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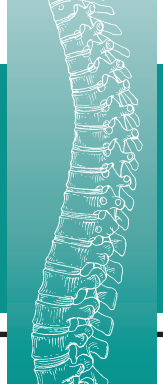

Rheumatoid Arthritis of the Cervical Spine

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LEARNING OBJECTIVES: After participating in this activity, the surgeon should be better able to:

1. Differentiate the three major patterns of cervical spine instability attributable to rheumatoid arthritis.
2. Describe the diagnostic workup of cervical instability.
3. Recall the common principles of surgical treatment for the major patterns of cervical spine instability

Rheumatoid arthritis (RA) involvement of the cervical spine represents a relatively common yet serious condition that frequently leads to morbidity and even death. RA is a chronic, inflammatory autoimmune disorder of unknown primary etiology that targets numerous joints throughout the body.[1] Symptoms result from chronic synovial inflammation that leads to progression destruction of joints, ligaments, and bone, especially at the atlantoaxial joint.[2] The three main patterns of cervical instability that result from RA—which may occur separately or in combination—include atlantoaxial subluxation (AAS), atlantoaxial impaction (AAI), and subaxial subluxation (SAS). Each form of instability can precipitate a range of symptoms and worsen to cause spinal cord compression and potentially death, thus necessitating prompt diagnosis and management to achieve an optimal outcome.

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PATHOPHYSIOLOGY

The prevalence of RA in the United States is 1%–3%.[3] Although much cervical involvement might not be apparent clinically in patients with RA, radiographic involvement is extremely common. Among patients with RA, cervical instability ranges from 17%–86%.[4] Cervical disease begins early (within the first 2 years after diagnosis)[5] and strongly correlates with metacarpophalangeal joint and carpal bone damage.[6] Anatomic abnormalities result from synovitic damage to joints, ligaments, and bone as a result of the inflammatory process. Joint damage can result from degradation of the articular cartilage, whereas distension and rupture of ligaments can alternatively promote instability. In bone, osteoporosis and erosion can lead to a loss of skeletal integrity that can contribute to instability.[7]

The natural history of RA involvement of the cervical spine is one of variable progression. A recent 10-year follow-up of 161 patients with RA noted radiographic progression of cervical subluxation in 57%, whereas other studies have documented progression in 15%–87% of patients.[8–10] Clinical progression, however, is less prevalent (10%–57%), and it is apparently not directly linked with radiographic progression.[11] Risk factors for clinical progression include male sex, rheumatoid factor seropositivity, higher initial C-reactive protein levels, presence of subcutaneous nodules, advanced peripheral joint disease, and use of corticosteroids.[2,10,12]

The three main patterns of cervical instability include AAS, AAI, and SAS. AAS results from either an incompetent transverse ligament or erosion of the dens. Most often subluxation is anterior (70%), although lateral, posterior, and rotational subluxations also can occur.[13] The anterior atlantoaxial interval can be used to measure AAS. The normal interval is 3 mm in adults. An interval greater than 3 mm but less than 7 mm suggests disruption of the transverse ligament, and an interval of 9 mm or more suggests disruption of the entire periodontoid-ligamentous and capsular structures (Figure 1).

AAI, also known as cranial settling, occurs primarily due to bone and cartilage destruction of the atlantoaxial and occipitoatlantal joints. An apparent cranial

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migration of the odontoid process and caudal settling of the cranium characterize it. This represents the most dangerous instability pattern, as there is an increased risk of sudden death from either static or dynamic stenosis of the foramen magnum and compression of the medulla oblongata. In some cases, fixed rotation of the head might occur due to unilateral involvement of the atlantoaxial and occipitoatlantal joints.[14]

SAS is the second most common instability pattern after AAS. It results from destruction of the facet joints, interspinous ligaments, and the discovertebral joints from inflammatory processes.[15] These pathologic changes promote longitudinal collapse, bony erosion, and sagittal plane instability along multiple segments. The final result of the latter change is the characteristic "stepladder" type deformity, indicative of multiple sequential spondylolistheses.

