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MAIN ARTICLE

Serum soluble tumour necrosis factor related apoptosis-inducing ligand level and peripheral eosinophil count in patients with nasal polyposis

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Abstract

Background: Nasal polyposis is one of the most common inflammatory pathologies of the nasal cavity. Eosinophilic inflammation plays an important role in the pathogenesis. This study aimed to investigate soluble tumour necrosis factor related apoptosis-inducing ligand levels and eosinophil count in nasal polyposis patients.

Methods: The study was performed on 24 adult nasal polyposis patients and 24 age-matched healthy individuals. The patients had not received any medical or surgical treatment. Pre-operative computed tomography scans were assessed using the Lund–MacKay grading system, and soluble tumour necrosis factor related apoptosis-inducing ligand levels were measured with a sandwich enzyme-linked immunosorbent assay.

Results: Compared with controls, eosinophil levels in nasal polyposis patients were increased ($p = 0.024$), but there was no significant difference in soluble tumour necrosis factor related apoptosis-inducing ligand levels ($p = 0.529$). The Lund–Mackay mean grading was 12.43 ± 6.9. There was no correlation between soluble tumour necrosis factor related apoptosis-inducing ligand level and Lund–Mackay grading and eosinophil count.

Conclusion: There was no relationship between soluble tumour necrosis factor related apoptosis-inducing ligand level and blood eosinophil or clinical markers; however, soluble tumour necrosis factor related apoptosis-inducing ligand level remains of interest for future studies.

Key words: Nasal Polyps; Eosinophils; Biological Markers

Introduction

Nasal polyps are the most common tumours arising in the nasal cavities.[1] They are thought to affect between 1 and 4 per cent of the population. Various conditions predispose to nasal polyp formation, and the mechanisms of these associations are in some instances still undefined. Many pathogenic theories have been proposed to explain the aetiology of nasal polyps. However, multiple factors may be involved in polyp formation, and the exact aetiology of nasal polyposis remains unknown.[1–3]

Although polyps are reported to contain inflammatory cells which could play important roles, the nature of nasal polyps is still uncertain. Recent studies have focused on the role of mediators such as neuropeptides, cytokines and growth factors in mucosal inflammation associated with nasal polyps.[4] Many studies suggest that apoptosis has a major role in the pathogenesis of nasal polyps.[5]

Tumour necrosis factor (TNF), which belongs to a superfamily of cytokines, comprises structurally related proteins that play important roles in regulating cell death, immune response and inflammation. Tumour necrosis factor related apoptosis-inducing ligand (TRAIL), a member of the TNF superfamily of cytokines, is an important component of the immune system.[6] Of the various molecules like Fas ligand that are known to play a role in nasal polyps, the recently defined TRAIL may hold a unique position.[7] Recent studies have reported a link between serum soluble TRAIL levels and many disorders, such as cancer, and cardiac, renal and even allergic diseases.[8–11] A relation to asthma therapy modalities has also been reported.[11,12]

The present study aimed to: (1) determine the serum levels of soluble TRAIL in a cohort of newly diagnosed nasal polyposis patients; (2) assess the relationship between soluble TRAIL and the presence of polyps

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according to computed tomography (CT) imaging findings and Lund–Mackay grading of the disease; and (3) evaluate the association between serum soluble TRAIL levels and eosinophil levels, as mucosa infiltration by eosinophils is one of the most characteristic features of nasal polyposis.

Materials and methods

Subjects

Twenty-four adult nasal polyposis patients and 24 age-matched healthy controls were included in this study. Written informed consent was obtained from all subjects. The study was approved by the Ethics Committee of the Antalya Education and Research Hospital, and conducted in accordance with the Helsinki Declaration and the World Medical Association. The diagnosis of nasal polyposis was based on each patient's medical history, and on the results of nasal endoscopy and CT.

Findings on CT scans were graded according to the Lund–Mackay scoring system. Mucosal abnormalities were graded as follows: 0 = no abnormality; 1 = partial opacification; and 2 = total opacification of the frontal, maxillary, anterior ethmoid, posterior ethmoid and sphenoid sinus, bilaterally. The ostiomeatal complexes were scored bilaterally as: 0 = not occluded or 2 = occluded. The maximum CT grading score was 24.

