**Intermittent Jaw Pain, Part II: Case Study**

**Arun Garg, DMD and Ghislaine Guez, MD, MBA**

**Case**

A 74-year-old female with a past medical history notable for ulcerative colitis, heart disease (posterior myocardial infarction at age 64), and depression, and a dental history significant for edentulousness and chronic denture use, presents to a dental-implant specialist for evaluation. She complains that her dentures do not fit her properly, of late, and that she has noted some soreness in her jaw associated with denture use, as well as when she chews. The soreness is most prominent on the left, though occasionally pain will radiate toward the right. She first noted the discomfort several months ago, though she was able to successfully ignore it with no loss of function until about 10 days ago, when the pain became so unbearable that she presented to her dentist and her physician seeking relief. Upon further prompting, she also reveals a history of low-grade fevers and night sweats for the past several months, occasional headaches, and at least a 15-pound weight loss over the course of one year, which was unintentional. The patient has a history of smoking, though she quit 30 years ago. The patient’s symptoms have prompted a more detailed workup by her primary care physician, which is ongoing. However, the patient reports that her physician informed her that she does not have any bacteria growing in her blood, but that she is anemic. The patient’s dentist confirmed that her dentures were ill fitting and that she looked chronically ill, with pallor and weight loss. The patient’s physician advised her to hold off on any invasive dental procedures until after the work-up was completed and a diagnosis was obtained; however, the patient felt so frustrated by the discomfort that she sought the opinion of a second dental expert.

In last month’s case discussion, cardiovascular disease, endocrine disorders (Paget’s disease and subacute thyroiditis), infections including vari-
cella-zoster virus, and rheumatologic processes like giant-cell arteritis were discussed in the setting of the patient’s intermittent jaw pain. The possibility of neoplasm and the relevance of this patient’s constitutional symptoms were also mentioned. In this month’s discussion of the case, temporomandibular joint disorders will be evaluated in the context of this patient’s pain. The relevant early aspect of this case, as mentioned in last month’s issue, is to start with a broad differential diagnosis, especially given her varied past medical and dental history, and then narrowing down based on clinical cues and relevant laboratory and radiologic imaging.

**Temporomandibular Disorders (TMDs)**

Because of the far-reaching scope of this category of pathologic processes, it will be discussed separately from the aforementioned differential diagnoses. The temporomandibular disorders are, according to *CURRENT Diagnosis and Treatment in Otolaryngology*, “a set of musculoskeletal disorders affecting the temporomandibular joint (TMJ), the masticatory muscles, or both.”¹ The cause of these disorders remains unclear, with various likely etiologies thought to contribute to a decidedly multi-factorial process; these include trauma (from direct and indirect impact on the jaw), stress, and clenching and grinding of the teeth. Surgical intervention in the mouth may or may not contribute to TMD, as will be discussed further below. Poor posture, nonrestorative sleep, and poor coping skills are, according to *CURRENT*, “perpetuating factors” in the disease.¹

The anatomy of the temporomandibular joint is as follows: components include the mandibular condyle, the glenoid fossa, and the articular eminence of the temporal bone. The presence of a fibrocartilaginous disk (the articular disk) essentially separates the joint into superior and inferior segments and helps distribute synovial fluid into the separate spaces of the joint. This increases joint stability and the evenness of force distribution. The disk also allows for two types
Table 1: Patient's laboratory values notable for anemia, renal failure, hypercalcemia, and hypoalbuminemia

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Value</th>
<th>Normal Range</th>
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<tr>
<td>Hemoglobin</td>
<td>8.0 gm/dL</td>
<td>11.2-15.7 gm/dL</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>25%</td>
<td>34%-45%</td>
</tr>
<tr>
<td>Platelets</td>
<td>110 x 103/mcL</td>
<td>145-370 x 103/mcL</td>
</tr>
<tr>
<td>Na</td>
<td>136 mMol/L</td>
<td>135-145 mMol/L</td>
</tr>
<tr>
<td>K</td>
<td>4.7 mMol/L</td>
<td>3.5-5 mMol/L</td>
</tr>
<tr>
<td>Cl</td>
<td>102 mMol/L</td>
<td>98-107 mMol/L</td>
</tr>
<tr>
<td>BUN</td>
<td>37 mg/dL</td>
<td>8-18 mg/dL</td>
</tr>
<tr>
<td>Cr</td>
<td>2.3 mg/dL</td>
<td>0.7-1.2 mg/dL</td>
</tr>
<tr>
<td>Ca</td>
<td>13.4 mg/dL</td>
<td>8.5-10.5 mg/dL</td>
</tr>
<tr>
<td>Albumin Level</td>
<td>2.2 gm/dL</td>
<td>3.2-5.2 gm/dL</td>
</tr>
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</table>

of joint motion — rotational and translational movement and is, thus, referred to as a ginglymoarthrodial joint — a hinge and a sliding joint. Muscles that are associated with the joint are involved in overall jaw function — the temporalis, masseter, mylohyoid, anterior and posterior digastrics, hyoglossus, and stylohyoid.²

