Serum KL-6 levels in haematologic malignancies and their clinical application


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KL-6 is a mucin-like high molecular weight glycoprotein, which is strongly expressed on Type II pneumocytes and respiratory bronchiolar epithelial cells in normal lung, and it also exists on esophageal epithelial cells, ductal epithelial cells of the pancreas and fundic gland cells of the stomach [1]. KL-6 levels have been shown to be useful for estimation of the disease activity of pneumonitis, such as idiopathic pulmonary fibrosis and hypersensitivity pneumonitis [1–5]. Furthermore, it has been demonstrated that KL-6 antigen was detected at elevated levels in the serum of patients with lung adenocarcinoma, pancreatic cancer, breast cancer and hepatocellular cancer [1].

With this in mind we examined whether KL-6 antigen may be detected at elevated serum levels in patients with haematologic malignancies. The serum KL-6 levels were determined by using an enzyme-linked immunosorbent assay kit for KL-6 (Sanko Junyaku Co. Ltd., Japan) in 110 patients, including 16 with myelodysplastic syndrome (MDS), 20 with acute nonlymphocytic leukemia (ANLL), 10 with acute lymphocytic leukemia (ALL), 11 with chronic myeloproliferative disorders (CMPD), 6 with Hodgkin’s disease (HD), 30 with non-Hodgkin’s lymphoma (NHL), 11 with multiple myeloma (MM), 6 with adult T cell leukemia/lymphoma (ATL/L) in this study. No patients diagnosed as interstitial pneumonitis in haematologic malignancies took part in this study. On entry, all patients had evidence of the respective active haematological disease and had not received previous therapy. In the fifty healthy adult volunteers, the normal reference

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value of serum KL-6 was 172 ± 9 U/ml (mean ± SE). The mean serum KL-6 value was 326 ± 61 U/ml in ANLL patients, 262 ± 72 U/ml in ALL patients, 317 ± 82 U/ml in MDS patients, 522 ± 138 U/ml in CMPD patients, 266 ± 35 U/ml in NHL patients, 210 ± 41 U/ml in HD patients, 186 ± 34 U/ml in MM patients, 316 ± 73 U/ml in ATL/L patients (Fig. 1). These data suggest that the KL-6 antigen might be expressed on the malignant cells in some haematologic malignancies. So, we studied the reactivity of antihuman KL-6 monoclonal antibody kindly provided (Eisai Co. Ltd., Tokyo, Japan) to leukemia cells in bone marrow using an immunohistochemical method according to a previously described procedure [6]. Leukemia cells showed positive staining, and other blood cells showed negative staining on the bone marrow biopsy specimen. The results indicated that KL-6 antigen was expressed on the leukemia cells.

Because KL-6 was detected at elevated levels in the serum of patients with some haematologic malignancies, we thought that KL-6 might be useful as a new indicative laboratory marker when differentiating the haematologic malignancies. To check this assumption, haematologic malignancies were classified into two groups, a leukemia group and a lymphoma group; the serum KL-6 levels between a normal control group and the leukemia group, or lymphoma group, respectively, were then statistically analysed in order to evaluate the clinical usefulness of KL-6 as compared to the clinical usefulness of two previously described diagnostic and prognostic markers, the soluble transferrin receptor (sTfR) and interleukin 18 (IL-18), in haematological malignancies [7–9]. The differences in mean serum KL-6 values between the normal control group and the leukemia group, and between the normal control group and the lymphoma group were analyzed using Dunnett’s Post-hoc Procedure, respectively. The serum KL-6 levels from CMPD in the leukemia group, and the AIL/L and NHL in the lymphoma group were significantly elevated, compared to the control group (Fig. 1). There was no significant difference in mean serum KL-6 level between ANLL and ALL in the leukemia group using Bonferroni/Dunn analysis. The sTfR levels in the sera from ANLL and MDS patients in the leukemia group, and from NHL in the lymphoma group were significantly elevated, as compared to that of the control group (Fig. 2). The IL-18 level in the sera from ALL patients was also significantly elevated, as compared with those from the control group (Fig. 3). There were however no significant correlations between the levels of sTfR and KL-6, and between those of IL-18 and KL-6, nor between IL-18 and sTfR, respectively, as shown in Fig. 4. These results suggest that these three parameters are clinically useful as independent diagnostic indicators in haematologic malignancies.

In conclusion, the KL-6 was detected at elevated levels in the serum of patients with some haematologic malignancies, although further studies with a larger number of patients are needed to evaluate the role of serum KL-6 levels as prognostic indicator in haematologic malignancies.