The exclusion criteria included: patients with a history of allergies or asthma; those who had undergone surgical treatment or received any medical treatment in the four weeks prior to the study; patients who reported atherosclerosis, hypercholesterolaemia, systemic sclerosis or other rheumatoid diseases; and those with cardiovascular disease or suspected renal failure.

The patients were grouped according to whether they were a heavy or social smoker; however, there was no difference in the smoking rates between the nasal polyposis and control groups.

Laboratory investigations

Blood samples, for all nasal polyposis patients, were taken prior to corticosteroid therapy. Routine blood sampling, blood biochemistry and urinalysis were performed to verify the presence of any illnesses relevant to the exclusion criteria. Serum eosinophil levels were evaluated in all patients.

We used the human soluble TRAIL/Apo2L enzyme-linked immunosorbent assay kit (catalogue number: 850.770.192; Cell Sciences, Canton, Massachusetts, USA) for the *in vitro* quantitative determination of soluble TRAIL in serum samples of the newly diagnosed, non-drug-using patients with nasal polyps. The absorbance of each patient sample was determined using a spectrophotometer at 450 nm and the concentration of soluble TRAIL (pg/ml) was measured.

Statistical analysis

Patient data were compared with those of healthy subjects. Data were analysed using the Statistical Package for the Social Sciences software, version 11.0 for Windows (SPSS, Chicago, Illinois, USA). The Mann–Whitney U test was used for comparing results from independent groups. Spearman's rank correlation test was used to examine the relationships between soluble TRAIL level, eosinophil count and CT score in the nasal polyposis patients. A p-value of less than 0.05 was considered to be statistically significant.

Results

The demographic data for the nasal polyposis patients and control group are shown in Table I. The patients and the controls were matched in terms of age, but not sex. However, as the results showed no difference between the groups in terms of sex (data not shown), male and female patients were grouped together for subsequent analyses.

The percentages of (heavy and social) smokers in the patient group and control group were 33.3 per cent and 26.8 per cent respectively; there was no significant difference between the groups.

With regard to the CT imaging results for the patient group, the mean Lund–Mackay grade was 12.43 ± 6.9.

The levels of eosinophils were elevated in 21.4 per cent of the nasal polyposis patients; in 78.6 per cent of the patients, the levels were within a normal range. Mean eosinophil levels were 502.14 ± 303.14 cells/μl (range, 88.00–1379.00 cells/μl) in the patient group and 338.95 ± 124.22 cells/μl (range, 135.0–670.0 cells/μl) in the control group (Figure 1). The difference between these two groups was significant ($p = 0.024$).

The mean serum soluble TRAIL level was 617.55 ± 82.42 pg/ml (range, 443.13–797.86 pg/ml) in the patient group and 633.76 ± 82.64 pg/ml (range, 501.31–808.29 pg/ml) in the control group (Figure 2). The difference between the two groups was not significant ($p = 0.529$).

We investigated whether there were any correlations between serum soluble TRAIL level and eosinophil level and Lund–Mackay score in the nasal polyposis

TABLE I
DEMOGRAPHICS OF NASAL POLYPOSIS PATIENTS AND CONTROLS

Parameter	NP patients	Controls	p
Age (mean ± SD; y)	43.86 ± 16.58	36.48 ± 8.32	0.08
Sex (%)			
– Male	76.2	52.4	0.05
– Female	23.8	47.6	0.02
Smokers (%)			
– All	33.3	26.8	0.07
– Heavy	9.6	7.8	0.09
– Social	23.7	19.0	0.08

NP = nasal polyposis; SD = standard deviation; y = years

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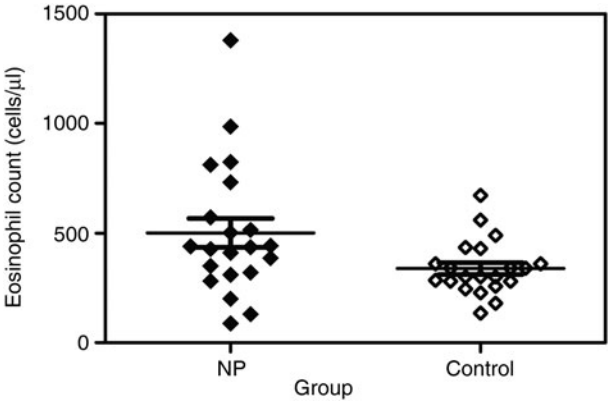

FIG. 1
Eosinophil counts of the nasal polyposis (NP) patients and controls.

patients. The findings indicated no correlations with soluble TRAIL level.

