Thymidine Phosphorylase is Increased in Patients with Infection and Could be a Prognostic Marker for Sepsis and Disseminated Intravascular Coagulation

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Abstract

Background: Sepsis, a serious condition caused by infection, can ultimately progress to life-threatening septic shock and multiple organ failure. Hitherto, no reliable markers could be used for the early diagnosis and sepsis is still a challenge for clinicians. We investigated the potential role of thymidine phosphorylase (TYMP) in infection and delved its value in diagnosing sepsis and disseminated intravascular coagulation (DIC).

Methods: This prospective study enrolled infection patients consecutively admitted to Beijing Friendship Hospital from November 2019 to January 2021. Non-infection volunteers were used as control (NIC). Blood sample were obtained on day 1, 2, 4, and 7 after admission. TYMP serum levels and its correlation with DIC scores, Sequential Organ Failure Assessment (SOFA) scores, and other laboratory parameters were analyzed using the non-parametric Mann-Whitney U test and the Spearman's Rank-Order Correlation analyses.

Results: Eighty-three infectious patients were enrolled. Forty-two patients were diagnosed as sepsis (SP) and 41 were non-septic infection (NSP). NIC group included 20 individuals without any infection. Serum TYMP levels were significantly higher in both SP and NSP groups when compared with the NIC group. TYMP serum levels was further higher in the SP than in the NSP group. The increase of TYMP was positively correlated with DIC scores. TYMP was higher in patients with DIC than those patients without DIC. A positive correlation presented between serum TYMP and plasma D-dimer levels. No positive correlations were found between TYMP and inflammatory markers. TYMP was higher in patients with SOFA score > 1 than those with SOFA score zero. The increase of TYMP is also positively correlated with SOFA score and death risk coefficient, and negatively correlated with oxygen index. By conducting receiver operating characteristic curve analyses, we found TYMP has a specific and sensitive predictive value for diagnosing sepsis and a modest value for DIC.

Conclusions: This study is the first time to determine the role of TYMP in infectious disease. TYMP is significantly increased in infectious patients and is further higher in patients with sepsis or DIC. TYMP is positively correlated with acuity markers and has a diagnostic and prognostic value for sepsis and DIC.

Full Text

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Tables

Table 1. Cases based on diseases.

	Sepsis	Non-sepsis
Prior Medical History		
Cardiovascular Disease	12	11
Respiratory Diseases	4	3
Kidney Disease	4	3
Liver Disease	4	1
Rheumatic Disease	3	7
Diagnosis		
Pneumonia	11	14
Lung abscess	2	0
Necrotizing fasciitis	1	0
Soft tissue infections	2	0
Urinary tract infection	3	6
Infective endocarditis	1	2
Meningitis	1	1
Abdominal infection	20	14
Anaplasma infection	1	0
Perianal infection	0	1
Acutesuppurative tonsillitis	0	1
Bacillary dysentery	0	1
Osteomyelitis	0	1
Death	5	0

Table 2. Age, gender, and laboratory tests.

	Sepsis	Non-sepsis	Control	P
Sample size (n)	42	41	20	NS
Age, mean (range)	58.43 ± 17.67	55.17 ± 17.87	43.13± 14.082	NS
Gender (male/female)	29/13	24/17	10/10	NS
BMI (kg/m ²)	25.22 ± 3.996	23.973 ± 3.844		0.178
TYMP expression				
Pulmonary infection	5.944 ± 1.215	5.102 ± 1.373		0.127
Soft tissue infection	4.095 ± 0.927	5.253		0.500
Urinary tract infection	6.361 ± 4.346	3.988 ± 0.880		0.629
Infective endocarditis	5.184 ± 1.404	2.823		0.667
Central nervous system infection	6.811	4.981		1
Digestive system infection	8.347 ± 6.753	5.143 ± 2.80		0.069
Laboratory tests				
	11.213 ± 14.587	9.801 ± 5.549		0.592
WBC (10 ⁹ /L)	88.916 ± 89.122	77.677 ± 82.034		0.566
CRP (mg/L)	7.655 ± 13.376	3.968 ± 4.731		0.264
D-Dimer (µg/ml)	202.63 ± 155.693	300.03 ± 144.582		0.001
PLT (10 ⁹ /L)	367.839 ± 141.398	444.818 ± 78.127		0.004
Oxygenation index	1.599 ± 5.801	0.465 ± 0.413		0.142
CK-MB (U/L)	2.86 ± 1.458	1.54 ± 1.051		0.000
DIC score	4.23 ± 2.577	0.27 ± 0.449		0.000
SOFA score	28.856% ± 20.461%	13.071% ± 9.882%		0.000
Death risk coefficient.	13.38 ± 6.226	8.82 ± 4.089		0.000
APACHE II	0.123 ± 0.522	0.016 ± 0.058		0.004
cTNI (ng/ml)	401.69 ± 371.327	244.64 ± 123.325		0.018
LDH (U/L)				

Figures

Figure 1

Serum TYMP levels are increased in patients with infection, especially in sepsis. Eighty-three infectious patients were divided into sepsis (SP, 43 patients) and non sepsis (NSP, 41 patients) groups according to the Third International Consensus Definition for Sepsis and Septic Shock (SEPSIS-3). Twenty healthy individuals were used as non-infection control (NIC). Blood drawn at the time of admission was used for preparing serum and TYMP expression was measured using ELISA

Figure 2

The increase of serum TYMP levels is correlated with the thrombotic event. A. Patients were stratified based on if they were diagnosed as having DIC or not and TYMP serum levels were compared. B to E, correlation analyses were conducted between serum TYMP levels and DIC scores (B), plasma D-dimer (C), platelet (PLT) counts (D), or plasma fibrinogen (E).

Figure 3

The increase of serum TYMP levels is not associated with white blood cell counts and plasma CRP levels. Correlation analyses were conducted between serum TYMP and white blood cell counts (A) or plasma CRP (B).

Figure 4

The increase of serum TYMP levels is positively correlated with scores of 24 acuity markers. A. Correlation analysis was conducted between serum TYMP levels and SOFA scores. B. Patients were stratified based on their SOFA scores and divided into SOFA 0 (n = 30) and SOFA > 1 (n = 53) two groups and TYMP expression was compared. C and D. Correlation analysis was conducted between serum TYMP levels and Death risk coefficients (C), or APACHE II scores (D).

Figure 5

The increase of serum TYMP is associated with cardiopulmonary dysfunction. Correlation analyses were conducted between serum TYMP levels and cTNI (A), CK-MB (B), LDH (C), or oxygen index (D).

Figure 6

The increase of serum TYMP could be a predictive marker for developing sepsis and DIC in patients with infectious disease. A. A receiver operating characteristic curve (ROC) analysis was conducted using serum TYMP levels in SOFA score 0 groups as control and SOFA > 2 as sepsis, and area under the curve (AUC) was calculated. B. ROC analysis based on TYMP levels in non-DIC (controls) and DIC patients

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