Article

Diagnostic significance of serum soluble transferrin receptors in various anemic diseases: the first multi-institutional joint study in Japan

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Abstract—Serum soluble transferrin receptor (sTfR) has been reported to be higher in patients with iron deficiency or with elevated erythropoiesis. In the present study, serum sTfR was measured in various anemic diseases and their clinical significance was examined in a multi-institutional joint study. Serum sTfRs in patients with the following anemic diseases were markedly higher than those in normal healthy adults: non-treated iron deficiency anemia (IDA) (9.13 ± 7.04 mg/l, n = 52, p < 0.0001), anemia of chronic disorders (ACD) (3.45 ± 1.38 mg/l, n = 20, p < 0.0001), hemolytic anemia (HA) (5.57 ± 3.26 mg/l, n = 17, p < 0.0001), and myelodysplastic syndrome (MDS) (4.03 ± 2.83 mg/l, n = 20, p < 0.0001). There were significant differences between IDA and ACD (p < 0.0001), between aplastic anemia (AA) (1.58 ± 1.26 mg/l, n = 16) and MDS (p < 0.001), and between AA and MDS with refractory anemia (MDS-RA) (4.16 ± 3.40 mg/l, n = 9) (p < 0.02). In patients with chronic renal failure (CRF), serum sTfR levels and serum sTfR/log serum ferritin ratios (sTfR/F index) were compared in the two classified groups according to Muirhead’s criteria, as IDA and non-IDA groups with or without recombinant human erythropoietin (rHuEPO) treatment. Significantly high levels of both serum sTfR (p < 0.0001) and the sTfR/F index (p < 0.0001) were observed in IDA without rHuEPO treatment. Especially in CRF with rHuEPO treatment, the sTfR/F index showed marked elevation in the IDA group (p < 0.0001) compared with serum sTfR (p < 0.001), indicating more diagnostic efficacy of the sTfR/F index for CRF with IDA. In conclusion, the serum sTfR concentration is a useful diagnostic tool for discrimination between IDA and ACD, and between AA and MDS-RA, and for the detection of iron deficiency in CRF patients in the Japanese population.

Key words: Anemia; iron deficiency anemia; anemia of chronic disorders; myelodysplastic syndrome; aplastic anemia; chronic renal failure; soluble transferrin receptor.

INTRODUCTION

Transferrin receptor (TfR), a membranous protein that regulates iron uptake into cells, is expressed strongly in erythroblasts, which are constantly reproducing in the bone marrow to internalize iron for the synthesis of haemoglobin, and also moderately in various cells in the proliferation phase [1–4]. On the other hand, the expression of TfR is regulated by iron regulating protein (IRP) in the cytoplasm [5]. In the iron deficiency state, IRP moves to combine with the iron reactive element (IRE) at the untranslated region on the 3'-end of TfR mRNA and protects mRNA against degradation by RNase, resulting in up-regulation of TfR [6]. Alternatively, the presence of excess iron leads to the dissociation of IRP from IRE, and RNase degrades TfR mRNA, resulting in a reduction of the translation of mRNA [7]. TfR on the cell membrane associates with iron-saturated transferrin (Tf) and this complex is internalized into cells. After delivering iron into the cytoplasm, TfR dissociates from Tf and binds again to the cell membrane for its recycling [8]. In the production and recycling process, some of the TfR leaks to the cell outside as soluble transferrin receptor (sTfR) [9]. It has been reported that the sTfR concentration reflects the total mass of TfR in a body [10].

Measurement of serum sTfR has been reported to indicate two different clinical symptoms. The major one is an indication of iron deficiency. Kohgo et al. have reported that they could even diagnose subclinical iron deficiency at the pre-anemic stage [11]. The second is the possibility to detect erythropoietic function, because erythroblasts strongly express TfR [10, 12].