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Rheumatoid Arthritis in the Cervical Spine: What You Need to Know

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Patients diagnosed with rheumatoid arthritis (RA) are among the most difficult for orthopedic surgeons to treat. Cervical spine involvement is the manifestation of RA that is most likely to cause rapidly progressive disability or sudden death. Management of the rheumatoid cervical spine remains a challenge for experienced spine surgeons and can be especially daunting for general orthopedic surgeons and nonspine specialists alike.

This complicated process is simplified by using a straightforward approach based on 5 fundamental questions: 1. What is the scope of the problem? 2. What should I look for in my patients? 3. What can I do for my patients? 4. When should I ask for help? 5. What can others do for my patients? In this review, we answer these questions and provide the information needed to evaluate the cervical spine in patients with RA.

1 What is the scope of the problem?

Epidemiology

In the US population, the incidence of RA is approximately 0.5% to 1.5%.[1] Although a predominance has been described for women, men are at higher risk for advanced cervical disease. Historically, about 50% of all patients with RA will become unable to work within 10 years of diagnosis.[2] The most common sites of involvement are hands, feet, and cervical spine. Depending on the series, cervical spine disorders are found in 17% to 86% of patients with RA.[3] A recent study found cervical involvement in 39% of patients 14 years after diagnosis and in 56% after 24 years.[4]

Pathophysiology and Pathoanatomy

RA is an inflammatory condition that affects synovial joints. The disease process is thought to be initiated by an autoimmune response to an antigen expressed on synovial cells. The ensuing inflammatory process causes the formation of rheumatoid pannus. The pannus contributes to chronic synovitis characterized by the release of enzymes capable of destroying ligaments, tendons, cartilage, and bone.

The cervical spine is composed of multiple small synovial articulations that make it particularly suscep-

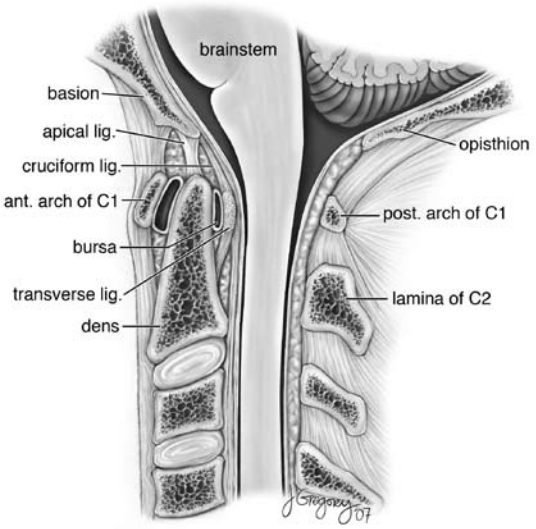

Figure 1. Normal upper cervical spine anatomy. ©2007, Continuum Health Partners, New York, NY.

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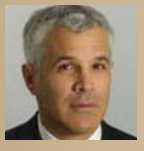

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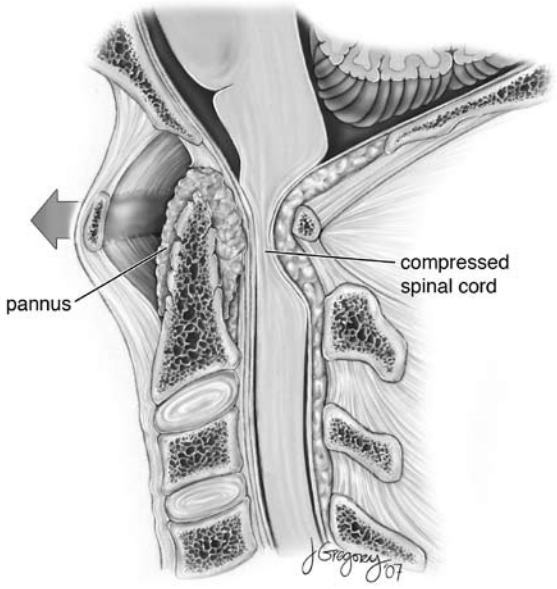

Figure 2. Atlantoaxial subluxation. Note the spinal cord compression caused by the forward shift of C1 on C2 and the rheumatoid pannus posterior to the odontoid. ©2007, Continuum Health Partners, New York, NY.

