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Multiple Sclerosis: Oral Manifestations and Dental Implications

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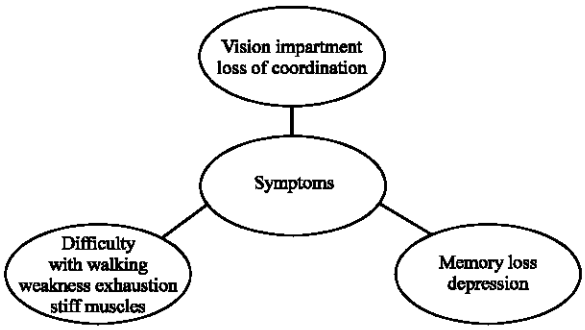
Abstract: Multiple Sclerosis (MS), a disease of the central nervous system, involves the nerves of the spinal cord and brain. Common early symptoms include visual disturbances, facial pain or trigeminal neuralgia and paresthesia or numbness of feet, legs, hands and arms. Also, many of the medications used in the symptomatic management of the condition have the potential to cause dry mouth and associated oral disease. Patients taking these medications have a predisposition to hemorrhage and are particularly susceptible to infection. The principal side effects of the medications in the oral cavity are: Stomatitis, ulcers, gingivitis, candidiasis and certain other opportunistic infections (e.g. herpes simplex). Dentists should also be aware of the importance of this disease in the diagnosis, treatment and prognosis of certain oro-facial lesions or conditions. This study reviews the oro-facial manifestations of the disease and discusses the dental implications.

Key words: Multiple sclerosis, oral manifestations, oral management, de oral disease, patients

INTRODUCTION

Multiple Sclerosis (MS), a disease of the central nervous system, involves the nerves of the spinal cord and brain (Bruck and Stadelmann, 2003; Frohman, 2003). MS symptoms, whether mild or severe, can include loss of muscle control or coordination. The symptoms range from mild ones such as slight numbness of the limbs to the more severe, such as loss of vision and paralysis (Connor, 2005; Sarlani *et al*., 2003; Sarlani, 2003). The causes of MS is not yet known but scientists theorize that it is the result of a virus or autoimmune condition in which the body becomes allergic to itself. In people with MS, malfunctioning T-cells (immune system cells that patrol the body for invaders) mistakenly attack the protective covering of nerve cells and expose bundles of long nerve fibers (Stefano *et al*., 2001; Markovic *et al*., 2004). That damage makes it difficult for the brain to transmit messages. Damage can result in various symptoms of the disease, depending on where in the central nervous system it occurs (Markovic *et al*., 2004).



Considered a lifelong disorder, the disease most often strikes between the ages of 20 and 30 and affects women twice as many times as men. Between 20 and 35% of all patients have a mild form of the disease and experience few, if any, symptoms. Another three to 12% of the patients have rapidly progressive multiple sclerosis while the majority of patients are somewhere in between the two extremes (Bruck and Stadelmann, 2003). Although not considered a hereditary disease, a family history of multiple sclerosis may make you more susceptible to the illness. Diagnosis of multiple sclerosis can be difficult because the symptoms of the disease can be very mild or non-existent and are similar to those of many other diseases. MS diagnosis is often done through a review of the patient's health history, a physical evaluation and various laboratory tests (Connor, 2002). There are approved drugs for multiple sclerosis treatment. Generally speaking, most physicians prescribe steroid medications to patients with multiple sclerosis to reduce the inflammation of the nerve tissue (Dhib-Jalbut, 2002; Goodin *et al*., 2002; McCormack and Scott, 2004; Sato *et al*., 2004). For certain patients, chemotherapy can be used as a treatment to interfere with the immune system that is attacking itself. New horizons in multiple sclerosis treatments and research advances are being made as research efforts reveal more information about multiple sclerosis (Dhib-Jalbut, 2002).

