Correlation of Otorhinolaryngologic Symptoms with Physical Findings in Behçet’s Disease

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abstract. Correlation of Otorhinolaryngologic Symptoms with Physical Findings in Behçet’s Disease. Objective: Behçet’s disease is a chronic systemic inflammatory disease of unknown etiology. We examined the correlation between otorhinolaryngologic symptoms and otorhinolaryngologic physical findings in patients with Behçet’s disease, in search of strategies to reduce the morbidity rates. Methods: Seventy-two patients diagnosed with Behçet’s disease were included. After giving a detailed history of oropharyngeal, nasal, laryngeal, and otic symptoms, patients were examined endoscopically by an otolaryngologist, and the findings were recorded. Results: Thirty-nine of the patients were male, and thirty-three were female. The mean age was 39.2±3.4, and the mean disease duration was 8.24±4.2 years. Statistically significant correlations were observed between ear lesions and ear symptoms (crusting and otic pain), nasal lesions and nasal symptoms (crusting and nasal pain), oropharyngeal lesions and oropharyngeal symptoms (pain and difficulty in swallowing), and laryngeal lesions and laryngeal symptoms (hoarseness, difficulty in swallowing, and pain). Conclusion: The results demonstrated a positive correlation between symptoms and otorhinolaryngeal examination findings in Behçet’s disease. Potential morbidities can be prevented by routine endoscopic otorhinolaryngeal examinations and symptom screening of patients with Behçet’s disease and arranging the therapy accordingly.

Introduction

Behçet’s disease (BD) is a vasculitis characterized by recurring oral and genital ulcers and eye problems, as well as involvement of the skeletal, nervous, and gastrointestinal systems. BD has a unique geographical distribution not seen in other systemic diseases, mainly affecting ethnic groups of Mediterranean and Eastern Asian origin and living along the historic Silk Road region, and usually starts between ages 20 and 35. In two studies conducted in Turkey, the prevalence of BD was reported as 110-420/100,000. The estimated prevalence of the disease is 13–20/100,000 in Japan and 1-2/100,000 in the UK and USA.

Aphthous stomatitis is observed in 97% of patients affected by BD and is universally recognized as a diagnostic criterion. Mucosal involvement is rare, except in the oral and genital areas. Only a few studies have reported involvement of the nasal mucosa, and a limited number of reports have addressed otorhinolaryngologic involvement in BD, usually focused mainly on one organ. In the study conducted by Shahram et al., the clinical parameters and the frequency of nasal involvement in BD were examined. Süslü et al. examined the effect of BD on hearing function using pure tone audiometry and distortion product otoacoustic emissions. In a review, Webb et al. reported on ear, nose, and throat manifestations of BD as examined by case screening.

The underlying pathology in BD is the inflammatory response involving the arteries and veins. Although in most cases the disease is self-limited, in others, posterior uveitis resulting in blindness, involvement of the central nervous system, and gastrointestinal involvement resulting in perforation can lead to serious morbidity and mortality. Because of these severe complications, early diagnosis with full assessment of clinical symptoms is crucial.

No studies investigating the relationship between symptoms and BD lesions of the nose, ear, pharynx, and larynx have been conducted. In the present
study, we examined symptoms and the BD lesions in those areas and investigated the correlation between them.

Material and methods

The Ethical Committee of Clinical Research approved the study on 25.02.2011 (no. 642). Seventy-two patients diagnosed by the Department of Dermatology with BD were included in our study. The following patients were excluded from the study: those with active upper respiratory tract and ear infections; previously diagnosed otolaryngopharyngeal pathologies; previously diagnosed BD, on medical therapy and asymptomatic during the past year; or diagnosed with any dermatological disease other than BD that may have caused upper respiratory tract and ear involvements. All patients signed informed consent. Patients previously diagnosed with BD and on follow-up were evaluated by the Department of Dermatology, and those patients with symptoms associated with oropharyngeal, nasal, laryngeal, and otic localizations were questioned by an otorhinolaryngologist and examined in detail endoscopically, and all results were recorded.

At follow-up of patients, data taken by the dermatology department assessed the presence or absence of oral and genital aphtha, eye and joint involvement, skin lesions, whether or not the patient received treatment, and the name and doses of the drugs used for treatment, if any. The otorhinolaryngology data taken in the follow-up document focused on ear symptoms (loss of hearing, crusting, hemorrhage, pain, and itching) and physical examination findings; nose symptoms (congestion, hemorrhage, crusting, pain, itching) and examination findings; oropharyngeal symptoms (pain, hemorrhage, burning, difficulty in swallowing) and examination findings; and laryngeal symptoms (hoarseness, difficulty in swallowing, pain) and examination findings.

In the symptomatic assessment of the patients, the existence (positive) or non-existence (negative) of the symptom was questioned. The criteria for accepting the symptom as positive were duration of at least 3 months, a negative effect on the patient’s daily life, and no additional pathologies that may have caused the same symptom.

