Original Article

Diffuse idiopathic skeletal hyperostosis: A functional enemy of vertebral stability – Case series and surgical consideration of craniovertebral junction involvement

ABSTRACT

Context: Diffuse idiopathic skeletal hyperostosis (DISH) or Forestier's syndrome may reduce vertebral mobility, thus affecting the stability of adjacent vertebral segments and promoting spinal stenosis, vertebral dislocation, and unstable fracture secondary to low-energy trauma.

Aims: This study aimed to contribute with a case series of three patients affected by DISH undergone surgery with occipitocervical fixation for craniovertebral junction (CVJ) instability since the poor literature about CVJ instability and surgery in patients affected by DISH.

Settings and Design: This was a multicentric case series.

Subjects and Methods: Literature about CVJ instability and surgery in patients affected by DISH is poor. Thus, we present a case series of three patients affected by DISH, who underwent surgery with occipitocervical fixation with different clinical and radiological patterns.

Results: CVJ represents one of the most mobile joints of the spine and is at greater risk for instability. Moreover, instability itself may act as *primum movens* for several degenerative conditions such as cervical spondylosis, ossification of the posterior longitudinal ligament, and cervical deformities. On the contrary, DISH itself may worsen CVJ instability because of subaxial spine stiffness. In case of DISH, the rigid unit formed by several ossified vertebral bodies acts as a long lever arm, increasing the forces applied to the hypermobile CVJ and reducing the dynamic buffer capability of ossified spine. On the other hand, vertebral instability increases the odds of fractures. In such cases, CVJ posterior instrumentation and fusion is an effective and feasible surgical technique, aimed to restore vertebral stability and to halt the progression of spinal stenosis.

Conclusions: Due to the altered dynamics cervical spine along with the possible comorbidities, treatment indication and surgery for patients affected by DISH must be tailored case by case.

Keywords: Craniovertebral junction, diffuse idiopathic skeletal hyperostosis, instability, occipitocervical fixation

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INTRODUCTION

The spine is frequently affected by several degenerative conditions, which may undermine vertebral stability. Among these, diffuse idiopathic skeletal hyperostosis (DISH) or Forestier's syndrome may segmentally reduce vertebral mobility, thus affecting the stability of adjacent vertebral segments. DISH was first described in 1950;[1] according to Resnick and Niwayama criteria, it is characterized by the presence of flowing calcification and ossification along the anterolateral aspect of at least four contiguous vertebral

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bodies with or without associated localized osteophytes at vertebral body-intervertebral disc junctions.[2] Moreover, the intervertebral disc height of the involved segment is preserved and radiologic features of intervertebral disc degeneration such as vacuum phenomena and marginal sclerosis are absent. It has been reported a general prevalence of more than 10% in a population over 50 years old.[3] The pathophysiology of DISH still remains unknown, whereas known risk factors are older age, male sex, obesity, hypertension, atherosclerosis, diabetes mellitus, and hyperuricemia.[4]

Vertebral hyperostosis causes cervical ankylosis, which leads to dysphagia and spinal stiffness that ends up with chronical pain, often without neurological impairments. The last consequence of cervical ankylosis is the abolition of cervical range of motion.[5,6]

The absence of apophyseal joint ankylosis and sacroiliac joint erosion, sclerosis, or intra-articular osseous fusion discriminates DISH from ankylosing spondylitis (AS).[2,7,8] As a result of ankylosis, DISH may promote segmental instability of the adjacent vertebral segments above and below the affected spine; this instability may be associated with spinal stenosis, vertebral dislocation, and unstable fracture such as odontoid fracture secondary to low-energy trauma.[9,10]

Odontoid fractures represent 9%–15% of all cervical fractures and are the most common vertebral fractures in patients older than 70 years.[11]

Odontoid fractures are categorized by several classifications; Anderson-D'Alonzo is the most commonly used classification; this categorizes odontoid fractures according to the location:[12]
- Type I: Oblique fracture through the odontoid tip
- Type II: Fracture through the base of the dens
- Type III: Fractures through the body of C2.

This classification has been improved by Grauer *et al*. in 2005 by the distinction of Type II fractures into three subcategories:[13]
- Type II A: Transverse fractures without comminution and with < 1 mm displacement
- Type II B: Fractures that pass from anterior superior to posterior inferior or displaced transverse fractures (>1 mm)
- Type II C: Fractures that pass from anterior inferior to posterior superior or fractures with significant comminution.