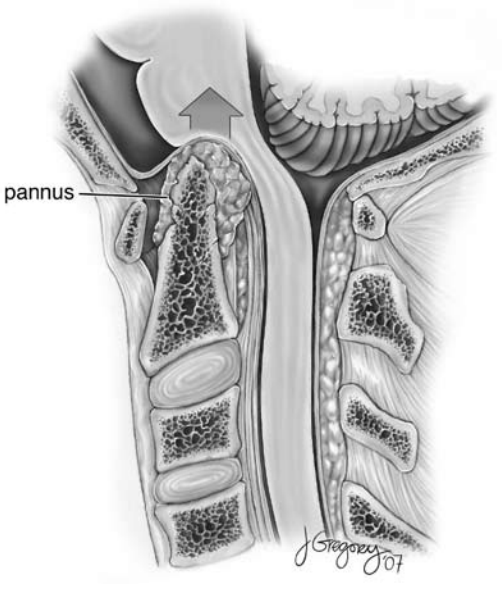

Figure 3. Atlantoaxial impaction. Superior migration of the dens into the foramen magnum and the rheumatoid pannus results in brainstem compression. ©2007, Continuum Health Partners, New York, NY.

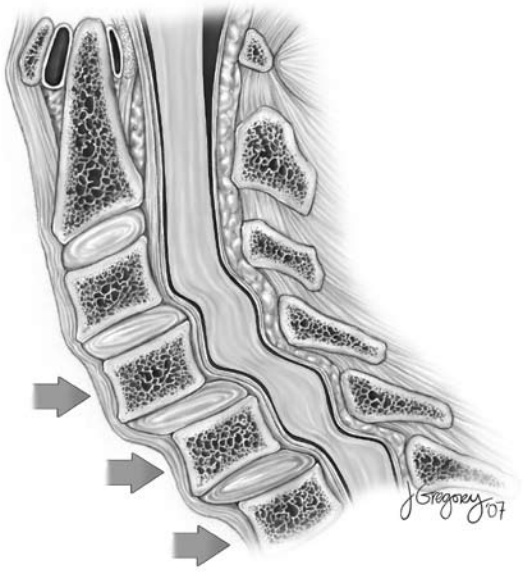

Figure 4. Subaxial subluxation. Note the stepladder deformity of the lower cervical vertebrae, which results in spinal stenosis at multiple levels. ©2007, Continuum Health Partners, New York, NY.

tible to RA involvement (Figure 1). The occipitoatlantal (occiput-C1) and atlantoaxial (C1-C2) joints are at high risk because of the extensive presence of synovial tissue in these regions. Soft-tissue destruction in the upper cervical spine causes instability because of lack of inherent bony stability in these articulations. Three patterns of cervical spine involvement have been described: atlantoaxial subluxation (65%), atlantoaxial impaction (20%-25%), and subaxial subluxation (10%-15%).

Atlantoaxial subluxation is the most common pattern of instability due to disease involvement of a bursa posterior to the odontoid, which causes destruction of the transverse ligament (Figure 2). Although the transverse ligament is the primary stabilizer of the C1-C2 joint, significant instability (>3-4 mm) occurs only with incompetence of the alar-apical ligament complex or erosion of the dens itself. Anterior translation of the C1 ring on the odontoid process of C2 is the most common type of atlantoaxial subluxation. Instability in the atlantoaxial region can cause spinal cord compression and neurologic problems.

Atlantoaxial impaction, also referred to as *basilar invagination, superior migration of the odontoid,* and *cranial settling,* is the result of bone and cartilage destruction at the occipitoatlantal and atlantoaxial articulations (Figure 3). This process causes a relative cephalad movement of the dens into the foramen magnum. When the amount of cranial settling is significant, direct compression of the brainstem and/or vascular compromise of the spinal cord can occur. In general, basilar invagination follows atlantoaxial subluxation. Patients with cranial settling typically present with more neurologic deficits and a worse prognosis than patients with isolated atlantoaxial subluxation.[5]

Subaxial subluxation involves the lower cervical spine from C2-C7 and usually occurs later in the disease process than do other forms of cervical involvement (Figure 4). Subaxial subluxation is characterized by the classic "stepladder deformity" with anterior translation of one vertebra on another at multiple levels. Often, cervical kyphosis is present as well. Subaxial instability can follow upper cervical fusion procedures because of resultant increased biomechanical stresses in the lower cervical spine.