Clinical findings associated with TMD include jaw, face, and head pain, often unilateral, with or without radiation to the ears or temporal and periorbital regions, as well as the posterior neck.² It should be noted that the temporomandibular joint is anatomically situated close to the external auditory canal and, for this reason, in part, patients report specific noises characteristic of the disease. Most patients complain of reduced opening of the mouth, “popping” and “clicking” noises, and appreciable joint sensations, such as “locking” and “sticking” when the mouth is opened. Prevalence, according to several studies, ranges between 40% and 75% of the population, with predominance in female patients (anywhere from 3:1 to 9:1 in terms of female-to-male ratio).

As with all specific patient complaints suggestive of a pathologic process, accurate and thorough history and physical exam is essential on behalf of the dental-implant practitioner. Documentation of degree of impair is useful, especially if treatment is required. Recommended in the evaluation of patients with TMJ complaints is a complete dental history, in addition to a physical exam that includes palpation on mandibular motion, assessment of range of motion, appreciation of co-occurring musculature, palpation for lymphadenopathy, and a detailed neurological exam, including evaluation of cranial nerve function; assessment of carotid arteries is also valuable. In a detailed review on the topic featured in a 2008 article in the New England Journal of Medicine, authors Scrivani, Keith, and Kaban suggest that a biobehavioral approach should be considered, given the significant coexisting psychopathology associated with chronic pain disorders like TMJ. As such, practitioners, if able, should screen for anxiety and depressive disorders, stress disorders, and evidence of past abuse.²

Imaging tests to assess the temporomandibular joint include panoramic radiographs and, increasingly, computed tomography (CT) to evaluate bone morphology, erosive changes, and pre-surgical appearance of the anatomical structures involved in the joint. MRI, a useful tool, can be used to evaluate the intra-articular disk at rest and in motion; it is recommended to evaluate soft tissue structures in fine detail. According to one study, articular disk displacement is visualized in 80% of MRI images in patients with DMD.³ MRI is considered the gold standard for evaluation of DMD.⁴ Damage to the disk seen by MRI includes disk perforation, joint effusion, osteoarthritis, and disk deformity. A direct “in the joint” evaluation is possible with arthroscopy, which is a minimally invasive surgical technique that can elucidate processes not otherwise seen with radiography, such as synovitis, cartilaginous changes, adhesions.

Interestingly, TMJ-related pain can be acute or chronic. Many acute cases resolve spontaneously. Chronic cases can be very difficult to manage and may require an interdisciplinary approach with the assistance of numerous providers (similar to the approach toward treating patients with chronic headache, fibromyalgia, and other long-standing, painful conditions). According to the New England Journal of Medicine, management of TMD “consists of a combination of home self-care, counseling, physiotherapy, pharmacotherapy, jaw-appliance therapy, physical medicine, behavioral medicine, and surgery.”³ Surgical intervention is only recommended to treat structural abnormalities, and can be controversial. One meta-analysis evaluating surgery as a cause of, or the treatment for, temporomandibular disorders found no evidence that dental surgery and subsequent malocclusion causes TMJ; nonetheless, patients feel strongly that it is, in fact, the case. The conclusion drawn by study authors suggests that more evidence is needed before adequate data analysis can occur. As it stands, in the 32 eligible articles reviewed, none of
these included data could be generalized in such a way as to combine criteria and increase overall study power. In fact, the very definition of TMD was different from study to study.

The International Research Diagnostic Criteria for Temporomandibular Disorders (RDC-TMD) Consortium is an association created for dental research on the topic, and provides practitioners with useful tools to diagnose and assess severity of TMD (accessible online at http://www.rdc-tmdinternational.org/). The tools on this site are useful for all dental practitioners, and serve as a valuable and underused resource for those doing research on TMD. Unfortunately, standardization of the disease process is difficult, as many of the patient complaints are subjective and difficult to quantify. Nonetheless, the group put together history, jaw function, pain, and demographic patient questionnaires, as well as a behavioral assessment. The booklet also expounds on specific measures for the administration of all patient questionnaires, as well as details on documenting physical-exam findings. Standardization criteria, such as the behavior assessment scale, are underutilized by practitioners, making meta-analyses nearly impossible.