Discussion

The lack of a causal link between soluble TRAIL and the clinical status of the nasal polyposis patients might be because our study group was small, which is a limitation of the study. However, a major advantage of this study concerns the fact that none of the patients were using any medication and had not undergone any surgical treatment, which eliminates any confounding influence of these factors on soluble TRAIL and eosinophil levels.

Recent studies have reported variable serum soluble TRAIL levels in many disorders, such as cancer, and cardiac, renal and even allergic diseases.[8–12] Furthermore, the biological effects of TRAIL are known to be largely receptor and cell type specific in autoimmune diseases such as diabetes and rheumatoid arthritis.[13–15]

Nasal polyposis is an inflammatory disorder of the nasal mucosa and paranasal sinuses. The aetiology of nasal polyposis, however, remains largely unknown. Numerous theories have been suggested to explain the cause of nasal polyposis. These include: adenoma and fibroadenoma, mucosal exudate, glandular cyst, blockage, new gland formation, ion transport, periphlebitis and perilymphangitis, excretory channel cystic dilation and vessel obstruction, and necrotising ethmoid sinusitis.[2,3]

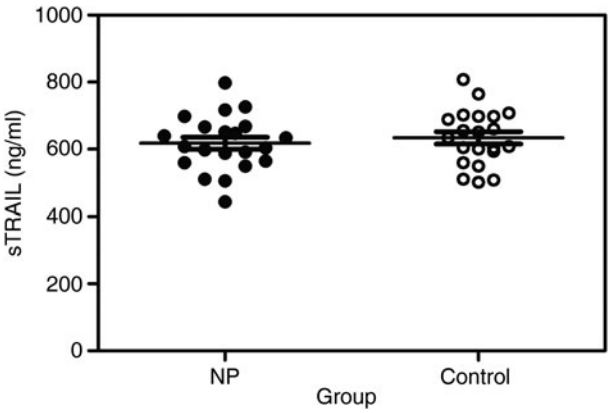

FIG. 2
Comparison of serum soluble TRAIL (sTRAIL) levels of nasal polyposis (NP) patients versus controls.

- **Tumour necrosis factor related apoptosis-inducing ligand (TRAIL), soluble TRAIL and its receptors have become valuable biomarkers for cancer and autoimmune diseases**
- **This study investigated the possible novel mechanism of soluble TRAIL in nasal polyposis development and its relation to clinical markers**
- **Eosinophil count was correlated with clinical markers of nasal polyposis, possibly reflecting the disease's pathophysiological process**

Apoptosis has an important role in the removal of unwanted cells associated with nasal polyps. Recent studies have suggested that delayed cellular apoptosis has a major role in the pathogenesis of nasal polyps.[16] Hence, the tumour necrosis factor superfamily member TRAIL might play an important role, and may contribute to defective apoptosis. However, our study findings revealed no statistically significant difference in circulating TRAIL levels between nasal polyposis patients and healthy individuals. Furthermore, there was no relationship between patients' clinical status (i.e. Lund–Mackay grade, assessed to examine disease severity) and soluble TRAIL levels. In addition, although eosinophil levels were elevated in nasal polyposis patients, no correlation was found between these levels and soluble TRAIL levels.

Conclusion

To the best of our knowledge, this is the first study to assess serum soluble TRAIL levels together with eosinophil count in nasal polyposis patients, and to evaluate the relationship with clinical status. In our study, there was no significant difference in soluble TRAIL levels between nasal polyposis patients and healthy individuals, and soluble TRAIL levels were not correlated with clinical status or eosinophil count. Nevertheless, eosinophil levels were increased in the nasal polyposis patients compared with controls, and these levels were correlated with clinical status in the patient group, as has been demonstrated in previous studies.[17,18] Further studies are needed to investigate whether the TRAIL system has any role in the molecular basis of immunological diseases.

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