CLINICAL PRESENTATION

Rheumatoid disease of the cervical spine is most commonly asymptomatic. The most common symptoms that arise, however, are neck pain, neurologic symptoms, and death. Neck pain results from peripheral erosive changes around the apophyseal joints and surrounding soft tissues, although occipital headaches often arise from cervical instability that can impinge on the posterior rami of the greater (C1) and lesser (C2) occipital nerves.[14] Patients often report a "clunking" sensation in the neck with movement. A careful physical examination is necessary to identify neurologic signs, which only occur in 7%–34% of patients.[11] Worsening instability can decrease effective spinal canal diameter and promote myelopathy, which is progressive but often difficult to identify by loss of fine motor control, gait imbalance, and global numbness of the hands. Hand deformities and decrease in ambulatory status may be confused with rheumatoid involvement of small and large joints, respectively.[14] More subtle neurologic findings include occipital neuralgia, facial pain from impingement of the trigeminal nucleus, vertebrobasilar insufficiency, and myeloradiculopathy.[2] Various classification systems exist to classify patients with RA of the cervical spine; two of note are the Ranawat system[16] (Table 1) and the more nuanced Zeidman and Ducker modification of the Nurick myelopathy scale[17] (Table 2).

IMAGING

Plain x-rays are an effective tool in assessment of patients with cervical instability. Standard views should include anteroposterior (AP), lateral, open mouth (odontoid), and flexion-extension images. Two measurements are used to assess AAS: anterior atlantodental interval (AADI) and posterior atlantodental interval (PADI). The AADI is measured from the anterior surface of the dens to the posterior margin of the anterior ring of C1, whereas the PADI is the distance between the posterior surface of the dens and the anterior margin of the posterior ring of C1. The normal AADI is 3 mm; a value greater than 5 mm indicates instability.[10,18] PADI, however, has been shown to be a more reliable predictor of neurologic outcome because it assesses the potential space available for the spinal cord.[19] A PADI less than 14 mm is highly (97%) predictive of paralysis, and patients with PADI less than 10 mm do not show neurologic recovery.[2,14]

Varying measures have been used to assess AAI. Based on lateral radiographic views, these methods have different degrees of sensitivity and specificity, so they are used in tandem. The

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Fig. 1 *A 57-year-old woman with a history of rheumatoid disease and painful deformities of the upper and lower extremities presented with a 5-month history of numbness and weakness in the hands. She also noted some clumsiness in walking and manipulating utensils. Lateral x-ray in the neutral position shows anterior atlantodental interval of 17 mm and posterior atlantodental interval of 8 mm, consistent with atlantoaxial subluxation. (Image courtesy of Howard An, MD.)*

majority of these techniques assess the relationship between the tip of the odontoid, the hard palate, and the skull base. McGregor's line connects the posterior margin of the hard palate to the caudal base of the occiput. AAI occurs when the tip of the dens is more than 4.5 mm above the line. This method is used frequently due to its simplicity. Because the dens is sometimes difficult to visualize if it is destroyed or osteopenic, the Redlund-Johnell and Ranawat criteria have been described. The Redlund-Johnell distance is measured as the perpendicular distance from the middle of the lower endplate of the axis to McGregor's line (AAI <34 mm in men, <29 mm in women).[20] The Ranawat criterion is the distance between the center of the pedicle of C2 and transverse axis of C1.[16] The Clark station method uses the position of the atlas in relation to the upper, middle, or lower third of the odontoid process in the midsagittal plane. If the anterior arch of the atlas is level with the middle third (station 2) or the caudal third (station 3) of the dens, AAI is present. Furthermore, Chamberlain's line is drawn from the hard palate margin to the posterior margin of the foramen magnum, and the odontoid tip should not project beyond 3 mm above this line. As no single screening test possesses sensitivity higher than 90%, a combination of three methods—Clark, Redlund-Johnell, and Ranawat—can be most effective. If all methods are used and at least one is positive, the sensitivity for AAI increases to 94%, with a negative predictive value of 91%.[21]

