Short communication

Urinary trypsin inhibitor levels in the urine of patients with haematological malignancies


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Abstract—The urinary trypsin inhibitor (UTI) levels in the urine of patients with various haematological malignancies were determined, using automated latex agglutination immunoturbidimetry. The mean UTI levels in urine in acute non-lymphocytic leukaemia, myelodysplastic syndrome, non-Hodgkin’s lymphoma, and multiple myeloma groups were significantly elevated, compared with the normal control group. It was found that the UTI level in urine changed from an elevated value to a normal value with haematological improvement by chemotherapy in a patient with myelodysplastic syndrome included in a previous study. These results suggest that UTI may be excreted from malignant cells of patients with certain haematological malignancies and that it may be useful as an indicator of chemotherapeutic effects against haematological malignancies.

Key words: Urinary trypsin inhibitor; immunoturbidimetry; haematological malignancies.

INTRODUCTION

Urinary trypsin inhibitor (UTI) is a physiological trypsin inhibitor that has been isolated and purified from human urine [1–9]. It consists of 143 amino acid residues with one glycosaminoglycan chain and one N-linked carbohydrate [10]; has a molecular weight of about 30 kD; and inhibits various serine proteases, such as plasmin, chymotrypsin, and neutrophil elastase [1, 11]. It has been reported that the mean UTI level in urine is elevated in all patients with haematological cancers and various solid tumours, compared with normal control individuals [12–15]. We prepared latex beads coated with an antibody to rabbit anti-human UTI by immunizing rabbits with a human UTI (urinastatin, Mochida Pharmaceutical Co.

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Ltd., Japan) and developed latex agglutination immunoturbidimetry for automated determination of the UTI level [16]. We then measured the UTI levels in the urine of patients with various haematological malignancies and evaluated the clinical significance of UTI, including the results of previous studies.

PATIENTS AND METHODS

Sixty-six patients, including 12 with myelodysplastic syndrome (MDS), 12 with acute non-lymphocytic leukaemia (ANLL), four with acute lymphocytic leukaemia (ALL), four with chronic myeloproliferative disorders (CMPD), three with Hodgkin’s disease (HD), 20 with non-Hodgkin’s lymphoma (NHL), ten with multiple myeloma (MM), and three with adult T-cell leukaemia/lymphoma (ATL/L), were analysed in this study. No patients with acute inflammation, infection or renal disease took part in this study, since the UTI concentration in urine is elevated several times above the normal level in individuals with bacterial infections or renal dysfunction. On entry, all patients had evidence of the respective active haematological disease and had not undergone previous therapy. We determined the UTI levels in urine as follows. Latex beads were coated with an antibody to rabbit anti-human UTI, obtained by immunizing rabbits with a human UTI (urinastatin, Mochida Pharmaceutical Co. Ltd., Japan). With these beads, the UTI level in urine was automatically measured using latex agglutination immunoturbidimetry (Eiken LX 2500, Eiken Chemical Co. Ltd., Japan). The unit of UTI (U) for inhibition of trypsin was equivalent to that of urinastatin, which was used as the standard. One unit inhibits 50% of the activity of 2 μg of trypsin. The UTI level was calculated based on the standard curve of urinastatin determined using LX-2500. Within-run CV ranged from 1.3% to 4.7% and UTI assay precision was good [16]. Spot urine samples of patients and healthy adult volunteers were stored at −80°C until analysis. In the 89 healthy adult volunteers (N), the normal level of UTI in urine was 18.2 ± 14.1 U/ml (mean ± SD). Differences in mean UTI values in urine between the healthy control group and the respective haematological malignancy groups were statistically analysed using Dunnett’s post-hoc procedure.

Among patients with previously determined UTI levels in urine not included in this study, we followed the changes of UTI levels and laboratory findings of a 54-year-old female with MDS (subtype, RAEB-t) with an elevated UTI level (395.5 U/ml) in urine before and after chemotherapy.

RESULTS

The respective UTI levels in urine in the various haematological malignancy groups and a healthy adult volunteer group are indicated as individual frequencies in Fig. 1. The mean UTI value in urine was 74.8 ± 49.7 U/ml in ANLL patients, 14.1 ± 12.8 U/ml in ALL patients, 59.5 ± 52.8 U/ml in MDS patients, 29.9 ± 44.5 U/ml