A RARE COMBINATION OF DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS AND CERVICAL SEPTIC SPONDYLODISCITIS

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Abstract. *Ossification of the anterior longitudinal ligament of the spine is a rare pathology with still unclear etiopathogenesis, although some authors associate it with metabolic diseases such as diabetes. Another rare disorder whose etiopathogenesis is also closely related to immunological disorders in diabetes is spinal epidural empyema. We present a case of a 62-year-old man with comorbidities of arterial hypertension and type II diabetes mellitus, with complaints of dysphagia and throat discomfort one and a half years prior to hospitalization. About a month before hospitalization, the patient reported pain with limited cervical mobility, followed by episodes of fever up to 38°C, with developing upper extremity muscle weakness and self-care incapacity. After imaging and laboratory studies, the patient was diagnosed with Forestier disease according to Resnick and Niwayama criteria, with ossification of the anterior longitudinal ligament and spondylodiscitis with epidural empyema in the cervical compartment. The patient was started on empiric antibiotic therapy and emergency surgery was undertaken for osteophytectomy, median corpectomy with medullar decompression and vertebrodesis. Postoperatively, the patient had improvement in dysphagia and upper extremity muscle strength – MRC 5/5 at the 6-month follow-up. Timely diagnosis and operative treatment with adequate decompression, anterior vertebrodesis and subsequent targeted antibiotic therapy are essential for a good outcome in the management of patients with this combined pathology.*

Key words: *diffuse idiopathic skeletal hyperostosis, Forestier disease, spinal epidural empyema, cervical septic spondylodiscitis, osteophytectomy, median corpectomy, anterior vertebrodesis*

Introduction

Ossification of the anterior longitudinal ligament of the spine was first described by Forestier et al. This pathology is also known in the literature as diffuse idiopathic spinal hyperostosis (DISH) or Forestier and Rotes-Querol disease [1, 2]. It is defined as a non-inflammatory hyperostosis on the anterolateral surface of the vertebral bodies, involving several spinal levels and affecting the paravertebral connective tissue and tendinous insertions [3]. Diffuse idiopathic spinal hyperostosis is more common in males and its incidence ranges from 3.8% to 25%, with an increase in incidence with advancing age [4]. The etiopathogenesis remains unknown, with some authors linking it to metabolic diseases such as diabetes and obesity [3]. The disease is usually clinically asymptomatic, but in about 10.7% of the cases it affects the cervical spine and may cause dysphonia or dysphagia [4]. Respiratory disturbances are less common but can be life-threatening [5]. Radiological investigations are crucial for the diagnosis of the disease based on the Resnick criteria [3].

Another rare disease whose etiopathogenesis is also closely related to metabolic and immunologic disturbances in diabetes is spinal epidural empyema. The combination of diffuse idiopathic skeletal hyperostosis and cervical septic spondylodiscitis with epidural empyema represents a rare combination requiring timely recognition of the two not directly related pathologies and subsequent treatment. This combination of the two nosologies poses surgical challenges because of the need for urgent anterior decompression when cervical epidural empyema is diagnosed and the changes resulting from the present diffuse idiopathic skeletal hyperostosis. A detailed search of PubMed and Medline databases was performed, using all non-repetitive synonyms of the two nosological entities listed in the MeSh and OMIM platforms as keywords. Inclusion criteria were the availability of full text or abstract of the publications found. For the given period from 1983 to 2023, our search did not find another submitted case with a similar combination.

Case report

We present a case of a 62-year-old man with comorbidities of arterial hypertension and type II diabetes mellitus. The patient's complaints date

back to one and a half years prior to hospitalization, presenting with dysphagia and throat discomfort. Approximately one month prior to hospitalization, the patient reported pain with limited mobility in the cervical region, with episodes of fever up to 38 °C starting immediately after the onset of pain. Empiric antibiotic therapy was administered without resulting in clinical improvement. The patient experienced a progression of pain with developing hand muscle weakness and self-care incapacity. At the time of hospitalization, the neurological status revealed a marked cervical vertebral syndrome with axial pain VAS 9/10, upper limb flaccid paraparesis MRC 2/5, spasticity and brisk tendinous reflexes for the lower limbs (3+), with maintained bladder control. After imaging studies (MRI, cervical and sacroiliac joint radiographs – Fig. 1, Fig. 2, Fig. 3, Fig. 4) given the clinical findings, the patient was diagnosed with Forestier's disease according to the criteria of Resnick and Niwayama(4,8), with ossification of the anterior longitudinal ligament and marked hyperostosis at the levels C2-C3-C4-C5-C6. In addition the MRI revealed cervical spondylodiscitis with epidural empyema at the C3-C4-C5-C6 levels ventrally.

Paraclinical findings revealed leukocytosis 14 x 10^9/L, ESR 80 mm/s and C-reactive protein 94.70 µmol/L. The patient was prescribed triple empiric antibiotic therapy with ceftriaxone, meropenem and vancomycin. The decision to perform surgical treatment on an emergency basis, using an anterior cervical approach to perform osteophytectomy at the levels described, median corpectomy at C4 and C5 levels, evacuation of the epidural empyema with debridement and decompression, followed by vertebrodesis with titanium intervertebral mesh and plate at C3-C6 levels, was made (Fig. 5).