Patients with BD were assigned into two groups for each otolaryngologic field (ear, nose, oropharynx, larynx) according to lesion positivity/negativity (Group 1: Lesion positive; Group 2: Lesion negative). Symptoms related to each localization were compared to age, sex, and duration of illness. The relationship between involvement in an otolaryngologic field and the symptoms was evaluated.

Statistics

Statistical analysis was carried out using the Statistical Package for the Social Sciences version 13.0 software for Window (SPSS Inc, Chicago, IL, USA). All quantitative variables were estimated using measures of central location (i.e., mean and median) and measures of dispersion (i.e., standard deviation (SD)). Data normality was checked using the Kolmogorov–Smirnov tests. Pearson Chi-square tests were used for the study of the relationship among symptoms, lesions, and gender.

In comparison of age and disease duration between groups, independent-t tests were used. The correlations between the variables were analyzed through Spearman’s rank correlation ratio. In all tests, p < 0.05 was accepted as statistically significant.

Results

Seventy-two patients were included. Thirty-nine were male, and thirty-three were female. The mean age of the patients was 39.2 ± 3.4, and mean disease duration was 8.24 ± 4.2 years.

During the study, all patients were on colchicine therapy; 57% were taking colchicine 0.5 mg t.i.d and 43% were taking it 0.5 mg b.i.d. None of the patients were taking any other drug during the course of the study. Physical examination revealed oral aphtha in all patients (100%), and genital aphtha in 83% of the patients. Skin involvement was observed, 41% as nodular lesions and 55% as papulopustular lesions.

Endoscopic ear examination of the patients revealed ear lesions in 26 patients (26/72, 36.1%) while no ear lesions were observed in 46 (63.9%) patients. In the lesion-positive group, crusting and pain were significantly higher than in the lesion-negative group (p = 0.040 and p = 0.012, respectively) (Table 1). The mean age of the patients was significantly higher in the lesion-positive group (p = 0.010) (Table 1). There were significant correlations between ear lesions and ear symptoms...
Endoscopic examination of the oropharynx revealed oropharyngeal lesions in 62 patients (62/72, 86.1%) while no lesions were identified in 10 (14.9%) patients. Pain, sore throat, and dysphagia were significantly higher in the lesion-positive group than in the lesion-negative group ($p = 0.001$, $p = 0.001$, and $p = 0.001$, respectively) (Table 3). Significant correlations were observed between the oropharyngeal lesions and the oropharyngeal symptoms (pain, soreness, and dysphagia in the oropharynx) in every patient ($r = 0.763$, $r = 0.601$, and $r = 0.738$, respectively) ($p < 0.05$) (Table 3).

Endoscopic examination of the larynx revealed laryngeal lesions in 28 patients (28/72, 38.8%) (crusting and pain in the ear) in all patients ($r = 0.412$ and $r = 0.753$, respectively) ($p < 0.05$) (Table 1).

Endoscopic nasal examination revealed nasal lesions in 38 patients (38/72, 52.7%) while no nasal lesions were identified in 34 (47.3%) patients. In the lesion-positive group, nasal crusting and nasal pain were significantly higher than in the lesion-negative group ($p = 0.005$ and $p = 0.049$, respectively) (Table 2). Significant correlation was present between nasal lesions and bleeding, crusting, and pain in the nose for every patient (respectively $r = 0.384$, $r = 0.508$, and $r = 0.829$) ($p < 0.05$) (Table 2).
A. Meric et al.

Discussion

BD is a systemic disease characterized by attacks that may involve multiple organs and in which the main pathology is vasculitis.\(^\text{10}\) BD is not limited only to oral, genital, and eye lesions but may progress systemically with articular, pulmonary, gastrointestinal, urogenital, cardiac, vascular, and neurological involvement.\(^\text{11}\)

The etiology and pathogenesis of BD are still under investigation. Research has demonstrated that multiple antigens generated by infectious agents trigger cytokine production by T-cells, thus activating neutrophils that promote endothelial damage, resulting in vasculitis.\(^\text{10}\)
Although BD may occur at all ages, it most frequently develops in the third decade and is rarely seen in children. Systemic involvement increases the mortality rate, particularly in young male patients. Death generally occurs because of the involvement of large vessels, as in the case of pulmonary artery aneurysm, or perforation following involvement of the gastrointestinal system, and also by neurological involvement. The natural course of the disease is not yet fully understood. BD follows a long-term course with unpredictable, recurrent episodes followed by asymptomatic periods. Delayed diagnosis and treatment appear to be important risk factors that might incite a more severe progression of the disease, and consequently, increase the mortality rate.

Because there are no definitive diagnostic laboratory tests and histopathological findings for BD, diagnosis is based on the clinical picture. Findings on the skin and mucosae, particularly oral and genital ulcers, skin symptoms, and a positive pathergy test are the common diagnostic criteria. In the majority of patients, skin and mucosa symptoms occur before organ involvement. Therefore, early recognition of cutaneous and mucosal symptoms is of prime importance for a rapid diagnosis, which may prevent probable serious complications by prompting the proper treatment.