ORAL SYMPTOMS

Individuals with disabilities are especially prone to dental problems. A silent epidemic of dental and oral

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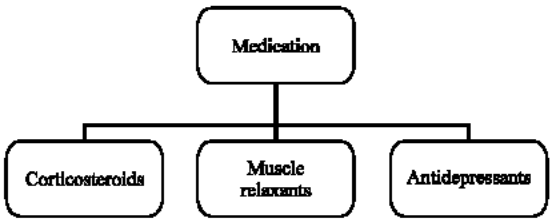
diseases affecting some population groups-including persons with disabilities-was recently brought to light in the first Surgeon General's report on oral health. Some authors announced that persons with disabilities and complex health conditions are at greater risk for oral diseases that, in turn, further complicate their health. The American Dental Association (ADA) is aware that persons with disabilities and chronic illnesses have special dental concerns that, to some extent, may inhibit self-care. The ADA says periodontal disease, untreated tooth decay and premature loss of teeth are particularly prevalent among this segment of the population, because other pressing health problems or poor self-care may overshadow the need for good oral hygiene. In addition, oral health can be affected by certain medications and treatments. Common early symptoms include visual disturbances, facial pain or trigeminal neuralgia and paresthesia or numbness of feet, legs, hands and arms (Bruck and Stadelmann, 2003). These, plus symptoms of spasticity, spasms, tremor, fatigue, depression and progressive disability, impact on the individual's ability to maintain oral health, cope with dental treatment and access dental services. Also, many of the medications used in the symptomatic management of the condition have the potential to cause dry mouth and associated oral disease (Chemaly *et al*., 2000).



Muscles of the oral cavity, pharynx and cervical esophagus are of the striated variety. These disorders may manifest as oral stasis of food, inability to initiate a swallow, premature spillage of food into the pharynx, pharyngeal stasis, nasal regurgitation, or laryngeal aspiration. Facial paralysis appears later in the course of the disease (Fig. 1). Up to 24.3% of MS sufferers may experience facial paralysis. Trigeminal Neuralgia (TN) (tic douloureux) also may be caused by demyelinating plaques of MS involving the trigeminal nociceptive pathway. It is, however, the first manifestation of the disease in 0.3% of cases (Bruck and Stadelmann, 2003; Devor *et al*., 2002; Love and Coakham, 2001; Matsuka *et al*., 2000; Sarlani *et al*., 2005; Zakrzewska, 2002). MS is diagnosed in 2-4% of patients with TN. Typically, patients with TN and MS are younger than those with idiopathic TN and are more likely to have