In patients with facial pain who do not have a structural defect requiring surgery, which makes up the majority of patients with TMD, treatment with reassurance and counseling, locally applied heat, and medications, such as non-steroidal anti-inflammatory agents and antidepressants (those that do not increase bruise), have all been shown to provide some degree of relief in a certain group of patients. Jaw appliances, while popular amongst patients and providers, have not been shown to improve TMD when used alone. In combination with other treatments, they have, however, been shown to improve patient discomfort. There is also evidence for biofeedback, stress management, and ongoing counseling/therapy in all chronic-pain syndromes, including temporomandibular joint disorders. Patients should be advised not to completely immobilize the mandible but to limit excessive opening, as well as limit stress-induced repetitive behaviors.

For patients who have evidence of disc displacement on MRI, all the aforementioned treatments should be tried before a more aggressive approach is taken. As with other joint disorders, injection of steroid or hyaluronic acid into the joint can improve patient symptoms in the short-term, but these treatments are temporary, carry specific risks, and are not recommended beyond a certain number of treatments. It should be noted that osteoarthritis of the temporomandibular joint can present in patients in their third and forth decades of life, and that it does not need to coincide with evidence of osteoarthritis in other joints.

**Case Progression**

While this elderly female patient is having some symptoms of myofacial pain, she is lacking the classic findings associated with TMD — no clicking or popping is noted. It does have a rapidly worsening course, and radiates in a way suggestive of TMD, but these factors alone do not point in a strong direction toward TMD. Additionally, the patient’s constitutional symptoms — weight loss, fatigue and malaise, night sweats, and fevers cannot be ignored. The patient’s primary care physician shared the patient’s recent lab data, as shown in Table 1.

The patient’s primary care physician ordered radiographs of the skull and spine, both pending at this time. Though not included in this patient’s laboratory data, the physician reports that the patient also has hyperproteinemia.

**Malignancy**

In last month’s issue of Dental Implantology Update, neoplasms that commonly metastasize to bone were briefly discussed. One malignancy not covered that also affects bone is multiple myeloma. Multiple myeloma is a hematological malignancy characterized by excessive monoclonal paraprotein, which presents with systemic toxicity and generally carries a poor prognosis. Plasma cells are immune-system cells that originate in the bone marrow and eventually differentiate to antibody-producing cells. Despite an overabundance of one particular type of antibodies, the immune system is actually compromised because the antibodies produced are impaired, related to a single clone, and rapidly destroyed. For this reason, patients have multiple recurrent illnesses including bacterial infections, such as pneumonia, with common pathogens being *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Klebsiella pneumoniae*.

Several other systemic processes are the direct result of the disease process and the presence of excessive monoclonal proteins in the blood, including renal failure, anemia, and bleeding. Renal failure is the result of deposition of aberrant protein (light chains) in renal tubules, as well as hypercalcemia and concurrent use of anti-inflammatory medications. Excretion of large amounts of protein in the urine may also lead to the diagnosis of multiple myeloma, especially with normal albumin levels and normotension. Anemia results from replacement of marrow by rapidly expanding plasma cells; this is also the cause of thrombocytopenia.

Multiple myeloma accounts for roughly 1% of all malignancies, and 13% of all hematological malignancies. The disease is twice as common in African-Americans, with a male-to-female ration of 3:2.

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An initial presentation of jaw pain alone is a rarity for patients with multiple myeloma; nonetheless, it is important to note multiple myeloma among relevant malignancies that may cause ostial pain located at the jaw or skull. Several case reports exist of patients presenting solely with mouth, jaw, and skull pain and, ultimately, receiving a diagnosis of multiple myeloma. Because of the numerous other systems complaints in patients with multiple myeloma, straightforward mandibular pain may suggest other etiologies; practitioners should, in the early phases of evaluation, stay broad, and narrow the differential diagnosis only after enough data have been gathered. Bone pain should not be ignored for this very reason. In fact, generalized bony pain (commonly at the spine and ribs) is one of the most common complaints of patients with the disease, and it often represents as a pathologic fracture. Bony lesions are lytic, and the classic radiographic appearance is the “punched-out” lesion readily visible on the calvarium. Patients generally present with some acute illness, evidence of renal failure and anemia, and bony pain. Diagnosis requires laboratory evaluation, summary of clinical symptoms, and a serum or urine M protein component.