Since the common incidence of DISH is in older age, odontoid fracture is often associated with several comorbidities. This aspect must be taken into account during treatment planning as it profoundly affects the choice of surgical strategy and postoperative outcomes.[11]

Literature about craniovertebral junction (CVJ) instability and surgery in patients affected by DISH is poor. Thus, we feel to contribute with a case series of three patients affected by DISH undergone surgery with occipitocervical fixation for CVJ instability.

SUBJECTS AND METHODS

We retrospectively reported clinical data of three patients affected by DISH, who underwent surgery for CVJ instability at two different Institutions (University of Palermo and Fondazione Policlinico Universitario "A. Gemelli" IRCCS). Patients' personal health records were analyzed and radiological images were retrieved. Patients' history, clinical presentation, indications and type of surgery, clinical course, and follow-up were reported and discussed.

RESULTS

Case 1
A 57-year-old man, with a recent diagnosis of seronegative spondyloarthritis (SA), complained of a 2-year history of recurrent paraparesis and frequent falls. Computed tomography (CT) scan and magnetic resonance imaging (MRI) examinations revealed high-density tissue at the posterior aspect of the odontoid, causing spinal canal stenosis and spinal cord compression; this tissue was associated with ossification of the anterior longitudinal ligament and posterior intervertebral ligaments. The absence of ossification of the anterior sacroiliac ligament was also evidenced by pelvis X-ray. CT angiography showed a normal course of the vertebral arteries with right dominance. Overall radiological findings were consistent with the diagnosis of DISH in the context of SA. Neurophysiological tests documented altered somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) [Figure 1].

Neurological examination revealed spastic tetraparesis with bilateral hyperevocable reflexes, achilleus clonus, and Babinski sign; autonomous walking was not possible, requiring a wheelchair.

Given these evidence, the patient underwent 1-stage spinal cord decompression through transoral approach, since it has been shown as the most convenient and safe anterior approach to CVJ,[14] in order to relieve the spinal cord ventral compression. Then, C0–C3 occipitocervical
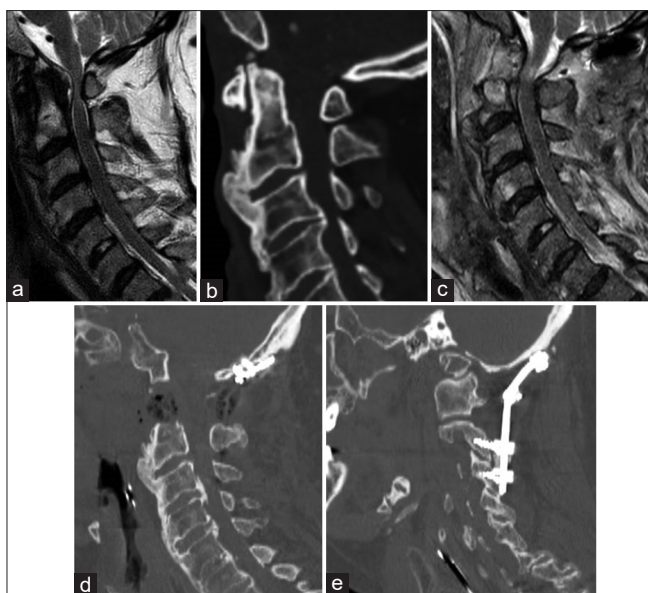
Figure 1: Preoperative sagittal T2-weighted magnetic resonance (MR) (a) and computed tomography (CT) scan (b) Ventral medullary compression and ossification of the anterior longitudinal ligament from C2 to C5 attributable to diffuse idiopathic skeletal hyperostosis, along with bulbomedullary compression. Postoperative sagittal MR imaging (c) and CT scan showing craniovertebral junction decompression and occipitocervical instrumentation (d-e)

fixation was performed, since C1 lateral masses were not suitable for Goel's C1–C2 instrumentation because of their reduced thickness and unfavorable angle due to occiput prominence. Fusion with autologous bone fragments and hydroxyapatite was performed. The postoperative course was uneventful despite a transient urinary infection treated with antimicrobial therapy. After surgery, the patient did not complain of any other neurological impairments or swallowing difficulties. The postoperative CT and craniocervical MRI showed bulbomedullary decompression and the correct placement of instrumentation. After hospital discharge, the patient underwent rehabilitation with gradual improvement of preoperative symptoms at 6 months and a progressive return to a near-normal quality of life 1 year after surgery.