Natural History

The fate of RA patients with cervical spine involvement was once considered benign. However, recent studies have found a risk for functional deterioration and sudden death. Pellicci and colleagues[6] prospectively studied 106 patients with RA and cervical spine involvement over 5 years and found progression of radiographic findings in 80% of patients and neurologic deterioration in 36%. Patients who develop myelopathy as a result of RA in the cervical spine have a particularly poor prognosis if left untreated. One study showed a 73% mortality rate within 5 years of symptom onset,[7] whereas another found a mortality rate of 100% after 8 years without treatment.[8] A significant cause of sudden death is medullary compression due to pannus and spinal deformity. A postmortem examination of 104 patients with RA demonstrated that 10% of subjects died as a result of brainstem compression due to atlantoaxial subluxation, and a large number of these were sudden deaths.[9]

Risk factors that portend a worse prognosis for patients with cervical spine involvement by RA include male gender, rheumatoid factor seropositivity, and severe peripheral disease. Although prolonged steroid use has also been shown to be a risk factor, this may simply reflect severe peripheral involvement. There is also an indication that increased C-reactive protein levels correlate with progressive spinal involvement.

2 What should I look for in my patients?

History and Physical Examination

As a result of frequently diffuse involvement, the physical examination of patients with RA can be difficult. An error in managing patients with RA is the attribution of minor functional changes to progressive peripheral disease. One study of patients with RA demonstrated a delay of more than 6 months between the onset of neurologic symptoms and the diagnosis of myelopathy.[10] Moreover, minor changes in the physical examination can be obscured by severe peripheral involvement with accompanying tendon ruptures; swollen, painful joints; decreased range of motion; and joint contractures. Nevertheless, it is critical that surgeons remain vigilant in their history taking and physical examination so as to avoid missing the subtle findings that suggest cervical involvement and neurologic impairment.

Although many RA patients with cervical spine disease are asymptomatic, neck pain remains the most common complaint. Pain may be described as a deep ache and can radiate throughout the head. Neck stiffness, painful range of motion, and crepitus are also common symptoms. Patients with cervical involvement may present with occipital or migraine headaches, and some experience the sensation that their head is falling forward during neck flexion. In the latter case, the patient may also report a clunking sensation with extension, indicating reduction of the atlantoaxial joint.

Presence of either of two syndromes, cervical myelopathy or vertebrobasilar insufficiency, suggests significant cervical involvement and portends a worse prognosis. Myelopathy, the more common syndrome, is suggested by difficulty walking, ataxia, and loss of fine motor control. Patients may report changes in handwriting and difficulty holding small objects, handling coins, or buttoning clothes. Although these changes may be seen in patients with severe peripheral disease, surgeons must not attribute these changes to the extremities without first ruling out cervical disease. Vertebrobasilar insufficiency is caused by occlusion of the vertebral arteries as a result of upper cervical spine deformity or instability. This may result in nausea, tinnitus, vertigo, loss of equilibrium, dysphagia, or visual disturbances. If the subluxation is dynamic, the symptoms may occur only intermittently, making the diagnosis more difficult.

The physical examination should be directed toward the diagnosis of cervical myelopathy. The hallmarks of the disease include lower extremity hyperreflexia and the presence of pathologic signs. Hoffman's sign, flexion of the thumb after flicking the distal interphalangeal joint of the middle finger into extension, may be present. Other signs of myelopathy include the Babinski reflex, an upgoing great toe with splaying of the lesser toes on stroking of the lateral sole of the foot, and clonus, repetitive, involuntary movement of the ankle after forceful dorsiflexion of the foot by the examiner. Lhermitte's sign, a sensation of electricity running down the torso or arms with flexion of the neck, indicates significant dynamic compression of the spinal cord. Motor weakness is a late finding in cervical myelopathy, as are changes in urinary and rectal function.

Diagnostic Tests: Imaging Studies

Using and interpreting appropriate imaging studies are among the most important and difficult aspects of caring for the necks of patients with RA. Despite the temptation to proceed directly to magnetic resonance imaging (MRI), plain x-rays remain the initial imaging modality of choice. Although various lines, indices, and other measurements have long confused orthopedists, knowing indications for x-rays and other studies as well as significant measurements makes the process manageable for the treating physician.