Case Conclusion

This II-part case series demonstrates the broad list of possible diagnoses in an elderly patient with jaw pain. Dental-implant practitioners must be aware of the nondentate issues so that he or she can make appropriate referrals to other medical providers or, if necessary, refer for an emergency evaluation (as in the case of referred cardiac pain or temporal arteritis). Serious, potentially fatal malignancies may present as jaw pain. Chronic sufferers, as in the case of individuals with temporomandibular joint disorders, may require referral to pain-control specialists and psychological counseling.

References


Nanotechnology: The Science of Small

Arun Garg, DMD

Nanotechnology is the study of matter and its application on the nanoscale, that is to say, from one billionth (1 x 10-9) of a meter, which is equivalent to 1 nm, to 100 nm. Over the last several decades, engineers and physicists have managed to miniaturize any number of computer processing elements, shrinking everyday devices from room-sized to desk-sized to pocket-sized. There seems no limit to the shrinking nature of things, and this is everything nanotechnology serves to accomplish. But mastering the minuscule does not stop with electronic devices; in fact, the biomedical application of nanotechnology is growing increasingly popular and prevalent, with sums of research dollars going toward the development of drug-delivery devices, molecular coatings, surgical instruments, and tissue-engineering processes. Scientists work tirelessly to create nanorobots that will allow practitioners to intervene in the complex processes that occur at the cellular level. The reshuffling of the atomic deck with particles that can move and change molecular processes seems almost the stuff of science fiction; but despite the fact that it cannot be seen by the naked eye (far from it, in fact), nanotechnology
is based on the laws of physics and chemistry, and its potential applications are being heralded.¹

In 2000, an article in the *Journal of the American Dental Association* stated simply “development of nanodontistry will make possible the maintenance of near-perfect oral health.”² The article described biotechnological advances making re-growth of native teeth a possibility, the treatment of dentin hypersensitivity at the level of the dentin tubules, of orthodontic nanorobots, and gingival anesthesia that is more microscopic than local. Though these goals have not been completely achieved, nanodontistry, as a field, is serving a reliably important role in the application of dental implants. Indeed, when considering anything on the nanoscale, it is the surface interaction between two materials, in this case the implant and the surrounding bone, that is relevant. Osseointegration, implant success or failure, patient healing times, even postoperative pain due to local inflammatory processes are all variables that can be affected by nanodontistry.

Two articles on the topic are especially relevant to the field, and shed insight on the growing discipline. In a 2010 review article entitled *Nanotechnology and Dental Implants*, authors Sandrine Lavenus, Guy Louarn, and Pierre Layrolle discuss the role of nanotechnology in osseointegration. From the outset, the authors clarify one of the well-understood principles of dental implantology — peri-implantitis can, and does, unanchor implants from surrounding bone, leading to implant failure. Peri-implantitis arises from pockets of bacterial colonization that develop between the implant and surrounding bone.³ The book *Implant Dentistry* nicely defines the three phases of osseointegration as the osteophilic phase, the osteoinductive phase, and the osteoadaptive phase.⁴ In the osteophilic phase, after a roughened surface implant is placed into the cancellous marrow space, only a small amount of trabecular bone within the marrow is in contact with the metal surface of the implant — the rest abuts fibro-fatty marrow space. In the early phase, osteoblasts migrate to the implant and osteoid production begins at the implant surface. Generally, it is understood that these cells respond to growth factors and mineral proteins resultant from the surgical intervention and disruption of bone. This phase lasts roughly one month.⁴ In the osteoconductive phase, bone cells spread along the metal surface, a process called osteoconduction, laying down osteoid and forming a thin layer of bone. This phase is complete four months after implant placement, when more stable and significant quantity of bone covers the implant, at which point no further bone growth is noted in contact with the implant.⁴ The final phase is termed osteoadaptive, and it is described as a steady state with bone turnover over the implant, with resorption and deposition much like typical bone undergoes.⁴ Authors Lavenus, Louarn, and Layrolle describe a period of instability between the osteophilic and osteoconductive phases before biological anchorage is complete. While many companies have offered novel surfaces of implants (designed to enhance clot attachment and formation), nanotechnology, as the authors explain, will include the surface of the implant, and take note, specifically, of the interactions with the protein and cellular layers of the surrounding biologic tissue. The authors describe a new coating technology that aims to improve the osteoconductive phase of osseointegration by applying hydroxyapatite and related calcium phosphates (CaP) onto the surface of dental implants:

“Many studies have demonstrated that these CaP coatings provided titanium implants with an osteoconductive surface. Following implantation, the dissolution of CaP coatings in the peri-implant region increased ionic strength and saturation of blood, leading to the precipitations of biological apatite nanocrystals onto the surface of implants.