The appearance of SAS on lateral x-rays includes listhesis of sequential vertebral bodies and posterior element changes

Table 1. Ranawat Classification of Rheumatoid Myelopathy

Class	Description
I	No deficit
II	Subjective weakness, hyperreflexia
IIIa	Objective weakness, ambulatory
IIIb	Objective weakness, nonambulatory

Table 2. Zeidman and Ducker Modification of Nurick Grading

Grade	Radiculopathy	Myelopathy	Gait	Hand Function
0	Present	Absent	Normal	Normal
I	Present	Present	Normal	Slight abnormality
II	Present	Present	Mildly abnormal	Functional
III	Present	Present	Severely abnormal	Unable to button
IV	Present	Present	Only with assistance	Severely limited
V	Present	Present	Nonambulatory	Useless

(Figure 2). Weakening of the interspinous ligaments along with facet joint destabilization creates a "stepladder" appearance. Subluxation most often occurs anteriorly, although lateral and posterior subluxation are possible. The critical measure on lateral flexion/extension views is the spinal cord diameter behind the slipped vertebra: if distance is less than 14 mm, cord compression is possible. Thus, an MRI scan should be ordered if canal diameter is less than 14 mm or if neurologic symptoms are present.

CT and MRI are two additional imaging modalities with a role in managing RA of the cervical spine. CT provides superior detail of bony anatomy and identification of cranial settling. With contrast infusion, CT myelography can demonstrate cord compression effectively. MRI can identify soft tissue irregularities and demonstrate erosion, periodontoid pannus, and inflammation. Importantly, MRI can be used to assess the craniomedullary junction, with a notable correlation between the presence of myelopathic signs and a cervicomedullary angle less than 135 degrees, which is an indication for surgery.[22]

SURGICAL EVALUATION

The goals of surgery should be pain relief, spinal realignment, and decompression to relieve neurologic deficits. Optimal preoperative treatment should include a rheumatologic evaluation and maximal treatment with nonsteroidal anti-inflammatory drugs (NSAIDs), disease-modifying antirheumatic drugs, and other pharmacologic agents for disease and pain control.[23] Because RA is a chronic, debilitating disease, conservative therapy does not typically alter the disease course. Boden et al. found in a series of 73 patients at 20 years of follow-up that all patients treated nonoperatively had worsening neurologic