Postoperatively the patient had improvement in dysphagia and upper extremity muscle strength – MRC 4/5. Microbiological examination isolated Staph. aureus (methicillin sensitive) and antibiotic therapy was optimized according to the antibiogram. Given the stable trend of decline in inflammatory markers, the patient was discharged on oral antibiotic therapy for 1 month as per the antibiogram, with weekly laboratory follow-up. At the 6-month follow-up the patient was without any residual or recurrent symptoms, with a restored upper extremity MRC 5/5 muscle strength. Follow-up imaging studies showed evidence of optimal positioning of the anterior cervical stabilization system (Fig. 6).

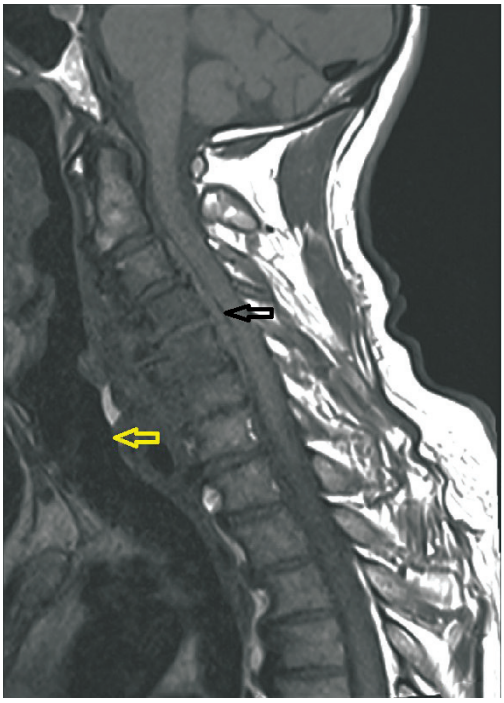


Fig. 1. MRI of the cervical spine, T1 sequence, preoperative: black arrow, empyema occupying the anterior epidural space with compression on the medulla; yellow arrow, displacement of the larynx and esophagus under the pressure of the ossified anterior longitudinal ligament



Fig. 2. MRI of the cervical spine, T2 sequence with evidence of myelopathy

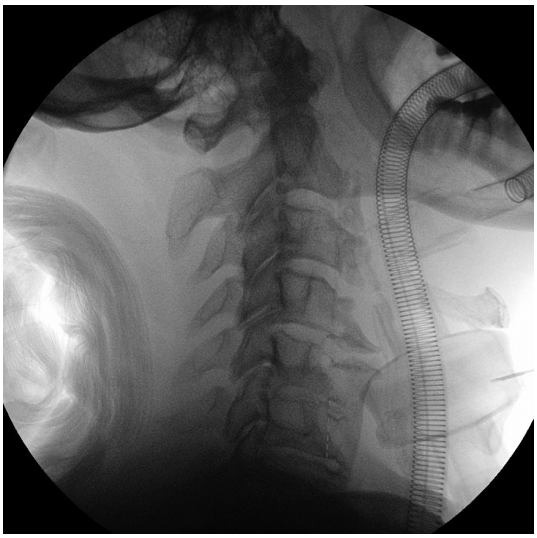


Fig. 3. Preoperative plain lateral radiograph of the cervical department. Pronounced hyperostosis of the anterior longitudinal ligament beyond the anterior marginal line (red dotted line) is visualized, with the facet joints and intervertebral discs intact



Fig. 4. Radiograph of sacroiliac joints – no evidence of involvement of the latter by the inflammatory process

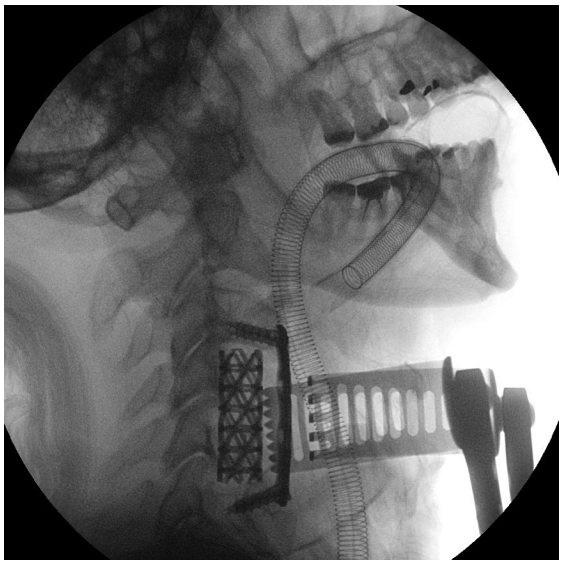


Fig. 5. Intraoperative plain lateral radiograph of the cervical compartment after median corpectomy at the C4-C5 level and anterior corporodesis with titanium intervertebral mesh and plate