Case 2

A 78-year-old man complained of a 1-year history of progressive spastic tetraparesis determining a reduction of the autonomy of daily activities. Cervical MRI and CT scan documented a multilevel cervical stenosis, an ossification of the anterior longitudinal ligament compatible with the diagnosis of DISH, and a focal ossification of the posterior longitudinal ligament (OPLL) at C3–C4 level determining a ventral compression of the spinal cord. Dynamic X-ray showed local instability. SSEPs and electromyography (EMG) showed sensory pathway impairments and a right C7 axonal chronic polyneuropathy. The absence of ossification of the
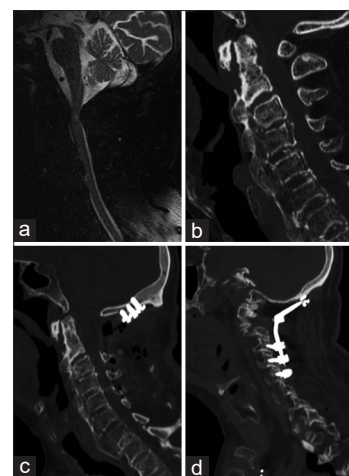

Figure 2: Preoperative sagittal T2-weighted magnetic resonance imaging (a) and computed tomography (CT) scan (b) showing stenosis of the central spinal canal and ventral spinal cord compression, consistent with ossification of the anterior longitudinal ligament and posterior vertebral arches ligaments. Postoperative CT scan (c) showing craniovertebral junction decompression and occipitocervical instrumentation (d)

anterior sacroiliac ligament was also evidenced by pelvis X-ray. CT angiogram showed an abnormal course of vertebral arteries [Figure 2].

Neurological examination showed moderate spastic tetraparesis affecting mostly right and lower limbs, hampered walking with small steps possible only with support, difficulty in postural changes, and urinary incontinence.

Given these evidence and the preoperative cervical instability, the patient underwent posterior cervical C1–C2 decompression and standard C0–C3–C4–C5 occipitocervical fixation. Fusion with autologous bone fragments and hydroxyapatite was performed. During the postoperative course, the patient showed a mild improvement of preoperative neurological impairments, without complaining of any swallowing difficulties attributable to the occipitocervical fixation. Postoperative craniocervical CT scan was performed and showing satisfactory bulbomedullary decompression without complications, and the correct placement of instrumentation. During follow-up, after physical therapy and rehabilitation, the patient showed a gradual recovery from preoperative neurological impairment with partial gait improvement at 12 months after surgery.

Case 3

A 77-year-old male presented to the emergency department after an accidental fall with head-and-neck trauma. His past medical history was positive for hypertension, chronic atrial fibrillation, diabetes mellitus Type 2, and benign prostatic hypertrophy and an inveterate dysphagia. At the admission,
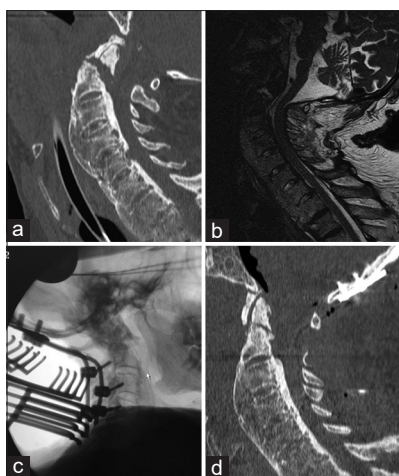
Figure 3: Cervical computed tomography (CT) scan showing the odontoid fracture with displacement of the odontoid process and the ossification of the anterior longitudinal ligament compatible with diffuse idiopathic skeletal hyperostosis (a). Cervical magnetic resonance imaging showing the odontoid fracture with displacement of the odontoid process and slightly stretched spinal cord (b). Intraoperative fluoroscopy showing occipitocervical fixation (c). Postoperative cervical CT scan with fracture reduction and occipitocervical fixation (d)

the patient complained of neck pain without any neurological impairments. Head-and-neck CT examination performed in emergency showed a Type II displaced odontoid fracture with cervical DISH [Figure 3].

During the hospitalization, the patient underwent cervical immobilization by using a hard cervical brace. A second CVJ CT and MRI scan confirmed the transverse odontoid fracture with posterior displacement of the odontoid process without spinal cord compression, tiny bone shards along the fracture lines with inflammatory/reactive imbibition, and the ossification of the anterior longitudinal ligament from C2 to T2. A subsequent preoperative CT angiogram showed the normal course and anatomy of the vertebral arteries. The absence of ossification of the anterior sacroiliac ligament was also evidenced by pelvis X-ray.

Given the higher risk of pseudoarthrosis with conservative management and the need for prolonged immobilization, the patient declined the conservative option, opting for the surgical strategy. Thus, a reduction and posterior C1–C2 fixation was planned, but due to cardiovascular instability with drug-resistant arterial hypotension, surgical procedure was prematurely interrupted, and the patient was transferred to intensive care unit (ICU) for vitals stabilization and a subsequent tracheostomy. After 10 days, finally the patient underwent surgical procedure.

