Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(5):1199-1202

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Comparison of Mannan-binding lectin-associated serine protease-2 (MASP-2) serum levels between children with acute lymphoblastic leukemia and healthy controls

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ABSTRACT

Mannan-binding lectin-associated serine protease-2 (MASP-2) is an essential component of the lectin pathway of complement activation. Its serum concentrations show a wide interindividual variability. The aim of our study was to determine if serum concentrations of MASP-2 differ between children with Acute lymphoblastic leukemia (ALL) and healthy age-matched controls. This study included 48 individuals: 37 children with Acute lymphoblastic leukemia (ALL) and 11 healthy age-matched controls. Serum levels of MASP-2 were evaluated by ELISA. The results showed that children with Acute lymphoblastic leukemia had higher median MASP-2 serum concentrations (509 ± 351.8 ng/mL) compared to healthy age-matched controls (284 ± 35.4 ng/mL), ($p<0.05$). This indicates the Acute lymphoblastic leukaemia associated with high levels of MASP-2 and suggests the possibility to use MASP-2 as diagnostic biomarker for Acute lymphoblastic leukaemia.

Key words: Acute lymphoblastic leukemia (ALL), innate immunity, Mannose-binding lectin-associated serine protease-2 (MASP-2).

INTRODUCTION

While the role of adaptive immunity and cellular components of innate immunity in cancer suppression and promotion have been extensively studied [1–3], little is known on the respective influence of soluble components of innate immunity.

The complement system provides an important effector mechanism of innate humoral defence. Activation of the complement system proceeds through three different pathways converging in the activation of C3. The classical pathway is typically initiated after antigen recognition by antibodies, the alternative pathway relies on interference by foreign substances in a delicate activation–inhibition balance and the third pathway, the mannan-binding lectin (MBL) or lectin pathway, is initiated when one of the molecules MBL, L-ficolin or Hficolin recognizes ligands arranged in patterns characteristic of microbial surfaces, pathogen associated molecular patterns or PAMPs [4-7].

Due to single nucleotide polymorphisms, deficiencies of MBL and MASP-2, two key components of the lectin pathway, are frequent in Caucasians, with an incidence of about 10% [8]. In adults, such deficiencies or the underlying genotypes seem to be associated with the incidence, or the prognosis, of different types of carcinoma both for MBL [9-13] and MASP-2 [14,15]. In young children, where adaptive immunity is still maturing, innate immunity may play a more important role in carcinogenesis or immunosurveillance. Despite this, nearly nothing is

known on components of the lectin pathway in children with cancer. We are aware of only one exception, a study on MBL genotypes in children with acute lymphoblastic leukaemia (ALL), who were found to have an increased frequency of low-producing MBL genotype compared to healthy adults [16]. The role of MASP-2, and of MBL phenotypes, in children with cancer versus healthy controls has not yet been studied.

This study aimed to determine if serum concentrations of MASP-2 differ between children with Acute lymphoblastic leukaemia (ALL) and healthy age-matched controls.

EXPERIMENTAL SECTION

Study Subjects: 37 patients below 15 years of age and diagnosed at Children University Hospital in Damascus, Damascus, Syria with Acute lymphoblastic leukemia requiring chemotherapy were eligible for this study. Excluded were patients with relapses or second malignancies, and those in which serum was not accessible. 11 healthy age-matched controls also participated to this study.

Sampling: Blood samples were collected (within 3 days of diagnosis and before starting chemotherapy for the patients) and after centrifugation, serum was acquired and aliquots were stored at -20πC until assay were done.

Assay: Serum levels of MASP-2 was measured using commercially available enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions.

Statistical analysis: data were analyzed using SSPS (version 21, IBM SSPS). Results were presented as mean ± SD. Comparison between the means of two independent groups was performed using Mann-Whitney'U-test.

RESULTS AND DISCUSSION

The table (1) and figure (1) show the comparison between MASP-2 serum concentrations in children with Acute lymphoblastic leukemia and healthy age-matched controls.