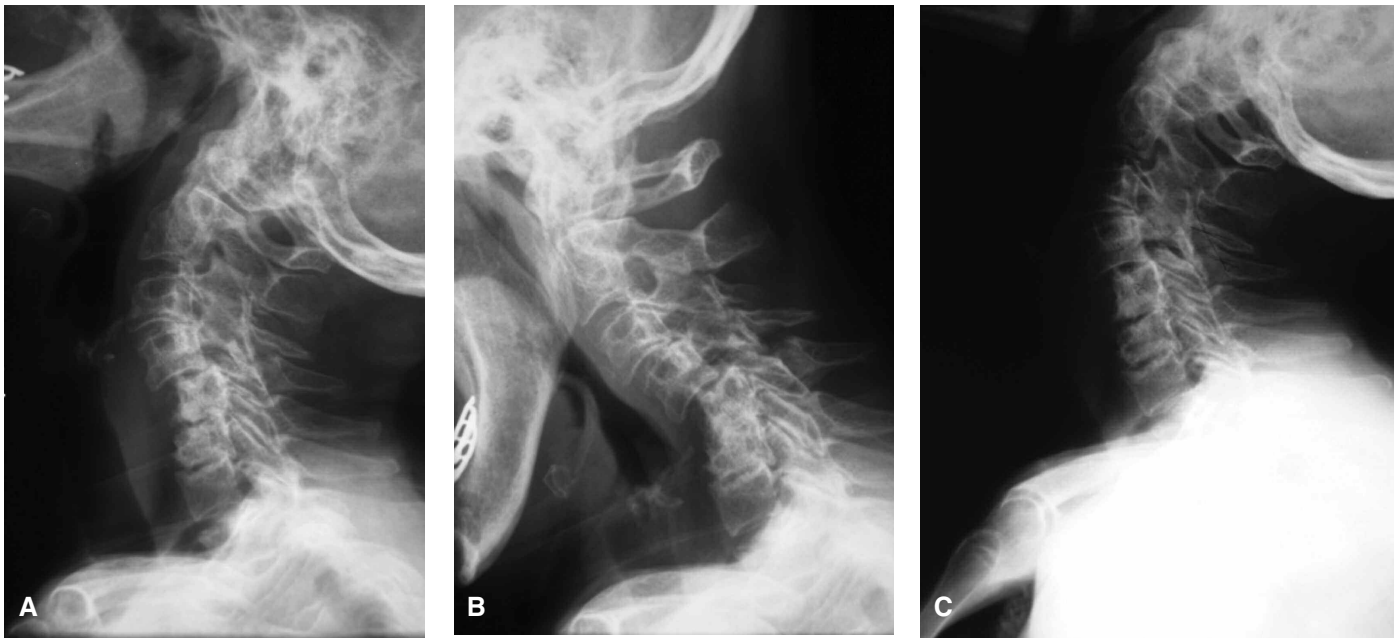

Fig. 2 *A 45-year-old woman with a history of advanced rheumatoid disease of the hands reported progressive neck pain and instability over a 9-month period. Lateral x-rays at the neutral position (A), in flexion (B), and in extension (C) demonstrate notable subaxial subluxation at the C4-C5 level. (Images courtesy of Howard An, MD.)*

Table 3. Surgical Indications in Patients With Rheumatoid Arthritis Of the Cervical Spine

Category	Description
Absolute	Neurologic deficit Intractable pain with spinal instability
Strongly indicated	Atlantoaxial subluxation with PADI ≤14 mm Atlantoaxial impaction ≥5 mm rostral to McGregor's line Subaxial subluxation with sagittal canal diameter ≤14 mm Space available for cord ≤ 13 mm Spinal cord diameter <6 mm in flexion Cervicomedullary angle <135 degrees

deficits.[19] Another study by Marks and Sharp noted a 50% mortality rate in patients with cervical myelopathy treated nonoperatively.[24] Consideration should also be given to the quality of bone stock, the presence of irreducible subluxations, the medical condition of the patients, and the need for fiberoptic intubation.

Decompression of nerve impingement is a frequently recognized indication for surgery. In neurologically intact patients without evidence of instability, however, surgery is controversial.[2] The current trend is toward prophylactic stabilization of the cervical spine in patients with RA to prevent irreversible neurologic deficits, which typically arise in the natural history of the disease. Surgical indications are listed in Table 3.

Imaging findings are often crucial to establish the severity of disease. Radiographically, Boden et al. found that PADI is the most effective tool in determining neurologic risk.[2,19] The criteria for determining whether to perform surgery in patients without neurologic findings, as determined by Boden et al., include the following: AAS with PADI 14 mm or less; AAI at least 5 mm rostral to McGregor's line; or SAS with sagittal canal diameter 14 mm or less.[19] MRI findings that suggest surgical intervention in patients with asymptomatic instability include cord space 13 mm or less, spinal cord diameter less than 6 mm in flexion, and a cervicomedullary angle less than 135 degrees.[22,25] Surgical treatment methods for the three different causes of RA cervical instability are considered separately.

