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LITERATURE REVIEW

Olfactory functions in Behçet's disease: A review

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ABSTRACT

OBJECTIVES. We reviewed the relationship between olfactory functions and Behçet's disease (BD).

MATERIAL AND METHODS. We searched Pubmed, Google, Google Scholar and Proquest Cebtral Database with the key words of "olfactory", "functions", "smell", "nasal" and "Behçet's disease".

RESULTS. Behçet's disease influences the nasal mucosa. Nasal mucosal inclusion causes mucosal ulcers, pain, burning, nasal obstruction, epistaxis, nasal itching and dysosmia. Nasal cartilage deformity is also reported. The higher rate of comorbid chronic rhinosinusitis (CRS) in BD patients may likewise be because of the complex mechanism of the disease inclining the host tissues to bacterial infections. Olfactory functions may decrease in BD. Odor identification may be lower in patients BD.

CONCLUSION. An olfactory dysfunction may be seen in patients with BD. BD patients should be evaluated for the involvement of the olfactory function and may require treatment because of a malfunction of the olfactory system that influences the quality of life. Neurological involvement associated with BD might play a more important role in causing olfactory dysfunction than mucosal involvement.

KEYWORDS: Behçet's disease, olfactory dysfunction, nasal involvement, epistaxis, nasal itching, mucosal ulcers.

INTRODUCTION

Behçet disease (BD) is an uncommon vasculitic disease that is described by "intermittent oral aphthous ulcers, genital ulcers, and uveitis"[1,2]. BD is a sporadic disease; however, there is a familial aspect[3]. Transporters of "HLA-B51/HLA-B5" have an expanded risk of creating BD contrasted and noncarriers[4]. HLA-B51 is the most grounded related hereditary variable and it has been appeared to be more common in Turkish, Middle Eastern, and Japanese population, comparing with a higher predominance of Behçet infection in these people[1].

Hulusi Behçet, a Turkish dermatologist, characterized Behçet's disease in 1937 as an intermittent aphthous ulcer, genital ulcer, and uveitis[1]. BD is a continuous, backsliding condition; it affects small vessels in the body with vast clinical signs such as vascular, visual, mucocutaneous, gastrointestinal, musculoskeletal and central nervous system. Clinical components of BD of the ENT include oral, oropharyngeal and laryngeal mucosal ulcerations and healing process with scar development[2]. In some studies, the association between sinonasal diseases and olfactory dysfunction, such as BD, has arisen[5,6].

In this paper, we explored the olfactory dysfunction in patients with BD. We searched Pubmed, Google, Google Scholar and Proquest Cebtral Database with the key words of "olfactory", "functions", "smell", "nasal" and "Behçet's disease".

EPIDEMIOLOGY

BD is more commonly seen in people between 20 and 40 years of age. The average age at initiation is 25-30 years. The cases that occurred before the age of 25 probably include eye disease and dynamic clinical disease[1].

In the United States, the prevalence of BD is calculated as 0.12-0.33 cases per 100,000 population[7]. Turkey has the most amazing prevalence of BD and has 420 cases for every 100,000 people. The prevalence of "Japan, Korea, China, Iran and Saudi Arabia" is in a range of 3.5-22/100,000. The dominance in Europe and North America is quite low with 1 case per 15,000-500,000 population[7,8].

In the Middle East, BD is seen more frequently

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among males than females with "3.8:1 (Israel), 5.3:1 (Egypt) and 3.4:1 (Turkey)" rates. In Brazil, Japan and Germany the infection is marginally more normal in women. In the USA, BD is more frequent in women. Women to men ratio is 5:1[7,8].

Males will probably create severe presentations of BD. In males, eye symptoms, thrombophlebitis and pulmonary aneurysms are more common. In females, skin lesions like erythema nodosum may be detected[1].

PATHOPHYSIOLOGY

Infectious triggers

Presentation to an infectious agent may trigger a cross-receptive immune reaction. Proposed suggested agents are "herpes simplex virus (HSV), *Streptococcus* species, *Staphylococcus* species, and *Escherichia coli*"[1].

T-cells and neutrophils

Systemic inclusion of numerous organs is seen in BD, established essentially in the advancement of vasculitic or vasculopathic injuries in the influenced regions. These regions may exhibit penetration of inflammatory tissue with neutrophils and T-cells[9-12].