The mean of MASP-2 serum concentrations was significantly higher in Acute lymphoblastic leukaemia (ALL) patients (509 ± 351.8 ng/mL) than control group (284 ± 35.4 ng/mL), ($p<0.05$).

Table (1): MASP-2 serum concentrations in children with Acute lymphoblastic leukemia and healthy age-matched controls

Group	Mean ± SD	N	Minimum	Maximum
Acute lymphoblastic leukemia patients	509 ± 351.8	37	87	1382
Control group	284 ± 35.4	11	217	339

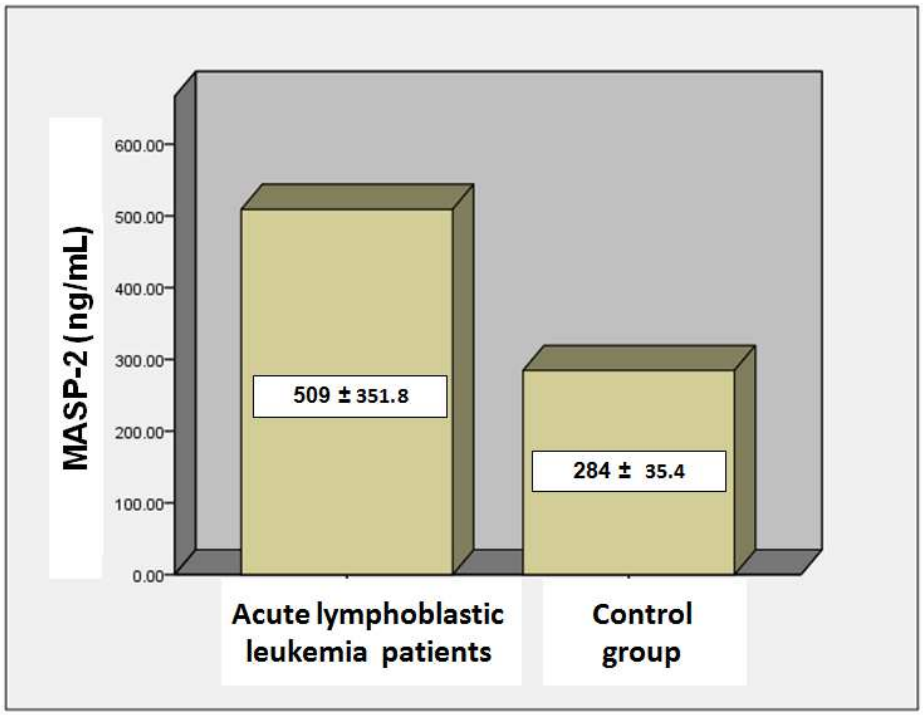

Figure (1): MASP-2 serum concentrations in children with Acute lymphoblastic leukemia and healthy age-matched controls

In this study, children with Acute lymphoblastic leukemia had higher median MASP-2 serum concentrations compared to age-matched controls. Similar results have been reported by Urs P. Fisch et al., who have noted that MASP-2 serum concentration was significantly higher in pediatric patients with ALL, NHL and CNS-tumours compared to age-matched healthy controls. They concluded that a role of MASP-2 in the initiation or progression of specific paediatric cancers, while other mechanisms remain possible as well [17]. In adult patients with colorectal cancer, higher MASP-2 serum concentrations than in healthy adults have as well been described [14]. Notably, high MASP-2 was associated with poor prognosis in adult colorectal cancer patients [14]. In contrast, high MASP-2 at diagnosis has been reported to be associated with a better prognosis in children with acute leukaemia and lymphoma [18].

