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Case Report

Sudden Loss of Olfaction and Gustation in a Patient with Multiple Sclerosis

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Abstract

Impairments in taste and smell are frequently encountered in multiple sclerosis (MS) patients. However, clinicians often fail to query patients about such symptoms and neither olfactory nor gustatory evaluations are carried out as part of routine physical check-ups. Furthermore, many patients are oblivious to their chemosensory deficits. Worsening of olfactory and gustatory perception is clinically relevant because it may reflect disease activity and progression of MS. Here, we describe the clinical course of a patient suffering from the relapsing-remitting form of MS who presented with an acute loss of taste and smell. Our article provides an overview of the current state-of-the-art regarding chemosensory dysfunction in MS.

Keywords: Olfaction; Gustation; Olfactory brain; Multiple sclerosis; MRI

Background

For a long time, the diagnosis and treatment of olfactory disorders has been regarded as an almost exclusive domain of the ear, nose and throat physician. Undoubtedly, this is largely due to the fact that the necessary workup may require specialized diagnostic procedures of that discipline which may go far beyond nasal endoscopy. Only in recent years has the role of chemosensory symptoms in neurodegenerative disorders such as Parkinson's disease and Alzheimer's dementia become fully apparent. In particular, impaired olfaction may be of considerable value for the early detection of Parkinson's and Alzheimer's disease [1,2]. Furthermore, olfaction testing may aid in the differential diagnosis of Parkinson syndromes because olfactory dysfunction seems to be more prevalent in idiopathic Parkinson's disease than in progressive supranuclear palsy or corticobasal degeneration [1,2]. Increased cerebrospinal fluid pressure such as occurs in idiopathic intracranial hypertension and, albeit only transiently, also in normal pressure hydrocephalus, may likewise adversely affect olfactory capabilities and damage olfactory structures [3,4].

Accumulating evidence has revealed that several neuroimmunological disorders may also impact the olfactory system on the functional and structural (e.g. magnetic resonance imaging, histology) levels [5-9]. Here, we describe the clinical course of a patient with relapsing-remitting MS who presented with an acute loss of olfaction and gustation. Furthermore, we discuss the current state-of-the-art vis-à-vis chemosensory complaints in MS.

Case Presentation

The 27-year-old patient presented with new-onset right facial hypesthesia as well as with hypesthesia and subtle motor skills deficits of the right hand. Furthermore, he complained of a sudden impairment and distortion of his sense of smell and an altered sense of taste.

The diagnosis of relapsing-remitting MS had first been made four years previously. The patient initially received immunomodulatory treatment with interferon β-1b. During this treatment, he suffered a severe attack with paraparesis and disturbed micturition which eventually resolved with plasmapheresis (initial intravenous steroid therapy with methylprednisolone had not yielded a sufficient therapeutic response). After two years, the patient was switched to 20 mg glatiramer acetate once daily, partly because of persistent influenza-like symptoms related to interferon β-1b. Treatment with glatiramer acetate resulted in a painful lump at the injection site. Furthermore, after six months on glatiramer acetate, the patient suffered another relapse with diplopia and ataxic gait which significantly improved with methylprednisolone pulse therapy. The patient was subsequently switched to 0.5 mg fingolimod once per day. On day 39 of treatment with fingolimod, the patient suffered the current attack described above.

On olfactory evaluation, the patient showed a normal response to trigeminal stimulants ammonia and formic acid. The extended Sniffin' Sticks procedure was carried out to test olfactory performance [10]. Odorants were presented for three seconds by placing pen-like devices approximately 2 cm in front of both nostrils to assess odor threshold (T), discrimination (D), and identification (I). The threshold test comprises 48 sniffing sticks with a 16-stage dilution series of n-butanol for determining the threshold of olfactory perception. The discrimination test also consists of 48 sniffing sticks to test the distinction of smells. Finally, the task of the identification test is to recognize everyday smells [10,11]. The patient showed a

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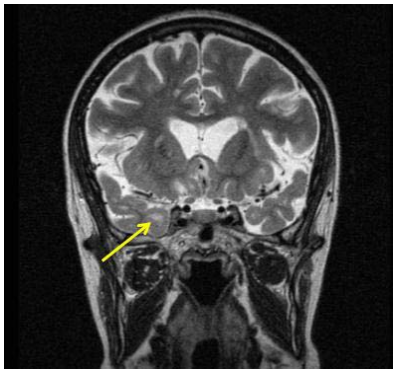

Figure 1: This T2-weighted image shows a subcortical lesion adjacent to the right entorhinal cortex (yellow arrow). Note other MS-typical white-matter lesions in the periventricular space and in subcortical gray matter.

composite TDI score of 15 signifying functional anosmia [12]. The detailed methods for subjective gustometry and the measurement of odor-evoked potentials (OEPs) have been described elsewhere [8,13]. Subjective gustometry yielded sensations for sour and salty tastes, although the patient was unable to recognize these taste qualities. The patient did not report any gustatory sensation for either sweet or bitter tastes even at the highest concentrations. OEPs could not be elicited by right-sided stimulation with olfactory stimulants phenylethyl alcohol and hydrogen sulfide. On the left side, OEPs after stimulation with phenylethyl alcohol were unremarkable whereas the response to hydrogen sulfide was doubtful. The trigeminal response to carbonation was observed on both sides. A comprehensive ear, nose and throat examination including nasal endoscopy did not yield any significant abnormalities. The patient's chemosensory complaints were therefore ascribed to the current relapse of MS. A cranial MRI scan showed no changes compared to two months earlier.

