Alopecia areata (AA) is a heterogeneous disease characterized by non-scarring hair loss on the scalp or other parts of the body. A wide range of clinical presentations can occur—from a single patch of hair loss (alopecia unilocularis, AUl), multiple patches (alopecia multilocularis, AM) to complete loss of hair on the scalp (alopecia totalis, AT) or the entire body (alopecia universalis, AU). The cause of AA is unknown although most evidence supports the hypothesis that AA is a T-cell mediated autoimmune disease of the hair follicle and that cytokines play an important role. The aim of the study was to evaluate serum concentrations of interferon-gamma (IFN-g) in patients with AA and healthy subjects and also to assess a possible association between IFN-g and clinical type and duration of the disease. Sixty patients with AA and 20 healthy controls were enrolled in the study. Serum concentrations of IFN-g were determined by ELISA method. The serum concentration of IFN-g in patients with AA was significantly higher than that in the control group (10.62±1.09 pg/mL vs 10.02±0.62 pg/mL, respectively). Significantly elevated serum IFN-g were noticed in patients with AU type (11.81±1.11 pg/mL), expecially those suffering from AT (12.30±0.93 pg/mL), compared with both patients with AUl (10.20±0.59 pg/mL) and patients with AM clinical type (10.21±0.78 pg/mL). There was no significant difference in serum IFN-g concentration between patients with AUl and AM group, as well as between patients with AT and AU. No correlations were found between duration of disease and the serum levels of IFN-g. Our findings confirm previously published data that the Th1 type cytokine IFN-g is elevated in the serum of AA patients. Key words: alopecia areata, interferon-gamma

1. INTRODUCTION

Alopecia areata (AA) is a heterogeneous disease characterized by non-scarring hair loss on the scalp or other parts of the body. A wide range of clinical presentation can occur—from a single patch of hair loss (alopecia unilocularis, AUl), multiple patches (alopecia multilocularis, AM) to complete loss of hair on the scalp (alopecia totalis, AT) or the entire body (alopecia universalis, AU). The histopathologic features of the AA consist of perifollicular lymphocytic infiltrates around anagen hair follicles, consisting of both CD4+ and intrafollicular infiltrates of CD8+ cells. Although the etiopathogenesis of the disease is not clear, several studies have shown that within the cascade of pathogenesis of AA, cytokines play a crucial role. The immune response presented in AA is associated with aberrant lesional expression of interferon-gamma (IFN-g), interleukin-2 (IL-2) and IL-1b, and overexpression of ICAM-1 and MHC molecules on hair follicle keratinocytes and dermal papilla cells.

IFN-g is produced by perifollicular or follicular antigen presenting cells and among several actions it also deprives dermal papilla cells of their ability to maintain anagen hair growth. The changes in serum IFN-g concentrations were found in many diseases, such as psoriasis and systemic lupus erythematosus. In some of these diseases, serum IFN-g concentration correlates with activity and intensity of the disease, and may be used as a prognostic factor.

The aim of our study was to evaluate serum concentrations of IFN-g in patients with AA and healthy subjects and also to assess a possible association between IFN-g and clinical type and duration of the disease.

2. MATERIAL AND METHODS

The study included 60 patients with AA (36 females and 24 males, median age 35.6). The patients who had received any treatment within previous 3 months were excluded from the study, as well as patients with any diseases based on the immune pathomechanism, which could influence serum concentrations of IFN-g.

According to the clinical type of AA, patients were divided into 4 groups: AUl (n=13, 21.6%) patients with alope-
Serum Concentrations of Interferon-gamma (IFN-g) in Patients with Alopecia areata: Correlation with clinical type and duration of the disease

Discussion

Although the etiopathogenesis of AA is poorly understood, most researches think that it is connected with immune processes. It has been reported that various autoimmune diseases often coexist with AA, and various autoantibodies against different tissues, including those directly against hair follicle, have been noticed in AA patients. The specific targets of follicular autoantibodies seen in AA include multiple components of anagen hair follicles.

The strongest evidence implicating autoimmune mechanism in the pathogenesis of AA has been provided by studies involving mice with severe combined immunodeficiency (SCID). In a set of experiments by Gilhar et al., AA was induced on human scalp explants transplanted onto SCID mice by incubation with IFN-g. The results are consistent with a clinical study performed by Arca et al. (15). They compared the serum levels of IFN-g in patients with AA and the control group and also they investigated the difference between the localized form of the disease with the extensive forms like AT and AU. It has been shown that serum levels of IFN-g are significantly higher in patients with AT or AU compared to controls, but no significant difference has been found in levels of IFN-g between localized AA and those with a CD4+ Th1 mediated response. By using immunohistochemical and in situ hybridization studies to demonstrate the persistence of proinflammatory as well as apoptotic mechanisms in the skin biopsies from patients with chronic AA, Bodemer et al. have confirmed the presence of a cellular infiltrate in close contact with the hair follicle, producing IFN-g in association with proinflammatory cytokine production (13). IFN-g is produced by perifollicular or follicular antigen presenting cells and among several actions it also deprives dermal papilla cells of their ability to maintain anagen hair growth (2).

To determine which cytokines may be involved with overexpression of ICAM-1 and MHC molecules on dermal papilla cells of affected hair follicles, Konig et al. were able to imitate the in vivo situation of AA (1). They found that incubation with IFN-g led to a time-dependent upregulation of the surface molecules, as well as to an overexpression of ICAM-1.

In addition, increased serum levels of IFN-g in patients with AA compared with normal controls has been reported, further suggesting a role for this cytokine. The results presented in our study demonstrate that the mean serum levels of IFN-g were significantly elevated in AA patients in comparison to healthy subjects. And also the serum levels of IFN-g in patients with AT and AU were significantly increased. These results are consistent with a clinical study performed by Arca et al. (15). They compared the serum levels of IFN-g in patients with AA and the control group and also they investigated the difference between the localized form of the disease with the extensive forms like AT and AU. It has been shown that serum levels of IFN-g are significantly higher in patients with AT or AU compared to controls, but no significant difference has been found in levels of IFN-g between localized AA and those with...
more extensive forms. Our findings are similar to the study of Lortkipanidze et al., who also recorded a significant increase in serum IFN-g in patients with AA (16). In the study of Teraki et al. (17), they compared the serum levels of cytokines, including IFN-g, TNF-a, IL-1a, IL-2, IL-4 and IL-6 in patients with the localized form and the extensive form and found that the serum levels of IL-1a and IL-4 were significantly elevated in patients with the localized form. In contrast, the serum levels of IFN-g and IL-2 were significantly elevated in patients with the extensive form. They said that these findings could be interpreted as an indication that Th1 type cytokines might be critical for the progression to the extensive form and that Th2 type cytokines may exert a more subtle influence on the inhibition of a cell-mediated attack on hair follicles. After that, Barahmani et al. analyzed serum cytokine profiles in 269 patients with AA and found that increased IFN-g levels is associated with AA regardless of disease severity (18).

5. CONCLUSION

In conclusion, IFN-g seems to be a useful indicator of the activity of AA and that it may play an important role in the development of this disease. Further investigations are required to clarify the pathogenic role and clinical significance of IFN-g, and these findings may provide important clues to assist in the development of new therapeutic strategies for patients with AA.

REFERENCES

3. Arican O, Aral M, Sasmaz S, Ciragil P. Serum levels of TNF-a, IFN-gamma, IL-6, IL-8, IL-12, IL-17, and IL-18 in patients with active psoriasis and correlation with disease severity. Mediators Inflamm, 2005; 24(5): 273-9.