This study cannot answer why MASP-2 serum concentrations in children with Acute lymphoblastic leukemia are higher than in controls. Several mechanisms are conceivable. First, individual MASP-2 concentrations might facilitate or hinder the development of malignancies. Specifically, high MASP-2 might act via increased complement factor C5a in the tumour microenvironment, which has been shown to enhance tumour growth in a mouse model of cervical cancer [19]. second, MASP-2 might be increased as part of the immunological response to malignancies themselves. third, MASP-2 might be actively expressed by malignant cells, as has been shown for oesophageal squamous cell carcinoma cells [15].

CONCLUSION

MASP-2 serum concentration was significantly higher in children with Acute lymphoblastic leukemia compared to healthy age-matched controls, so this suggests the possibility to use MASP-2 as diagnostic biomarker for Acute lymphoblastic leukaemia.

Acknowledgement
The authors are sincerely thankful to Prof. Khalil Al Kwatli & Prof. Shaden Haddad, Department of Biochemistry and Microbiology, Faculty of Pharmacy, Damascus University, Damascus, Syria, for their useful advices and help.

REFERENCES

[1] OJ Finn, *N Engl J Med*, **2008**, 358, 2704–2715.
[2] T Lehrnbecher; U Koehl; B Wittekindt et al, *Lancet Oncol*, **2008**, 9, 269–278.
[3] KE de Visser; LM Coussens, *Cancer Immunol Immunother*, **2005**, 54, 1143–1152.
[4]U Holmskov; S Thiel; JC Jensenius, *Annu Rev Immunol*, ***2003***, 21, 547.
[5] CA Janeway; P Travers; M Walport; M Shlomchik. Immunobiology, 5th Edition, Garland Publishing, New York, **2001**.
[6] RA Goldsby; TJ Kindt; BA Osborne. Immunology, 4th Edition, Freeman, New York, **2000**.
[7] M Matsushita; T Fujita, *Immunol Rev*, ***2001***, 180, 78.
[8] S Thiel, *Mol Immunol*, **2007**,44, 3875–88.
[9] H Ytting; JC Jensenius; IJ Christensen; S Thiel; HJ Nielsen, *Scand J Gastroenterol*, **2004**,39,674–9.
[10] A Baccarelli; L Hou; J Chen J; J Lissowska; EM El-Omar; P Grillo et al, *Int J Cancer*, **2006**,119,1970–5.
[11] AS Swierzko; K Florczak; M Cedzyński; J Szemraj; D Wydra; L Bak-Romaniszyn et al, *Cancer Immunol Immunother*, **2007**, 56, 959–71.
[12] T Bernig; BJ Boersma; TM Howe; R Welch; S Yadavalli; Staats B et al, *Carcinogenesis*, **2007**, 28, 828–36.
[13] FY Wang; T Tahara; T Arisawa; T Shibata; H Yamashita; M Nakamura M et al, *Dig Dis Sci*, **2008**, 53, 2904–8.
[14] H Ytting; IJ Christensen; S Thiel; JC Jensenius; HJ Nielsen, *Clin Cancer Res*, **2005**, 15, 1441–6.
[15] A Verma; A Matta; NK Shukla; SV Deo; SD Gupta; R Ralhan, *Int J Cancer*, **2006**, 15, 2930–5.
[16] K Schmiegelow; P Garred; B Lausen; B Andreassen; BL Petersen; HO Madsen, *Blood*, **2002**, 15, 3757–60.
[17] P Fisch; A Zehnder; A Hirt; FK. Niggli; A Simon; H Ozsahin; LJ Schlapbach; RA Ammann, *Swiss Med Wkly*, **2011**, 144, 1-5.
[18]A Zehnder; U Fisch; A Hirt; FK Niggli; A Simon; H Ozsahin; LJ Schlapbach; RA Ammann, *Pediatr Blood Cancer*, **2009**, 53, 53–7.
[19] MM Markiewski; RA DeAngelis; F Benencia; SK Ricklin-Lichtsteiner; A Koutoulaki; C Gerard et al, *Nat Immunol*, **2008**, 9, 1225–35.