The patient again received intravenous methylprednisolone pulse therapy. His right-sided sensorimotor syndrome quickly faded. In parallel, the patient's perception of his sense of taste and smell returned to normal. The patient's subjective improvement in olfactory performance was mirrored by an increase in the composite TDI score of the Sniffin' Sticks procedure to 22 points. Nevertheless, it should be noted that this score is still indicative of absolute hyposmia, which is defined as the tenth percentile TDI score of 16-35 year old subjects [12]. The patient was subsequently also able to recognize and detect the taste qualities of sour, salty and bitter while he still could not detect sweet tastes even at the highest concentration. On one-year follow-up, he reported further improvement of chemosensory function. Importantly, the patient had regained the ability to taste sweet tastes. There have been no further MS relapses for more than 1.5 years while the patient has remained on 0.5 mg fingolimod.

Discussion

The clinical case of a patient with relapsing-remitting MS reported in this paper highlights chemosensory dysfunction as one of the chief complaints associated with a relapse. Here, functional anosmia was confirmed objectively by measuring OEPs. Since OEPs could not be elicited by right-sided olfactory stimulation, it is somewhat unfortunate that the Sniffin' Sticks procedure was not used to test each nostril of our patient separately. It should also be noted that our

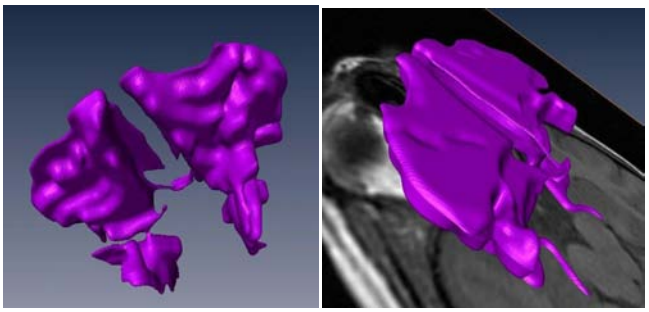

Figure 2 (A,B): 3-dimensional rendering of the segmented olfactory brain. The following structures were included: Primary olfactory cortex with the anterior olfactory nucleus, piriform cortex, amygdala, entorhinal cortex and olfactory tubercle, anterior insula and secondary olfactory cortex (basal frontal cortex) as well as white matter connecting these structures. The segmented olfactory brain can serve as a map for analysis of functional imaging data such as DTI.

case is not entirely uncommon in that cranial MRI frequently does not yield an MS lesion that clearly fits the clinical syndrome. This may be due to the fact that normal-appearing white matter (NAWM) may still be affected [14]. However, MS lesions may also be found in the central olfactory system as illustrated by the MRI scan of a different MS patient shown in Figure 1.

It remains to be elucidated which central structures are involved in the processing of olfactory information. New insights may come from the analysis of diffusion tensor imaging (DTI) data volumes. Fractional anisotropy (FA) serves as a DTI measure of the directionality of water motion [7]. A recent DTI study of olfactory structures in MS patients revealed a decrease in FA suggesting disturbed microstructural integrity of neuronal tissue in the olfactory brain of MS patients [7]. Figure 2 illustrates a 3-dimensional segmentation of the olfactory brain which may also serve as a map for the analysis of functional imaging data associated with olfaction [7].

Based on the Sniffin' Sticks procedure, up to 41% of MS patients show evidence of olfactory dysfunction. It seems that the prevalence of impaired gustatory function in these patients is somewhat lower [5,8,9]. The degree of olfactory dysfunction may vary. Typically, olfactory impairment is mild or moderate and falls into the category of functional hyposmia. Importantly, the majority of MS patients are not aware of this deficit [8]. The patient reported here suffered from relapsing-remitting MS. It should therefore be noted that chemosensory complaints are frequently also observed in patients with primary and secondary forms of disease progression. In particular, a marked reduction in the volume of the olfactory brain seems to be more common in these forms of MS. One likely explanation for this finding is that, in these progressive forms of the disease, demyelination is accompanied by axonal degeneration [9]. It has also been shown that reduced olfactory bulb volume (OBV) is associated with an increased number of MS lesions in the olfactory brain [9]. It is to be expected that new imaging technologies, especially high-resolution ultrahigh-field MRI, will shed new light on pathological alterations of the olfactory brain in MS [15].

A recent study of a human autopsy cohort of confirmed cases of demyelinating disease (MS, n=17; neuromyelitis optica [NMO], n=3; acute disseminating encephalomyelitis [ADEM], n=7) confirmed histopathological alterations in the olfactory structures [6]. The

authors detected demyelination of the olfactory bulb/tract in 70.6% of MS cases, 42.9% of ADEM cases and 66.7% of NMO cases. Furthermore, olfactory bulb/tract axonal loss was most severe in MS where it was significantly correlated to the extent of demyelination [6].

Finally, we would like to note that our patient was switched to fingolimod because, in our considered opinion, he suffered from highly active relapsing-remitting MS. It has been established that the beneficial effect of fingolimod on relapse rates only appears after a period of treatment with a range, depending on the study, from 64 to 82 days [16]. Our patient relapsed on day 39 of fingolimod treatment. Furthermore, he has remained clinically stable with continued fingolimod for 1.5 years.

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