After the odontoid fracture, reduction was verified by intraoperative fluoroscopy. Subsequently, due to bone

inconsistency, an occipitocervical decompression and fixation with C0–C2–C3–C4 screws was performed. Since the lack of spinal cord compression, C1–C2 laminectomy was not deemed necessary. Fusion with autologous bone fragments and hydroxyapatite was performed. Intraoperative neurophysiologic monitoring, performed by evaluation of MEPs, SSEPs and EMG, showed no changes throughout the procedure.

After the surgical procedure, the patient was transferred again to ICU for postoperative care. Immediate postoperative course was uneventful and postoperative CT scan showed the reduction of the odontoid fracture and the proper CVJ fixation.

In ICU, the patient's clinical course was complicated by respiratory dysfunction, thus tracheostomy was maintained. In addition, the patient developed renal failure, thus he underwent dialysis; then, he also developed liver failure and pressure ulcers for prolonged bedding, which were medicated daily with collagenase ointment, dressings with polyurethane patch, and paraffin greasy gauze and finally with surgical curettage. The progressive worsening of systemic conditions over 3 months finally led to multi-organ failure and the patient's death.

DISCUSSION

Ossification and atlantoaxial instability
The concept of atlantoaxial instability (AAI) is well known in the literature. Since CVJ represents one of the most mobile joints of the spine, it is at greater risk of instability and AAI is the most common among other spinal segments.[15] AAI can be determined by several variables, but the dysfunction of ligamentous complex is primarily responsible for CVJ instability. The subsequent clinical presentation may vary according to the severity of CVJ instability. Chronic instability can lead to a permanent lengthening of a ligament over time, which causes abnormal joint loads, chronic subluxation, and subsequent worsening of instability.[16] It has been postulated that instability itself may act as *primum movens* for several conditions such as cervical spondylosis, OPLL, cervical kyphotic and scoliotic deformities, fibrous abnormal proliferation, Chiari malformation, syringomyelia, and basilar invagination.[17-22] According to these premises, every condition causing subaxial spine stiffness may worsen CVJ instability. This condition may be represented by DISH, which is responsible for ossification and greater stiffness of the subaxial spine.

Regarding pathophysiology, although DISH clinically differs from OPLL, some molecular pathways may be shared by OPLL

and DISH itself. In particular, growth factors (e.g., insulin, insulin-like growth factor 1, transforming growth factor-β1, platelet-derived growth factor-BB, prostaglandin I2, and endothelin 1) may promote the transformation of mesenchymal cells into fibroblasts and osteoblasts. Reduced activity of inhibitors of bone-promoting peptides (e.g., matrix Gla protein, bone morphogenetic protein-2 inhibition, or Dickkopf-1) may also promote ossification. Regarding the natural history of DISH, hyperostosis initially involves cortical bone of the anterior surface of vertebral bodies. Because of hyperostosis, osteophytes gradually form at vertebral margins, particularly at the inferior lip of the vertebral body, progressively expanding across the intervertebral space sparing intervertebral disks, projecting forward to the neck soft tissues. and even displacing pharyngeal structures.[3] Thus, the ossification of contiguous vertebrae causes cervical stiffness. In this way, the rigid unit formed by several ossified vertebral bodies acts as a long lever arm, increasing the forces applied to the hypermobile CVJ and reducing the dissipation capability of the ossified spine. In this scenario, vertebral ossification promotes CVJ instability and increases the likelihood of vertebral fracture along the ossified spine. In addition, the CVJ instability results, as an initially compensatory phenomenon, in the production fibrous tissue, which, in turn, results in spinal cord compression.[3,21,23]

In front of vertebral instability and subsequent spinal stenosis caused by progressive ossification, spinal decompression and vertebral fixation are two surgical procedures aimed together to restore the vertebral canal caliber and to counteract CVJ instability, thus preventing further ossification and halting the pathophysiology of spinal stenosis in DISH.[24]

Ossification and odontoid fracture

Odontoid fracture is a common type of injury in the geriatric population. Surgical treatment is recommended for odontoid Type II fractures in patients ≥7 years of age with displacement ≥5 mm, or signs of instability/nonunion despite halo vest, concomitant myelopathy, and disruption of the transverse ligament, which increases the risk of delayed instability. Otherwise, management of odontoid Type II fractures may be conservative with prolonged immobilization with cervical brace or halo vest and staged clinical-radiological follow-up.