Although there is no consensus about indications for cervical spine x-rays in patients with RA, it is reasonable to order x-rays for patients with long-standing neck pain, neurologic symptoms, or a rapid decline in general function. X-rays should also be considered in patients with progressive, destructive peripheral disease. The initial screening examination should consist of anteroposterior, lateral, and open-mouth views in neutral alignment as well as lateral views in flexion and extension. Follow-up x-rays for stable patients should consist only of lateral views in flexion and extension and should be performed every 2 to 3 years. However, new studies should be obtained sooner for an RA patient with a sudden or significant deterioration in function or a worsening neurologic condition.

Asymptomatic patients who are being managed for peripheral RA without any of the aforementioned signs do not require neck x-rays. The exception is an asymptomatic patient scheduled to undergo a procedure that requires general endotracheal intubation. For patients who will undergo procedures under conscious sedation or local anesthesia, x-rays should be obtained as well, because of the possibility of conversion to general anesthesia. Asymptomatic patients who have had x-rays taken within the preceding 2 to 3 years do not require new x-rays before surgery, but new x-rays should be obtained if more than 3 years has elapsed.

When interpreting cervical spine x-rays in patients with RA, it is first necessary to look for atlantoaxial subluxation. Historically, the anterior atlanto-dens interval (AADI) was considered the most important indicator of C1-C2 subluxation (Figure 5). AADI is determined by measuring the distance between the posterior aspect of the anterior ring of C1 and the anterior surface of the odontoid process. In adults, AADI should be no more than 3 mm. Although it is still important to measure AADI, studies now suggest that the posterior atlanto-dens interval (PADI) is the more important measurement at the C1-C2 articulation. PADI is determined by the distance from the posterior aspect of the odontoid to the anterior surface of the posterior C1 ring and is normally more than 14 mm. In one important study, Boden and colleagues[11] found that PADI was significantly correlated with both paralysis and neurologic recovery after surgery, whereas AADI had no predictive value. The authors reported that all nonambulatory patients had preoperative PADI of less than 14 mm and that no neurologic recovery was seen when preoperative PADI was less than 10 mm.

Traditional measurements of cranial settling, such as Chamberlain's, McRae's, and McGregor's lines, focus on the relationship between the tip of the odontoid and the base of the skull. Several indices that avoid the need to find the top of the dens have also been devised, including the Clark station, the Redlund-Johnell method, and the Ranawat index. In a recent study, Riew and colleagues[12] found that no single measurement alone is sufficient to identify atlantoaxial settling. They recommended using the Clark, Redlund-Johnell, and Ranawat measurements in each patient. In so doing, the sensitivity is 94% when 1 of these 3 measurements is positive, and the negative predictive value is 91% when all 3 measurements are negative.

On plain x-rays, subaxial subluxation is measured by the amount of displacement of one vertebra on another. Classically, translation of more than 3.5 mm signifies clinically relevant subluxation. More recent studies suggest that the diameter of the spinal canal is a more important predictor of neurologic function than is the amount of subluxation. Canal size is determined by measuring the distance from the posterior aspect of the vertebral body to the spinolaminar line. As with PADI, sagittal subaxial canal diameter is significantly correlated with both paralysis and neurologic recovery after surgery (Figure 6).[11]

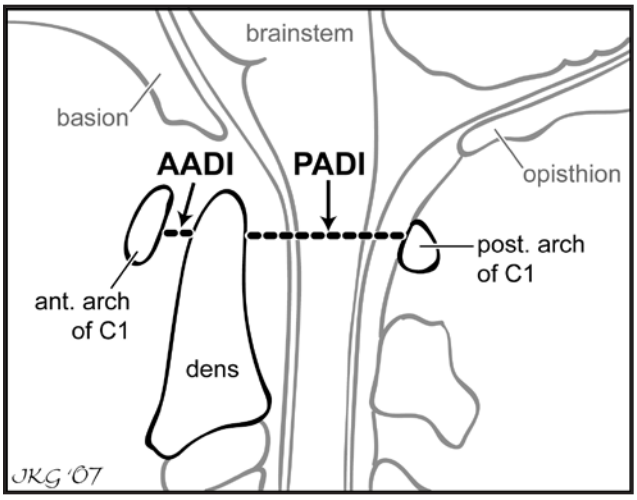

Figure 5. Measurements of atlantoaxial subluxation. Compared with the anterior atlanto-dens interval (AADI), the posterior atlanto-dens interval (PADI) is a more predictive measurement of paralysis and neurologic recovery after surgery. ©2007, Continuum Health Partners, New York, NY.