SURGICAL TREATMENT

Atlantoaxial Subluxation

The approach to treatment of patients with AAS hinges on whether the deformity is reducible. If it is reducible, potential treatment techniques include posterior atlantoaxial fusion using a Gallie or Brooks wiring approach (with bone graft), C1-C2 lateral mass screw technique, or C1-C2 transarticular Magerl screw technique.[26] For the Gallie wiring method, a sublaminar loop is placed around C1, and a second wire is placed through and around the base of the spinous process of C2, with both wires piercing iliac crest strut grafts.[27] The Brooks variation uses bilateral sublaminar wires beneath C1 and C2, as opposed to only C1.[14] The advantages of screw fixation, however, are that it allows for segmental fixation, deformity reduction, and enhanced biomechanical rigidity.[28] If AAS is nonreducible, screw fixation with a C1 laminectomy or occipitocervical fusion is indicated. If bone does not impinge upon the cord anteriorly, an odontoid resection may not be warranted, as MRI studies demonstrate pannus resorption after stabilization.[29] The Harms technique is an effective method of fixation that has been popularized recently. This method allows for segmental posterior fixation, can be used in

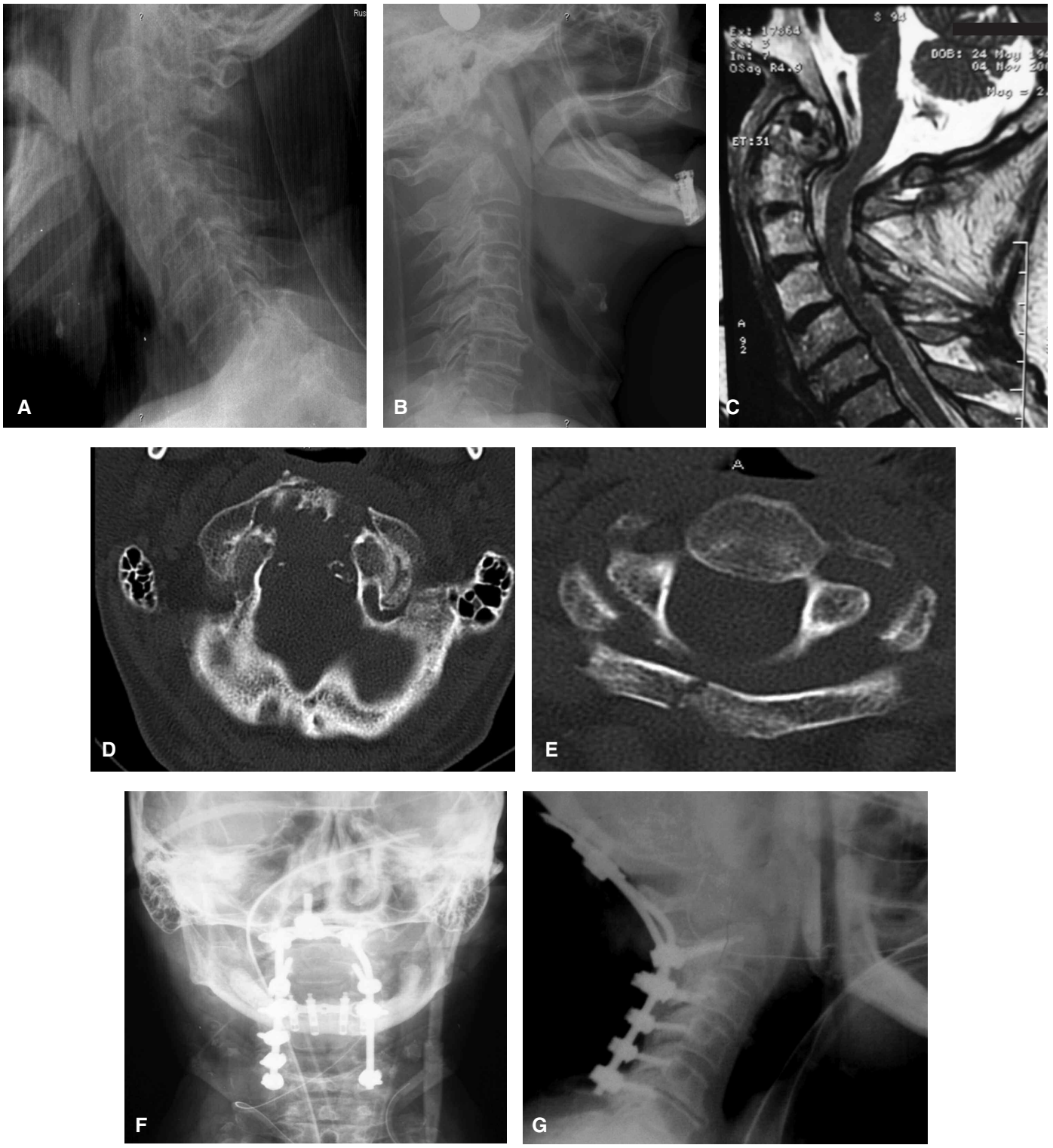

Fig. 3 *A 65-year-old man with a history of rheumatoid arthritis (including multiple joint deformities) and chronic methotrexate/corticosteroid use presented with a 6-month history of progressive neck pain. He also experienced difficulty walking and dysarthria/dysphagia of 1 month's duration. Lateral x-rays from the left side were taken before (A) and after (B) the application of 25 pounds of traction to the neck. Note the presence of subaxial subluxation at C4-C5 and the erosion of C2 at the C1-C2 junction. After traction, symptoms improved, and the overall cervical alignment improved. C, Preoperative sagittal MRI scan demonstrates pannus posterior to the C1 vertebra. In addition, there is cord effacement in the subaxial spine most notably at C3-4 and C4-C5. D, Axial CT scan at the C1-C2 level demonstrates extensive destruction of the C1-C2 joint articulation. E, Posterior fracture of the C1 ring is also visible. Postoperative anteroposterior (F) and lateral (G) x-rays show occipitocervical fusion with screw fixation. (Images courtesy of Kern Singh, MD.)*

the setting of anomalous vertebral arteries, and allows for reduction of previously "irreducible" C1-C2 deformities.