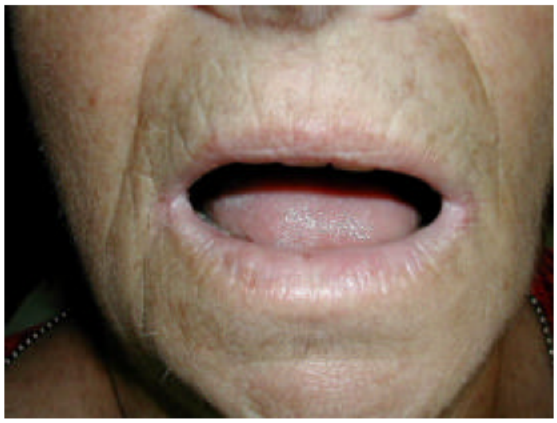


Fig.1: Facial paralysis of a patient with MS

bilateral facial pain. In the vast majority of cases, TN develops later in the course of MS; occasionally, however, TN may appear first. TN's development in patients younger than 50 years of age may be the first manifestation of MS, as was the case in our patient. A demyelinating plaque extending into the root entry zone of the trigeminal nerve is a common finding among patients with TN and MS, while plaques in other CNS regions do not seem to be associated with TN (Matsuka *et al*., 2000). Meaney and colleagues reported that vascular compression may be the underlying cause of TN, even in patients with MS. The authors demonstrated vascular compression of the root entry zone in a subset of these patients, with subsequent elimination of the TN pain after decompression of the nerve root. Pain attacks are episodic, last only seconds to a few minutes and may recur in clusters. The pain is characterized by sudden onset and cessation and the patient is completely asymptomatic between attacks (Sarlani *et al*., 2003; Zakrzewska, 2002). Pain paroxysms may be provoked by innocuous sensory stimulation of trigger zones in the receptive field of the affected branch. Common daily activities such as talking, eating, drinking, swallowing, exposure to cold air, shaving, brushing the teeth or washing the face can trigger the pain, significantly compromising the patient's quality of life. The trigger zone always is ipsilateral to the pain; however, it may not coincide with the area of pain. Common extraoral trigger zones occur above the supraorbital foramen, the inner canthus of the eye, lateral to the ala nasi and over the mental foramen (Matsuka *et al*., 2000). Typically, immediately after a jab of pain, there is a refractory period during which further pain attacks cannot be evoked. TN is characterized by spontaneous remissions that may last months or even years. Nevertheless, with time, pain attacks become more frequent, while remissions occur less often and last for a shorter period. In prolonged cases,

patients may develop atypical features, such as persistent pain between episodes.Continuous pain is more common in symptomatic TN, as in the case discussed here. Dentists should be competent in the differential diagnosis of trigeminal neuralgia from other facial pain causes, including dental pathology (Sarlani *et al*., 2005).

ORAL INVOLVEMENT CORRELATED TO SYSTEMIC TREATMENT

It is essential to manage the symptoms of the condition to improve the quality of life of the patient. One of the principal steroids used is prednisone, which counters the progression of multiple sclerosis and has anti-inflammatory properties (Dhib-Jalbut, 2002). This medication, taken orally, has numerous side effects (Fig. 2 and 3). In severe cases, steroids may be administered intravenously for a short period and subsequently taken orally. Dentists should be careful when treating patients on steroid therapy, as such patients may suffer from adrenal atrophy which can lead to adrenal crisis (shock, nausea, vomiting, abdominal pain, diarrhea and further complications including death). Because these patients are more prone to bacterial infections, a dentist performing a surgical intervention should place such a patient on a course of prophylactic antibiotics. Furthermore, it is important to avoid prescribing aspirin and NSAIDs (nonsteroidal anti-inflammatories) for these patients as they greatly raise the risk of gastric and duodenal ulcers. The interferons used to combat multiple sclerosis are powerful medications with numerous side effects. Those most commonly used, Beta 1-a interferon (Rebif) and Beta 1-b interferon (Betaseron), have anti-viral properties and modify the immune response (McCormack and Scott, 2004). Their action against multiple sclerosis isn't fully understood. We do know, however, that their effectiveness diminishes after prolonged use. Interferon reduces the frequency of active periods of the disease. It is self-administered by means of subcutaneous injections which can provoke local reactions of inflammation, pain and necrosis at the injection site. Flu-like symptoms (fever, shivering, fatigue, headaches, myalgia) can also appear at the beginning of treatment with interferon (Dhib-Jalbut, 2002; Goodin *et al*., 2002). These symptoms can be relieved by acetaminophen. Psychiatric problems ranging from depression to suicide can also arise. Finally, interferon can modify certain hematological parameters, notably: hematocrit, hemoglobin and platelet and white cell counts (Dhib-Jalbut, 2002). The dentist may notice certain oral side effects of the medications such as: cheilitis, gingivitis, stomatitis, xerostomia and candidiasis, dysgeusia or certain changes secondary to neutropenia and thrombocytopenia. Some cases of salivary gland