Although many physicians feel most comfortable ordering advanced imaging of the cervical spine in patients with RA, there are specific indications for doing so. Computed tomography (CT) scans should be reserved for preoperative evaluation by spine surgeons. MRI, the preferred modality for RA patients with significant cervical involvement (Figure 7), provides information about the size of the rheumatoid pannus, the extent of bony and soft-tissue destruction, the status of the spinal cord, and the relationship between structures in the upper cervical spine. Nevertheless, MRI should be ordered only in patients with neurologic deficits or with plain x-rays showing PADI or subaxial spinal canal diameter of less than 14 mm or basilar invagination. MRI allows for determination of the true space available for the spinal cord, which may be less than predicted on plain x-rays because of pannus in the canal. CT myelogram can be used to assess the neural elements in patients who cannot tolerate MRI.

3 What can I do for my patients?

The general orthopedic surgeon or the non-spine specialist can play a significant role in managing the cervical spine in patients with RA. In general, treatment goals include managing pain and other symptoms, avoiding permanent neurologic deficits and disability, preventing sudden death due to brainstem or spinal cord compression, and helping patients avoid unnecessary surgery.[13] Given these goals, the mainstay of cervical spine treatment in patients with RA remains nonoperative management.

All patients with RA should be evaluated and followed by a rheumatologist. Despite what we might think, many patients with RA have never seen a rheumatologist. Some patients present first to an orthopedic surgeon, without

