Raised serum interleukin 15 levels in Kawasaki disease

G-C Jang, H-Y Kim, S-Y Ahn, D-S Kim

Background: Interleukin (IL)15 is a novel cytokine that induces T cell proliferation, B cell maturation, natural killer cell cytotoxicity, and may have a pivotal role in the pathogenesis of inflammatory diseases, acting as an upstream signal for tumour necrosis factor α (TNFα). Kawasaki disease (KD) is an inflammatory disease, in which serum levels of inflammatory cytokines such as TNFα and IL6 are increased.

Objective: To examine the serum levels of IL15 in KD and to evaluate the role of IL15 in estimating the severity of inflammation in KD.

Results and conclusion: There was a significant increase in the mean (SD) serum levels of IL15 measured in the acute phase of KD (11.5 [5.8] pg/ml) compared to those in the subacute phase (11.8 [5.8] pg/ml) (p<0.01) and normal controls (10.4 [4.9] pg/ml) (p<0.01). The increase in IL15 correlated with the increase in TNFα (r=0.66, p<0.01); however it did not correlate with the levels of erythrocyte sedimentation rate and C reactive protein, suggesting that IL15 may not be a useful marker in estimating the severity of inflammation in KD.

Subjects and methods

Subjects
Forty serum samples were obtained from 20 patients (12 male) both in the acute (0–2 weeks) and subacute stages (2–4 weeks) of KD. These patients were all admitted to the Severance Hospital, Yonsei University College of Medicine, Seoul, Korea. All patients fulfilled at least five of the six criteria for the diagnosis of KD. Atypical KD was excluded in this study. The control sera were obtained from 10 age matched children (six male) who were having routine blood samples taken before elective surgical procedures. The mean (SD) age of patients and control groups was 2.1 (0.7) years and 2.7 (0.9) years, respectively. There was no difference in the age and sex ratio between the patients and the control groups. Informed consent was obtained from the parents of the children included in the study.

IL15 and TNFα levels by enzyme linked immunosorbent assay (ELISA)

Serum was stored at −70°C until measured for levels of IL15 and TNFα by an ELISA kit (Endogen, Woburn, MA, USA). ELISA was performed according to the manufacturer’s manual.

Measurement of erythrocyte sedimentation rate (ESR) and C reactive protein (CRP)

CRP was measured by TDx equipment (Abbott Inc, North Chicago, IL, USA). ESR was measured by the Westergren method.

Statistical analysis

A paired t test was used to compare the paired levels of IL15 and TNFα in the acute and subacute phase serum samples. The Wilcoxon signed rank test was used to compare the values of the IL15 levels in the acute phase of KD groups and control groups. The correlation between IL15 level and TNFα, CRP, and CRP was measured by the Spearman’s rank correlation test. A value of p<0.05 was regarded as significant.

Results

The mean (SD) IL15 level was 11.5 (5.8) pg/ml in the acute phase, higher than in the subacute phase (11.8 (5.8) pg/ml) (p<0.01). The serum IL15 level of control groups was 10.4 (4.9) pg/ml (p<0.01). There was no significant difference between controls and the subacute phase of disease (fig 1). The mean (SD) TNFα level was 24.1 (9.4) pg/ml in the acute phase, higher than in the subacute phase (11.8 (5.8) pg/ml) and in controls (10.4 (4.9) pg/ml) (p<0.01).

The serum IL15 level correlated with the TNFα level, which means that IL15 level was high in patients whose TNFα level was high (p<0.01, r=0.66) (fig 2). On the other hand, the IL levels did not correlate with other inflammatory indicators and IL15 levels.

Abbreviations: CRP, C reactive protein; ELISA, enzyme linked immunosorbent assay; ESR, erythrocyte sedimentation rate; IL, interleukin; KD, Kawasaki disease; TNFα, tumour necrosis factor α.
and decrease when the disease improves. Bowel diseases IL15 levels increase as the disease progresses, increase in some inflammatory diseases. In inflammatory inducing inflammation. It has been reported that IL15 levels in the acute phase than in the subacute phase and controls. Conversely, we found that IL15 levels were higher in the subacute phase, and controls, we found that IL15 levels were related to TNFα levels. As IL15 levels increased, so did TNFα levels. According to our results, the inflammatory precursor IL15 increases in the acute phase of KD, which induces TNFα proliferation and leads to an inflammatory reaction.

Besides TNFα, other inflammatory indicators such as CRP and ESR were measured in order to determine whether IL15 might be used as an effective indicator for assessing the degree of inflammation in KD.

Contrary to our expectations, there was no correlation between IL15 and either CRP or ESR. The acute phase reactants were affected by TNFα, IL6, or other various inflammatory cytokines. IL6 was especially more closely related to the acute phase reactants. For this reason, it was thought that the IL15 level did not correlate with both indicators.

Because coronary artery disease is an important inflammatory reaction in KD, the clinical and immunological role of IL15 in coronary artery disease must be researched. Among the 20 subjects of our study, however, only one patient had coronary artery disease. Therefore it was impossible to determine the correlation between IL15 levels and coronary artery disease.

With a larger number of patients, we should define the pathological role of IL15 in KD by comparing IL15 levels in patients with and without cardiovascular complications. Also the source of the increased serum IL15 levels must be found and the role of IL15 in KD elucidated.

CONCLUSION
Serum IL15, which induces inflammation in KD, increases in the acute phase and decreases in the subacute phase. We found a correlation between IL15 and TNFα levels. However, there was no significant correlation between IL15 levels and the acute phase reactants CRP and ESR. Thus, IL15 cannot be an effective indicator in assessing the degree of inflammation in KD.

ACKNOWLEDGEMENT
This work was supported by BK21 project for medical science, Yonsei University.

REFERENCES