Atlantoaxial Impaction (AAI)

Management of AAI requires a high degree of vigilance due to the capacity of impaction to worsen, causing brainstem herniation and death. A preoperative halo brace is recommended to attempt reduction of the deformity. If successful, occipitocervical fusion is indicated.[30] This can be accomplished through either wiring or plating. Wiring constructs offer a successful basis for fusion, even when the bone stock is poor; however, they require use of an external orthosis postoperatively. Occipitocervical plating offers a more rigid level of fixation, provided adequate bone stock is present.[31] This technique may be technically challenging to produce, given the difficulty in producing the correct amount of contour at the base of the skull. If reduction cannot be accomplished, symptomatic decompression with transoral odontoidectomy or C1 laminectomy with posterior stabilization is necessary.[26]

Although posterior stabilization is the mainstay of AAI surgical therapy, anterior approaches (either transoral or extrapharyngeal) are occasionally necessary. An anterior approach may be needed if there is evidence of significant anterior pannus, marked vertical translocation of the odontoid greater than 5 mm, or persistent neurologic deficits in which the anterior pannus has not resolved after a solid posterior fusion has been performed. A major disadvantage of the transoral anterior approach is the potential infection from the mouth flora, which is not present in the extrapharyngeal approach. The results from anterior odontoid resection are variable, in part due to the baseline severity of patient disease, and supplemental posterior fixation may also be required.[32]

Subaxial Subluxation

The treatment for SAS is variable, dependent on whether it is fixed or mobile. Preoperative halo use can provide temporary stabilization in both types of SAS, often with immediate improvement in neurologic deficits.[31] If a fixed subluxation is present that cannot be reduced, anterior decompression with corpectomy and reconstruction with strut graft may be necessary.[16] Strong consideration should also be given to supplemental posterior fixation, as graft resorption and settling can cause anterior column instability. Mobile subluxations are best treated with traction and instrumented posterior fixation with lateral mass screws (Figure 3).