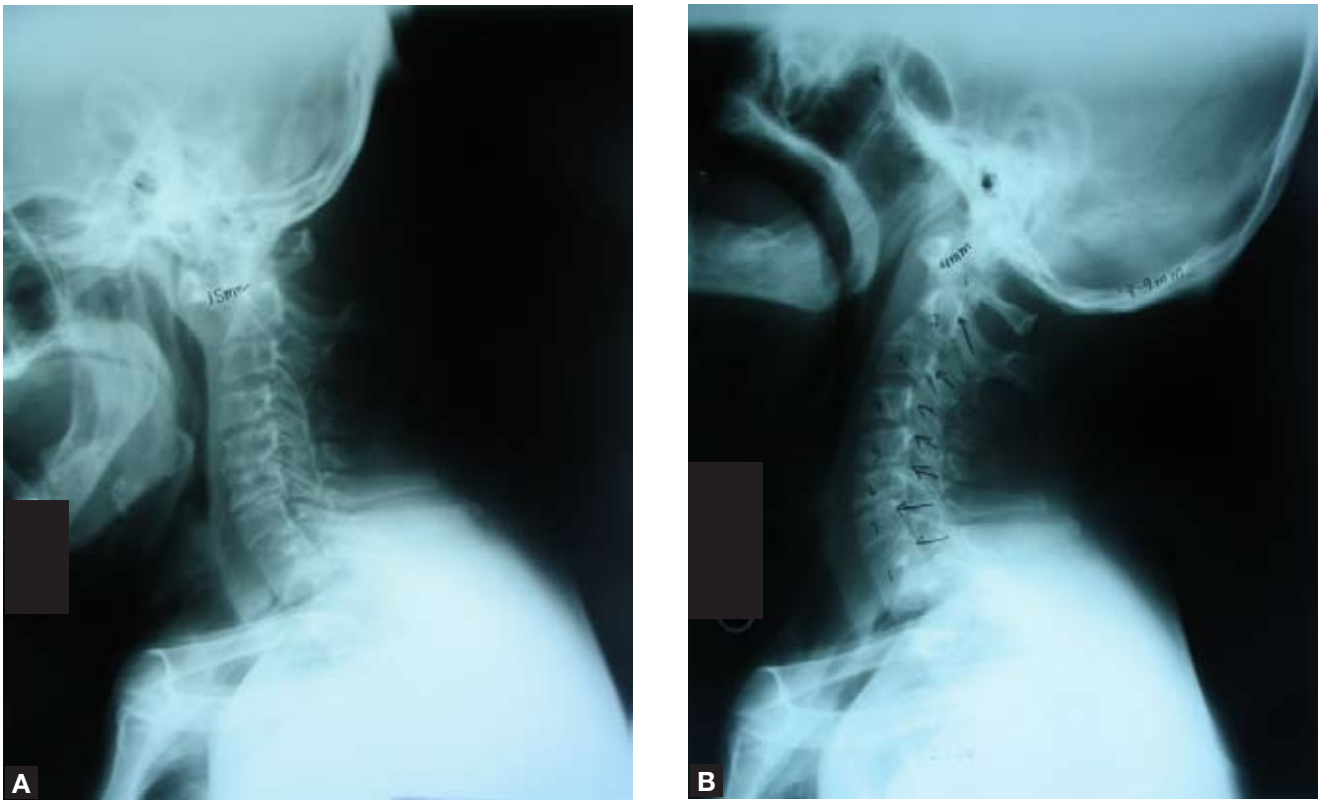

Figure 6. A 56-year-old man with rheumatoid arthritis and cervical myelopathy. Lateral x-rays in flexion **(A)** and extension **(B)** show dynamic C1-C2 instability, basilar invagination, and subaxial involvement by the rheumatoid process. Images courtesy of John Olsewski, MD, Bronx, New York.

having a known diagnosis of RA, while others seek care only for their extremity symptoms and neglect the medical management of their condition. It is critical that orthopedic surgeon and rheumatologist remain in close communication, especially when the disease is in an advanced stage.

Nonoperative management of RA often involves use of disease-modifying antirheumatic drugs (DMARDs), such as steroids, methotrexate, antimalarial drugs, gold, and sulfasalzine. Early, aggressive use of a combination of DMARDs may prevent the onset of cervical spine involvement.[14] Newer medications (etanercept, infliximab, leflunomide), which block tumor necrosis factor α, also appear to lead to improved outcomes. Although orthopedic surgeons may not wish to prescribe DMARDs themselves, they should be aware of the efficacy of these medications and ensure that patients receive them when appropriate.

Other nonoperative interventions are cervical collars, physical therapy, and patient education. Soft cervical collars may provide some pain relief for patients with minor symptoms and for patients who are not surgical candidates. It is important to avoid prolonged use of collars to prevent deconditioning the cervical musculature. Use of neck braces does not alter the natural history of rheumatoid disease in the cervical spine, does not significantly limit spinal motion, and will not prevent progression of neurologic symptoms. Physical therapy focused on the paracervical muscles and posture has been shown to provide symptomatic improvement. Patient education should center on the importance of posture, avoidance of neck flexion, and warning signs of impending neurologic and functional deterioration. One study found lasting pain relief with a comprehensive program consisting of patient education, physical therapy, cervical collars, practical aids, symptomatic treatment, and DMARD use.[15]

4 When should I ask for help?

Although it is never inappropriate to seek a consultation from a spine surgeon for a patient with RA, this resource is especially valuable for patients with significant cervical involvement. Undoubtedly, any RA patient with cervical myelopathy, progressive neurologic deficit, rapid decline in function, or recent loss of ambulation should be evaluated by a spine surgeon. In addition, referral should be made to a spine specialist for any patient with RA and significant atlantoaxial subluxation (as demonstrated by PADI of <14 mm), any amount of cranial settling, or subaxial subluxation with a sagittal canal diameter of less than 14 mm. Patients should have recent cervical spine x-rays and an MRI before visiting the spine surgeon.

Perhaps the most difficult patients to counsel are asymptomatic patients with radiographic evidence of cervical disease. These patients are at risk for neurologic

deterioration, paralysis, and sudden death. Patients at highest risk have PADI of less than 14 mm, basilar invagination, or a subaxial canal diameter of less than 14 mm. Thus, consultation with a spine surgeon is indicated for asymptomatic patients with significant radiographic findings and for cases in which there is a question about the condition of an RA patient's cervical spine.