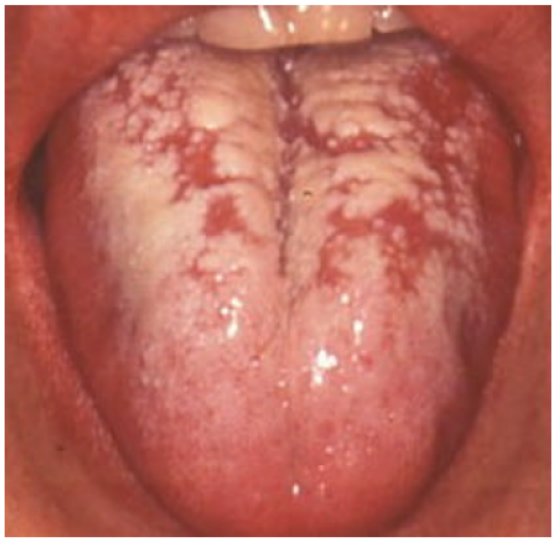


Fig. 2: Oral candidiasis associated to systemic corticosteroid treatment

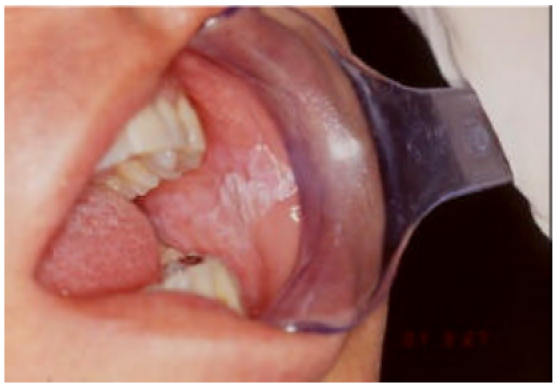


Fig. 3: Oral disease associated to systemic interferon treatment

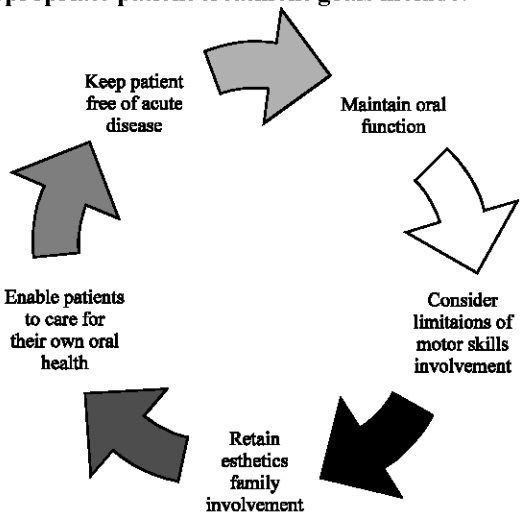
hyperplasia have also been noted (Dhib-Jalbut, 2002). ACTH, or corticotrophin, is used during acute crises because it stimulates the production of steroids produced by the adrenal gland. We should be cautious about prescribing NSAIDs in combination with ACTH because of the elevated risk of gastro-intestinal ulceration. Among the immunosuppressants prescribed, azathioprine and methotrexate work to inhibit T lymphocyte production (Goodin *et al*., 2002). The secondary effects of these medications (anemia, neutropenia and thrombocytopenia) have important implications for dentists. Patients taking these medications have a predisposition to hemorrhage and are particularly susceptible to infection. The principal side effects in the oral cavity are: stomatitis, ulcers, gingivitis, candidiasis and certain other opportunistic infections (e.g. herpes simplex). Finally the long-term use of immunosuppressors can raise the risk of developing

malignant neoplasias. Other medications can be prescribed to treat or reduce the symptoms of multiple sclerosis. Examples are muscle relaxants, anticonvulsants, antidepressants, anticholinergics and amantadine (Goodin *et al*., 2002). The principal muscle relaxants prescribed are baclofen (Lioresal) and diazepam (Valium) which relieve muscle spasms by blocking Gamma Amino Butyric Acid (GABA) and by inhibiting mono- and polysynaptic reflexes in the spinal cord (Goodin *et al*., 2002). The most common secondary effects of these drugs are: Fatigue, somnolence, blackouts, dizziness, hypotension and ataxia. The anticonvulsants are administered to control the pain of tic douloureux. The most commonly prescribed are carbamazepine (Tegretol), phenytoin (Dilantin) and gabapentine (Neorontin) (Sato *et al*., 2004). The main oral side effect of Dilantin is gingival hyperplasia. Tegretol can provoke bone marrow suppression, leading to anemia, neutropenia and thrombocytopenia. This must be taken into account when planning dental treatment for these patients. Anticholinergic agents are used to treat the bladder problems experienced by many patients. Amantadine (Symmetrel) seems to be effective in reducing the fatigue caused by multiple sclerosis (Goodin *et al*., 2002).