The investigation of T lymphocytes suggested that there is a predominant reaction of T helper 1 (Th1). Both "CD4+ and CD8+ lymphocytes" exhibit higher concentrations in the peripheral blood when comparing the height of trademarks and cytokines "[interleukin (IL)-2 and interferon-γ (IFN-γ)]". The concentration appeared to be increased and potentially reacted with reduced levels of bronchoalveolar lavage in BD patients with lung features and disability of natural killer cells[13].

The T-cell and IL-17 pathways are dynamic and play an imperative part, especially in BD's acute attacks. Neutrophil action is increased in BD, and the influenced organs demonstrate an invasion of lymphocytes and neutrophils. IL-17 and HLA-B51 are thought to play a role in the activation of neutrophils[2].

Genetics

BD is a diffuse sporadic disease, but familial collapse is striking[3]. Hereditary elements have been extensively researched and the association with HLA-B51 is still the main genetic susceptibility factor[2]. "HLA-B51 / HLA-B5" carriers have the risk of BD formation compared to non-carriers[4]. HLA-B51 is the most common hereditary redundant variable and it is more prevalent in the Middle Eastern, Turkish and Japanese populations. Its presence in these populations is associated with a high incidence of BD. At the same time the presence of HLA-B51 seems to have no influence upon symptoms severity.

OLFACTORY DYSFUNCTION

Olfactory receptor neurons specifically communicate with the outer condition in a way that contrasts with different neurons, i.e. they have a one of a kind capacity to recover. Be that as it may, neural improvement and separation inside the olfactory system is yet to be totally clarified[14]. Although frequently dismissed by patients and clinicians, the olfactory sense is of most extreme significance to people, since it contributes fundamentally to wellbeing and personal satisfaction[15].

The most widely known etiologies of olfactory dysfunction are "sino-nasal diseases and head injuries"[16,17]. Olfactory dysfunction can also be present in neurodegenerative diseases, endocrine diseases (diabetes mellitus, hypothyroidism), intracranial tumors, schizophrenia, endoscopic sinus surgery and nasal surgery. The etiology of olfactory dysfunction is frequently unexplained, and this is named "idiopathic olfactory dysfunction"[17-19].

Olfactory impairment is related with a decreased taste perception; consequently, taste perception is emphatically impacted by olfaction[20]. Smell and taste assume a part in invigorating gastric discharges with regard to the typical stomach-related physiology, and furthermore fill in as an early cautioning framework against harmful substances[21,22]. Olfactory dysfunction has been related to psychiatric and neurological diseases[19,23]. Olfactory dysfunction is likewise required in different autoimmune diseases, for example, systemic lupus erythematosus (SLE)[24].

Nasal mucosa involvement has been accounted for in different vasculitic and connective tissue diseases, for example, "Wegener granulomatosis[25], Churg–Strauss syndrome, systemic lupus erythematosus[26,27], Sjogren disorder, systemic sclerosis[28,29], and relapsing polychondritis"[30].

A few types of BD are known to include the central sensory system. The commonness of such neuro-Behçet is 5–15%[31]. Olfactory dysfunction can be a sign of neurological involvement in BD or ensuing to mucosal contribution. In opposition to desires, olfactory scores were somewhat higher in Behçet patients with nasal mucosal discoveries. This unexpected outcome led us to believe that the neurological contribution related with BD may assume a more vital part in creating olfactory dysfunction as contrasted with mucosal involvement[5].

Neurological involvement in BD was originally discovered by Knapp in 1941[32]. The reported recurrence rate of the sensory system is "5.3% to 38%"[33]. The neurological contribution in BD can be ordered into two remarkable meetings[34]. A framework is a provocative disease in the small vessels of the parenchyma in the central sensory system (CNS), a

central or multifocal relationship, and it is known as "intra-pivotal neuro-Behçet disorder (NBD)". The most common clinical picture is known as mind stem disorder. Cranial nerve involvement and sensory symptoms are regularly less frequent. The other form is known as "extra-axial NBS", where the underlying damage is not coordinated with CNS parenchyma, more often with the addition of cerebral venous or blood vessels[35].

NASAL AND OLFACTORY MANIFESTATIONS IN BD

Sinonasal findings are rare in BD and not very normal for this disease[36]. In the study of Shahram et al.[37], sinonasal side effects were detected in 31/400 (8%) BD patients. Nasal obstruction and dysosmia were most commonly observed. Different findings include ulcers, burning sensation and rhinorrhea. This arrangement excludes any instances of nasal itching and nose bleeds[37]. Nasal examination revealed cartilaginous distortion, non-aphthous and crust ulcers. There are no anterior rhinorrhea, nasal scars or deformities, septal perforation or granulomatous or nodular ligament injuries[37]. Despite the fact that sinonasal indications are rare, a systematic investigation of the nostrils may reduce other inflammatory conditions that occur as a result of the procedure at this level, similar to Wegener's granulomatosis[36,38].