5 What can others do for my patients?

Surgical Indications

Any RA patient with a progressive neurologic deficit, myelopathy, or severe, disabling neck pain despite nonoperative treatment should be considered for surgical management. In addition, patients with PADI of less than 14 mm, basilar invagination, or subaxial sagittal canal diameter of less than 14 mm should have advanced imaging. In these patients, surgery should be performed, regardless of presence of symptoms, when the true space available for the spinal cord is less than 13 mm or when there is significant flattening of the cord or angulation of the brainstem.[13] Two important caveats to these indications must be mentioned. First, not all patients with RA and significant radiographic or neurologic findings are candidates for spinal surgery. Treatment should be tailored to the individual based on his or her nutritional status, bone quality, and general functional capacity. Patients with long-standing paralysis or severe spinal deformity may not recover function. Second, some surgeons will observe patients who have basilar invagination but lack clinical or radiographic evidence of neurologic compromise. This conservative approach to cranial settling is potentially perilous; patients should be cautioned about the risks associated with postponing surgery and should be followed closely for any change in functional status or radiographic findings.

Surgical Management

Spinal fusion is the hallmark of surgical management of the rheumatoid neck. For patients with significant atlantoaxial subluxation, C1-C2 fusion is the procedure of choice. Traditional wiring techniques, such as the Brooks or Gallie procedures, are commonly used, but newer procedures, such as the Magerl technique and the Harms fusion, are stronger and avoid the need for a cervical collar after surgery. Cranial settling requires an occipital-cervical fusion to stabilize the upper cervical spine. Occipital-cervical fusion can be obtained by a variety of methods, including the Bohlman triple-wire technique, as well as by the use of newer plates, rods, and screws. Treatment of subaxial subluxation also requires spinal fusion. In almost all circumstances, the procedure is performed through a posterior approach using a variety of instrumentation techniques. The one true indication for an anterior approach to the subaxial rheumatoid cervical spine is significant kyphosis. It is critical to stabilize all involved areas of the spine when choosing surgical management of the rheumatoid neck. Progression of instability is almost certain when all aspects of a combined deformity are not included in the fusion (Figure 8).

Figure 7. Sagittal T_2-weighted magnetic resonance image of the patient in Figure 6 shows severe compression of the spinal cord as a result of atlantoaxial subluxation and basilar invagination. Extensive subaxial involvement is also visible. Image courtesy of John Olsewski, MD, Bronx, New York.

Surgical Outcomes

In recent studies, the results of cervical spine surgery in patients with RA have improved. Earlier diagnosis of cervical myelopathy and significant radiographic instability combined with better surgical techniques and perioperative care have contributed to these improved outcomes. Investigators who found high rates of mortality in untreated patients also found significant improvement with surgical management. One study showed 27% mortality 5 years after surgery (73% in untreated myelopathy) and 55% return to walking in nonambulators.[7] Another study showed that 84% of patients were alive 5 years after surgery, and 37% were alive 10 years after surgery, whereas nonsurgical management had a mortality of 100% at 8 years; neurologic improvement was seen in 68% of patients treated surgically.[8]

The best results with surgery appear to be in patients who remain ambulatory despite neurologic deficits. Patients who are unable to walk before surgery are at increased risk for perioperative complications and mortality; in addition, these patients appear less likely to recover neurologic function. According to one report, neurologic improvement occurred in only 62% of nonambulatory patients versus 100% of patients who remained ambulatory despite objective weakness.[11] Worsening of neurologic condition has been reported after surgical intervention; this worsening may be the result of permanent damage to the spinal cord caused by long-standing compression or instability.

Perioperative complication rates are higher for patients with RA than for patients without the disease. Notably, patients with RA are at increased risk for wound complications, infection, pseudarthrosis, and hardware failure. The perioperative mortality rate is approximately 5% to 10%. The rates of these and other complications have been shown to be higher in patients with advanced myelopathy than in less severely affected patients.