PLANNING DENTAL TREATMENT

The Dental team plays an essential role in ensuring that Oral health impacts positively on general health. Patients suffering from multiple MS are taking medications, either short- or long-term, that can have important implications for the planning of dental treatment. The dentist should be particularly prudent in providing treatment to patients taking interferon, steroids or immunosuppressors. In particular, because interferon and immunosuppressors cause anemia and neutropenia, the dentist should prescribe a course of prophylactic antibiotics before performing surgery. These drugs also may give rise to thrombocytopenia, which may greatly elevate the risk of post-operative hemorrhage. A complete blood count must be instituted before embarking on invasive treatment for patients taking immunosuppressors or interferon. Patients taking steroids will have adrenal hypofunction and have heightened susceptibility to infection. The dentist should keep in mind that the cardinal signs of inflammation are masked in patients taking steroids or immunosuppressors and that aspirin and NSAIDs significantly increase the risk of ulcers of the digestive tract in patients taking steroid therapy. A certain number of drugs currently prescribed by dentists may interact with medications prescribed for multiple sclerosis. This is the case with aspirin, NSAIDs, acetaminophen, narcotic analgesics and erythromycin. Aspirin and NSAIDs should be used very prudently with patients taking methotrexate. Through various mechanisms (inhibition of tubular secretion, modifying albumin fixation sites, etc.), these drugs have the effect of increasing the amount of free methotrexate, thereby amplifying its cytotoxicity. It is better to avoid the long-term use of acetaminophen in patients taking Dilantin and Tegretol because these medications, which induce the production of microsomial enzymes, can lead to the accumulation of certain hepatotoxic derivatives of acetaminophen. Narcotic analgesics have a tendency to amplify the central nervous system depression caused by Tegretol and tricyclic antidepressants and thus should be used with prudence with multiple sclerosis patients taking these drugs. Finally, erythromycin diminishes the clearance of Dilantin and Tegretol (inhibition of cytochrome P-450), thereby amplifying the toxic effects of these drugs. Anesthesia risks are generally not great for persons with MS-except for those with severe, advanced disease who may be seriously weakened by MS or have respiratory problems. The NMSS says there is no reason for a person with MS to avoid local anesthesia unless there is allergy to common local anesthetics such as Novocaine. The ADA provides guidelines to help dentists administer anesthesia and pain control in the safest manner possible. However, it is critical that persons with MS make dentists aware of their health status, medications (prescription or nonprescription) and any allergies or allergic reactions to medications or anesthesia. Despite the identical term, there is no relationship between dental "plaque" and Multiple Sclerosis (MS) "plaques." The latter term refers to areas of loss of myelin (the fatty envelope around nerve fibers in the brain, of the nerve and spinal cord). Dental plaque refers to deposits at the gum line caused by mouth bacteria.

Appropriate patient treatment goals include:



Clinical considerations:

- Patients with severe MS require short appointments
- Patient may have to be transferred from wheel chair to dental chair.
- patients may have difficulty localizing intraoral pain and discomfort; all diagnostic tools must be used before performing extractions or endodontic therapy.
- some patients develop trigeminal neuralgia (tic douloureaux), usually bilaterally.
- these individuals develop severe respiratory problems, due to the disease's effect on the muscles that control breathing and deficits in protective airway reflexes; rubber dam may be useful if the patient can breath through the nose.
- patients should not be placed in a supine position (to protect airway); can be placed at 45 degrees.
- sedation, general anesthesia, or hospitalization may be required prior to providing treatment.

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