Posteriorly, several methods of lateral mass screw fixation can be used, although we prefer the method popularized by An et al.[33] Nevertheless, all of the techniques for lateral mass screw fixation avoid damage to the vertebral artery, which lies anterior to the lateral mass. Notably, the C7 lateral mass is thin and may require screw fixation in the pedicle as opposed to the lateral mass or supplemental posterior wiring between the C6-C7 spinous processes. Fusion should extend at least to the distal involved level, although some authors recommend extending to T1 or T2 to minimize the risk of adjacent level instability.[34,35]

CONCLUSION

Cervical instability is a serious yet not altogether rare complication of RA. Although radiographic changes frequently accompany arthritic changes, the incidence of significant neurologic deficits is relatively small. Thus, the goal for treatment of cervical instability is to avoid irreversible neurologic deterioration if possible, and prophylactic stabilization remains a popular option given the natural history of disease progression. X-rays represent the most effective imaging modality to determine cervical involvement, and various criteria have been described that offer definitive indications for surgical intervention. Overall, careful patient selection and advances in medical therapy and surgical techniques may now allow for significant improvement in neurologic symptoms, pain relief, and avoidance of the severe complications associated with cervical instability from rheumatoid disease.

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1. The most common pattern of cervical involvement in rheumatoid arthritis (RA) is
A. basilar invagination
B. subaxial subluxation
C. atlantoaxial subluxation
D. atlantoaxial impaction

2. Lateral x-rays reveal subaxial subluxation in a 70-year-old man with RA who reported neck pain. He is positive for rheumatoid factor and has notable rheumatoid involvement of the metacarpophalangeal joints of both hands, with subcutaneous nodules on several bony prominences. Which one of the following factors is *not* associated with clinical progression of disease?
A. Male sex
B. Advanced age
C. Positive rheumatoid factor
D. Presence of subcutaneous nodules

3. A 40-year-old woman with RA presents with severe neck pain and right arm numbness of 3 months' duration. X-rays confirm likely impingement of the spinal cord at the C6 level. On physical examination, she is able to walk normally except for a slight wobble. Her hand function is not grossly abnormal, although hand grip strength is 4 of 5. Her classification according to the Zeidman and Ducker system is grade
A. I
B. II
C. III
D. IV

4. Which one of the following radiographic measurements is *most* indicative of neurologic injury from atlantoaxial subluxation?
A. posterior atlantodental interval = 15
B. posterior atlantodental interval = 12
C. anterior atlantodental interval = 3
D. anterior atlantodental interval = 5

5. A combination of which three radiographic measurements has been shown to be most effective in measuring atlantoaxial impaction?
A. McGregor's line, Redlund-Johnell distance, Clark station
B. McGregor's line, Chamberlain's line, Ranawat criterion
C. Clark station, Redlund-Johnell distance, Ranawat criterion
D. Redlund-Johnell distance, Ranawat criterion, Chamberlain's line

6. In patients with potential subaxial subluxation, when should an MRI be ordered?
A. Neurologic symptoms are present.
B. The space behind the slipped vertebra is less than 14 mm.
C. Multiple levels of listhesis are present, creating a "stepladder" deformity
D. A and B

7. Surgical intervention should be considered in patients with asymptomatic cervical instability and all of the following MRI findings, *except*
A. cervicomedullary angle less than 135 degrees
B. cord space 13 mm or less
C. inflammation, periodontoid pannus, and bony erosion
D. spinal cord diameter less than 6 mm in flexion

8. The most common presentation of RA disease of the cervical spine is
A. neck pain
B. neurologic symptoms
C. death
D. no symptoms (asymptomatic)

9. An anterior approach should be used to treat atlantoaxial impaction when the patient has
A. significant anterior pannus despite posterior stabilization
B. preoperative neck stiffness
C. horizontal translation of the dens greater than 1 mm with neck movement
D. previously undergone posterior cervical surgery

10. Which of the following is/are an advantage of halo bracing prior to definitive surgical treatment?
A. Stabilization of the spine
B. Improvement in neurologic deficits
C. Determination as to whether instability is reducible
D. All of the above