In search of novel strategies to cope with serious morbidity rates, we investigated correlations between otorhinolaryngologic symptoms and otorhinolaryngologic lesions in patients with BD. Previous studies on ear involvement in BD investigated audiological functioning. Such studies reported that the frequency of hearing loss in BD varied from 12% to 64.3%. In our study, sensorineural hearing loss affecting higher frequencies was observed in only 12.5% of the patients, which is compatible with relevant literature. There was no significant correlation between hearing loss and the pathological lesions (p = 0.397).

Brama and Farinatu demonstrated that inner ear involvement in BD patients occurred only after a prolonged disease duration. Those findings may explain why not all patients who have ear lesions have hearing loss and suggest that inner ear involvement can occur in patients with ear lesions at a much later period in the course of the disease. In our study, 26 of 72 patients (36.1%) had ear lesions. Crusting and pain were significantly higher in the lesion-positive group than in the lesion-negative group (respectively p = 0.040 and p = 0.012) (Table 1). These findings suggest that ear lesions predominantly cause pain and crusting, which may be the prodromal symptoms of internal (inner?) ear involvement that may manifest later in the course of the disease.

In our opinion, the treatment of patients with such lesions can be started at once to help prevent later morbidity.

Systemic diseases may create symptoms and lesions in the nasal region. A limited number of studies have been conducted on nasal mucosal involvement in BD. In a previous study, no significant differences were detected between clinical and paraclinical parameters of patients with and without nasal mucosal involvement in BD, with the former observed in 17% of the patients. As the authors noted, the study had a limited capability of detecting the actual prevalence of nasal involvement. In our study, nasal mucosal lesions were detected in 52.7% of the study group (Table 2). Additional studies are needed to determine the prevalence of nasal involvement in BD. Bleeding, nasal crusting, and pain were significantly higher in the lesion-positive group (p = 0.005, p = 0.049, p = 0.008 respectively) (Table 2). Significant correlations were present between nasal lesion positivity and related symptoms (bleeding, nasal crusting, and nasal pain). Such nasal symptoms may alert to potential hazardous pathologies that may develop later during the course of the disease, like conchal destruction and septal perforation. A case presentation reported a BD patient who had pansinusitis, conchal destruction, and septal perforation. Because nasal symptoms may herald such deleterious consequences, they need to be carefully questioned and detected in an attempt to prevent potential morbidities.

Recurrent oral ulcers are the most frequent symptoms of BD. BD should be suspected if six or more painful ulcerous lesions of different sizes with surrounding erythema are observed at the soft palate or oropharynx, especially those with scar tissue. Such ulcers considerably deteriorate the patient’s quality of life. It is reported that BD with oropharyngeal involvement causes pharyngeal stenosis in advanced stages. In our study, the oropharyngeal symptoms (bleeding, crusting, and dysphagia) were significantly higher in the lesion-positive group (Table 3). These findings suggest
that treatment should be initiated at once for such patients, together with frequent monitoring, to prevent further pathologies like pharyngeal stenosis. BD may also, although rarely, present with a major ulcer in the hypopharyngeal area, which can alert the clinician to the need for endoscopic oropharyngeal examination, supporting the objective of our study.

There is only one case in the medical literature reporting oropharyngeal involvement in BD. In that case presentation, edema, swelling, and omega epiglottis were observed at the laryngopharyngeal wall. A total of 38% of patients included in our study had laryngeal lesions. Laryngeal examination revealed diffuse laryngeal hyperemia and edema and ulcers on the surfaces of the epiglottis. The laryngeal symptoms (hoarseness, pain, and dysphagia) were significantly higher in the lesion-positive group (Table 4).

Our study suggests that irreparable damage may be prevented by routine inquiry about laryngeal symptoms in BD patients. This report is a first in the medical literature about laryngeal involvement in BD, and our findings, with a 38% rate of laryngeal involvement, indicate the necessity of routine endoscopic laryngeal examination in BD patients.

In our study, statistically significant correlations were also detected between certain symptoms and physical examination findings of different localizations: Pain symptoms in the ear were significantly related to nasal lesions; itching in the ear was significantly related to laryngeal lesions; nasal congestion was significantly related to laryngeal lesions; nasal pain was significantly related to ear lesions; and nasal pain was significantly related to laryngeal lesions. This report describes the first correlations between symptoms and physical examination findings in BD. Those correlations may be explained by reflected pain or result from the fact that BD is a systemic vasculitis. Additional studies with comprehensive series are needed to clarify these possibilities.

**Conclusion**

Our study revealed the relationships between the symptoms of BD and the orthonasal physiology examination findings. We propose routine endoscopic orthonasal laryngeal examination and symptom screening in all patients with BD, and when necessary, modifying the treatment accordingly, thinking that such an approach would help to reduce potential long-term morbidity and mortality.

**References**


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