Odontoid fractures and concomitant cervical DISH have been rarely reported. Literature about cervical spine fractures with underlying DISH is scarce.[21,25-27] Among the available case series and reports, very few cases of odontoid fracture with 1 concomitant DISH were reported and they are summarized 2 in Table 1.[5,28,29]

Management considerations

The treatment of odontoid fracture in DISH is tailored to the specific case since defined guidelines still lack. In the case published by Omar and Mesfin in 2017,[5] the patient reported Type II odontoid fracture falling after a syncopal event. He was neurologically intact and was treated with a nonsurgical approach through immobilization with a rigid cervical brace. A different choice was taken in the case described by Tsuji *et al.*[28] where a patient reported a misdiagnosed fracture after a bicycle fall. Three months later, an odontoid fracture with concomitant DISH was diagnosed by cervical CT scan and the patient underwent two-step surgical approach: first, the patient underwent reduction of odontoid fracture and immobilization; then, subsequent occipitocervical fixation was performed. Finally, Whang *et al.*[21] reported a case of a patient with posttraumatic C2 fracture causing complete sublesional anesthesia and tetraplegia, who underwent external immobilization with halo vest.

The management of odontoid fracture in elderly patients is complex and must consider several factors and possible comorbidities.[30] Taking into account only general trauma, the mortality increases with age: 2% mortality rate in patients younger than 65 years, 5% in patients older than 65 years, and up to 9% in patients older than 85 years. Another factor to consider is the longer length of stay (LOS) in the ICU. In fact, in elderly patients, it is about 6.7 ± 9.2 days and tends to be significantly longer in cases of preexisting comorbidities such as diabetes or pulmonary disease, having a negative impact on outcome and prognosis.[31] Early postoperative mobilization can mitigate the odds of complications; however, early mobilization may not be always possible due to the patient's specific conditions and comorbidities.[32]

In our cases, all the patients underwent decompression and fusion.

Table 1: Summary of literature review about C2 fracture with concomitant cervical diffuse idiopathic skeletal hyperostosis

Author and year	Type of article	Age, sex	Clinical manifestation	Level of fracture	Treatment
Omar, 2017[5]	Case report	73 years, male	Neck pain	C2	Halo vest
Tsuji, 2015[28]	Case report	73 years, male	Neck pain	C2	Surgery + halo vest
Paley, 1991[29]	Case report	N/A	N/A	C2	C1–C2 fixation
Whang, 2009[21]	Clinical series	N/A	ASIA: A	C2	Halo vest

N/A: Not available, ASIA: American Spinal Injury Association Impairment Scale

Patient 1 (57 years old) was approached both with anterior and posterior decompression and fusion due to the presence of anterior fibrous tissue compressing the cord and the absence of clinical contraindications. The younger age along with the favorable general conditions allowed one stage combined approach without complications.

In case 2 (78 years old), due to the prevalence of posterior compression, a single posterior decompression and fusion approach was preferred and the postoperative follow-up was uneventful.

In case 3 (77 years old), due to the prevalence of posterior compression, a single posterior decompression and fusion approach was preferred, but the patient's preoperative chronic atrial fibrillation, hypertension, and diabetes mellitus negatively contributed to intraoperative management and the global postoperative course. In fact, in these patients, comorbidities increase the odds of complications both in case of conservative treatment and surgery. In particular, pulmonary complications (e.g., respiratory failure or pneumonia) are commonly reported, followed by pressure sores and cardiocirculatory complications.[33,34] Regarding surgery, the operative risks and the odds of postoperative complication are burdened by DISH.[35]

These general aspects are fundamental not only for the evaluation of intraoperative complications but also for the prediction of postsurgical outcome.

In case 3, the patient's LOS was longer, considering also the preoperative transfer to ICU because of the cardiovascular instability encountered during the first procedure. In this case, the patient's mobilization was delayed because of the progressive development of respiratory and renal failure, thus he underwent only passive mobilization. For these patients, not only the operative risks but also the general conditions and possible postoperative complications must be focused.

CONCLUSIONS

Ossification of the spine, such as in DISH, increases cervical stiffness, which then rebounds onto the mobile adjacent segment, affecting CVJ stability, increasing the odds of C2 fractures and spinal cord compression with myelopathy. CVJ anterior decompression along with posterior decompression and fixation are the strategies. Tailored therapy is required in each patient. Occipitocervical fixation is an evergreen, effective, and feasible surgical technique, aimed to restore vertebral stability and to halt the progression of spinal stenosis. Finally, patients with DISH may have various comorbidities, which could hamper the peri- and postoperative course. For these reasons, the treatment and surgical indication must be tailored case by case.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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