patients with leukemia, lymphoma, pancreas and lung cancers. They found that the level of LSA was significantly higher in cancer patients especially with active disease as compared with healthy control.

In view of the above, the elevation of LSA in serum of leukemic patients is not surprising. However, the mechanism is very complex and can be related to the intensified cell metabolism and
increased serum sialytransferase activity expressed by the tumor cells (22) (23).

Elevated LSA concentration has also been reported in patients with chronic non-malignant disease as compared with healthy individuals. This was within the agreement with the previous studies conducted by Seider(15), Okennedy(18) and Brockhausen (24). They reported that LSA concentration was elevated in patients with bacterial infections and rheumatoid arthritis. This increase in serum LSA concentration may occurred through changes in the biosynthesis and post-translational glycosylation processing of the acute-phase glycoproteins in the liver (25).

REFERENCES