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<tr>
<th>Role for nanotechnology in implant dentistry</th>
<th>Examples</th>
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<tr>
<td>General surface modifications</td>
<td>Surface roughness of metals (grit blasting, acid-etching, ionic implantation) Coatings with osteoconductive properties</td>
</tr>
<tr>
<td>Hematologic interaction with surfaces</td>
<td>Hydrophilic surfaces (better for blood coagulation) Coating with cell-binding domains for interaction with integrin</td>
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<tr>
<td>Stem cell interactions with implant surfaces</td>
<td>Chemotaxis of mesenchymal stem cells; inflammatory phase reactants and chemo-attraction of clot matrix at implant surface. ‘Nanorough’ Ti and ‘nanostructured’ Ti preferred. Nano-pores enhance osseointegration</td>
</tr>
<tr>
<td>Tissue integration at implant surface</td>
<td>Goal is to decrease tissue healing times, improve clinical success rates.</td>
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This biological apatite layer incorporates proteins and promotes the adhesion of osteoprogenitor cells that would produce the extracellular matrix of bone tissue. In some ways, these types of coatings might modify the osteophyllic and osteoconductive phases into one, shorter peri-implant period, with faster and stronger osseointegration. In this detailed review article, the authors go on to discuss four modifications and interactions at the nanosurface level that can, and will, play an important role in improving dental-implant procedures and tolerability; these are listed in Table 1.

The second important article on nanodentistry comes from authors Shivani Sharma, Sarah Cross, Carlin Hsueh, Ruseen Wali, Adam Stieg, and James Gimzewski, entitled Nanocharacterization in Dentistry. The article mentions nanotechnology and implant dentistry, but expands to other aspects of dentistry, including biofilm formation, salivary characteristics, and dentine tubules. Ten years after the aforementioned 2000 Journal of American Dental Association article was released, these authors again state the potential application for nanodentistry, in that 80% of the population is affected by some dental issue. They write, “using nanocharacterization tools, a variety of oral disease can be understood at the molecular and cellular levels and, thereby, prevented. Nano-enabled technologies, thus, provide an alternative and superior approach to assess the onset or progression of disease, to identify targets for treatment interventions, as well as the ability to design more biocompatible, microbe-resistant dental materials and implants.” The authors review various materials with atomic force microscopy (AFM) to assess biological and artificial surfaces in the mouth. Understanding the surface of structures at a new nanolayer level promises to uncover remedies to improve conditions like osteoporosis, chronic pain, and hypersensitivity, even caries. In one example, AFM was used to observe dentine tubules before and after treatment with a desensitizing prophylaxis paste. Typically, the study of dentine hypersensitivity involves the patient’s subjective experience of the pain, with little to no objective data measured. Yet in the investigation of the treatment of dentine hypersensitivity using nanotechnology, the physical structure of the dentine tubule can be assessed before and after treatment — a novel and quantifiable concept. Beyond this, the very definition of dentine hypersensitivity was assessed (degree of open tubules, helical structure). Degree of bone development and mineralization can also be detected and quantified in this manner,
especially before and after implant placement (and consequentially if implant failure could be predicted days after the procedure).

Understanding surface dynamics also applies to bacterial and host cells, with implications for understanding (and possibly altering) platelet aggregation and healing, cytokine activation, bacterial agglutination (biofilm formation), and the development of caries. The authors also note the relevance of subcellular salivary biomarkers and the role of nanotechnology in the early diagnosis of oral and pharyngeal cancer.

Clearly, there is great promise in nanotechnology. Still in its infant stages, the field is ripe with opportunity for growth and change in an increasingly technology-oriented health sector. Though it has been heralded since the 1980s, and may offer solutions to common problems associated with dental implants and oral care as a whole, nanotechnology has been, to a certain extent, overlooked by modern dental practitioners. It could be that the promises of as-of-yet created technology seem too good to be true, buffered by a healthy degree of skepticism on behalf of those in the dental community. Or, it could be that negative press is keeping nanotechnology at bay. Some worry about the effect of nanotechnology on the population, on agriculture, on viruses and bacteria should human-engineered nanorobots enter the natural environment unregulated and dramatically alter the nature of all cells. Doomsday scenarios abound. Certainly, as researchers go deeper into the molecular level of bone formation and the early phases of biofilm adhesion, they will uncover the roles of highly specialized physiologic pathways of disease. Nanotechnology may, quite literally, fill in these gaps and offer diagnostic and therapeutic solutions to numerous dental problems.

References