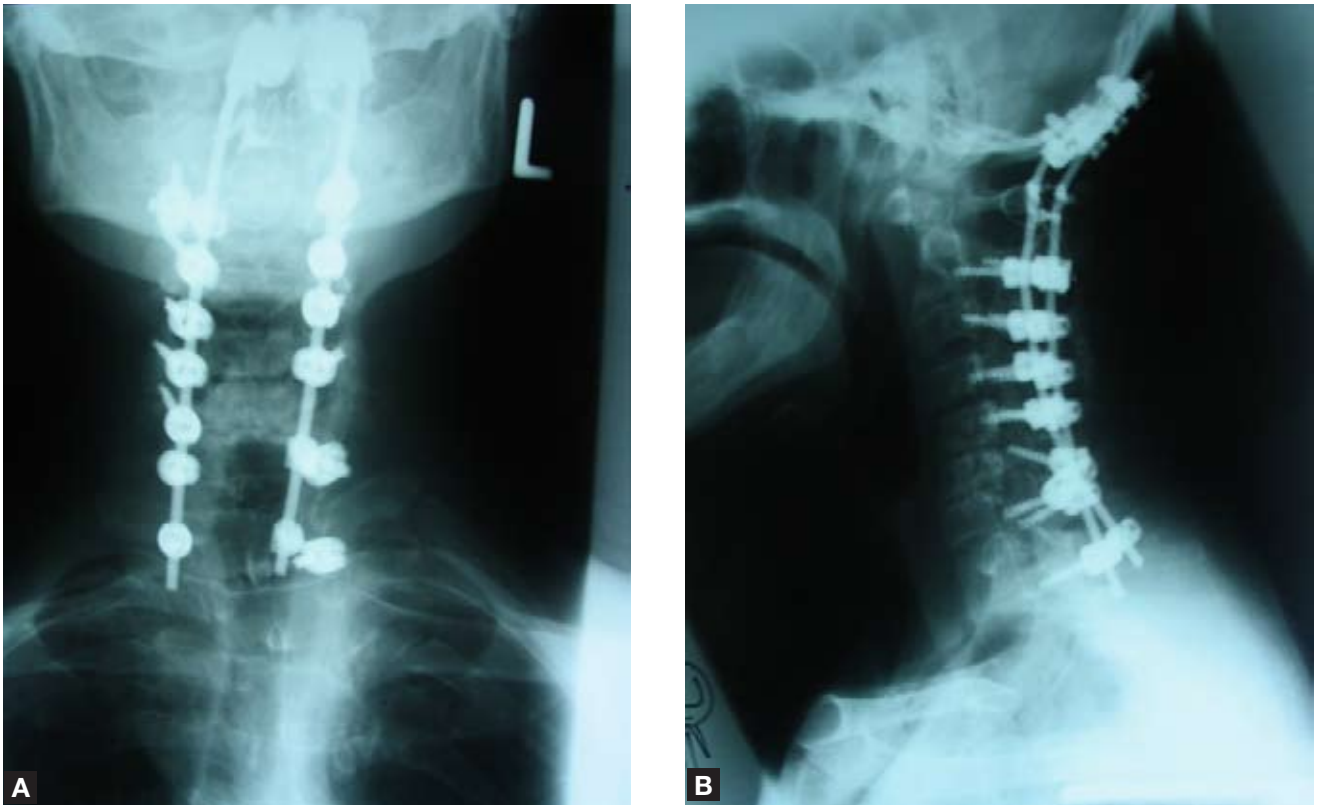

Figure 8. Postoperative anteroposterior **(A)** and lateral **(B)** x-rays of the patient in Figures 6 and 7 show treatment by means of occiput-to-T1 fusion. A combination of screws and wires was used to restore a normal relationship between C1 and C2 and to stabilize all involved segments of the cervical spine. Images courtesy of John Olsewski, MD, Bronx, New York.

Conclusions

Although the prospect of managing RA patients with cervical spine pathology may seem intimidating to the general orthopedic surgeon or nonspine specialist, the simplified approach described in this article will assist in the process. The cervical spine is often involved in the rheumatoid disease process, but not all patients with radiographic findings require surgical treatment. Indications for imaging studies, spine surgeon consultation, and surgery have been presented to guide the treating physician. Certainly, the mainstay of treatment for the rheumatoid neck remains nonoperative, and a rheumatologist should be part of management discussions. All patients undergoing procedures that require anesthesia should have recent x-rays of the cervical spine. Most important, RA in the neck can lead to profound disability, neurologic impairment, and sudden death. There are indications for surgery in asymptomatic patients, and the results of treatment are better in less profoundly affected patients. When doubt exists regarding treatment of the cervical spine in patients with RA, referral to a spine specialist is always prudent.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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