Meric et al.[39] investigated the correlation between the symptoms of ENT diseases and ENT physical findings in BD patients. They found that there were important connections between ear, nasal, oropharyngeal and laryngeal symptoms. Ear symptoms were crusting and otic pain. Crusting and nasal pain were nasal symptoms. Oropharyngeal signs were difficulty in swallowing and pain. Laryngeal symptoms were hoarseness and pain. There is a positive correlation between manifestations and ear-nose-throat examination findings in BD.

Morales-Angulo et al.[36] investigated the ENT appearances in 33 patients with BD and the mouth ulcers were the most commonly known (97%), followed by oropharyngeal ulcers (24%) and audiovestibular side effects (vertigo, sensorineural hearing loss, bilateral vestibular hypofunction; 15%)[36]. One patient showed significant side effects with vestibular neuritis as the main sign and this being also the sign of the onset of neuro- Behçet's disease. In 12% of patients, odynophagia and oropharyngeal lesions, such as tonsillitis (acute or recurrent), were detected as the primary symptoms and signs of the disease. They were observed alone or with ocular and cutaneous lesions[6,36].

BD is an immune disorder which is mediated by Th1 lymphocytes and it may begin in a similar range as other comorbidities (chronic rhinosinusitis without nasal polyposis - CRSsNP, Th1 intervention subclass)[40,41]. Another explanation for the greater predominance of chronic rhinosinusitis (CRS) in BD patients is that the immunosuppressive drugs used as treatment during patient active times may increase the incidence of different inflammatory conditions.

Furthermore, the high proportion of comorbid CRS in BD patients may also be due to the complex mechanism that directs the host tissues of the disease to bacterial infections[42]. The presence of Th1 pathology is clearly associated with the presence of another Th1 comorbidity[43]. Thus, the change in nasal polyps associated with Th2-interceded CRS or "hyperplastic eosinophilic sinusitis" indicates that it is more dominant when considering a Th2-mediated immune disorder (atopy, asthma)[44].

BD additionally influences the nasal mucosa[6]. The prevalence of nasal mucosa inclusion in BD patients was researched by Shahram et al.[37]. Of 400 patients, 67 detailed a history with nasal mucosa contribution, despite the fact that not the majority of the patients had nasal association at the time of the study. Nasal mucosa inclusion (mucosal ulcers, burning, pain, post-nasal discharge, epistaxis and nasal obstruction) was detected. The most widely recognized nasal manifestation was dysosmia, which was seen in 15 patients. Deformity in nasal cartilage, non-aphthous and crusted ulcers were also present[37].

Akyol et al.[15] assessed the olfactory capacity of patients diagnosed with BD. "Odor identification scores" were essentially lower in the BD group compared to the control group. There were no significant differences in "odor discrimination scores" between the groups ($p>0.05$). They recommended that the olfactory function of BD patients should be evaluated for its impact on the quality of life.

Veyseller et al.[5] examined the effects of BD on the olfactory function, nasal signs and mucosa. On endoscopic examination, nasal mucosa injuries were detected in 16 of 30 BD patients. The injuries were not specific to BD and were mostly in Little's region and the nasal septum. They were mostly erosions, crusts and hemorrhagic ulcers. Nasal symptoms were related to the nasal lesions. However, there was no association between olfactory functions and nasal findings.

Verim et al.[41] assessed the recurrence of chronic rhinosinusitis in BD patients and controls, and discovered prevalence rates of "23.2 % and 2.7 %", with a statistically significant difference between groups.

Özbay et al.[6] evaluated the effects of Behçet's in-

fection on the mucociliary clearance of the nose. They suggested that clinicians should closely follow BD patients for infections of the sinonasal region and ears and diseases of the respiratory tract.

CONCLUSIONS

The olfactory dysfunction may be seen in patients with BD. BD patients must be assessed for the involvement of the olfactory function and may need treatment due to a malfunction of the olfactory system affecting the quality of life. BD-associated neurological involvement may also cause olfactory dysfunction.

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Nuray Bayar Muluk: Planning, designing, literature survey, writing.

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