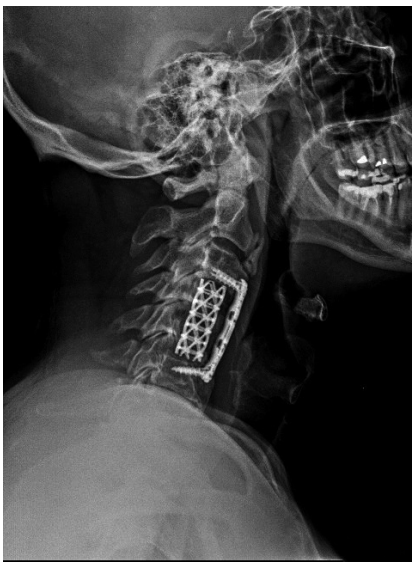


Fig. 6. Follow-up plain lateral radiograph of the cervical spine 6 months postoperatively with evidence of optimal implant position and fusion at C3-C6 levels

Discussion

Diffuse idiopathic skeletal hyperostosis more often affects elderly male patients, as in the presented case. Histopathologically, the following findings are characteristic of the disease: focal and diffuse ossification of the anterior longitudinal ligament and paraspinal connective tissue, ossification of the anulus fibrosus with degeneration of its peripheral fibers, hypervascularity, chronic infiltration with inflammatory cells, and periosteal ossification on the anterior surface of the vertebral bodies [6]. Recent studies regarding the complex etiopathogenesis of DISH have focused on the presence of a genetic predisposition, but a direct pathogenetic link between a particular genotype variant and the disease has not been demonstrated [7]. In a study by Parreira evidence of familial predisposition to the disease was found, pointing out to the presence of a genetic predispo-

sition in combination with common environmental factors, as the PPP2R2D gene variant may contribute significantly to the development of the disease [8]. Of the collagen (COL1A1, COL6A1, COL11A2) and vitamin D receptor (VDR) gene polymorphisms studied, only COL6A1 was associated with ectopic bone formation in the vertebral ligament region [9, 10]. Another study found an association between two variants of the gene for fibroblast growth factor (FGF2) and Forestier disease [11]. According to an earlier study, about 1/3 of DISH patients are positive for HLA-B27, which makes it necessary to always consider another ossifying spinal enthesopathy – the ankylosing spondylitis, in the differential diagnosis [12]. Table 1 presents a comparison between the radiological criteria for the diagnosis of the two diseases [3, 6, 13].

The frequent asymptomatic course of Forestier's disease and its easy differentiation from Bechterew's disease by imaging characteristics make radiological criteria more reliable than clinical ones. The most common clinical findings in Forestier disease are ankylosis in the thoracic region with limited respiratory capacity and a significantly increased risk of unstable spinal fractures [3]. A rarer clinical presentation of the disease is dysphagia, which occurs in 17-28% of cases with hyperostosis in the cervical compartment, which in turn is found in only 10.7% of cases [5, 4]. In our presented clinical case, the patient meets the radiological criteria, and there is a corresponding clinical manifestation of the disease. The pathogenetic mechanism of dysphagia is complex – mechanical compression with esophageal obstruction and irritation of the pharyngoesophageal tract with a local inflammatory response, which lead to a reflectory cricopharyngeal spasm and subsequently to denervation of the esophagus [5]. Treatment is based on exercise and analgesics to suppress the pain syndrome. Surgery is indicated in severe cases of dysphagia or neurological manifestations. In such cases, usually osteophytectomy via an anterior cervical approach results in alleviation of the dysphagia [5, 14].

Cervical epidural empyema is rare phenomenon with an incidence of 0.2-1.3 cases per 10,000 [15]. Empyema is often preceded by spondylodiscitis, which in 85% of cases affects a single level. The most commonly affected levels in the cervical compartment are C4-C5 and C5-C6 [15]. On MRI examination, empyema is visualized as an epidural collection, isointense in T1 and hyperintense in T2 sequence, with contrast enhancement ranging from homogeneous (phlegmon) to sparse at the periphery (abscess) depending on the phase of the process. The presence of T2 hyperintensity of the spinal cord is a poor prognostic marker for recovery of motor function [15]. This finding is in contrast to myelopathy related to degenerative changes in the cervical spine, in which case the presence of a hyperintensity simultaneously also in T1 is a negative prognostic marker regarding recovery of motor function. This highlights the more rapid development of irreversible neurological deficits in compression from empyema, which precede the more scant radiological features of myelopathy. In addition to the more rapid development of symptoms, this compartment has a significantly higher mortality rate than other spinal compartments – 21% compared with 3.6% for the thoracic and lumbar compartments combined [15]. MRSA/MSSA are the most commonly isolated causative agents, with gram-negative and other causative agents of cervical spondylodiscitis being rare, which determines antibiotic therapy and treatment success. Studies have shown an increase in the incidence of this phenomenon, with clinical presentation at a more advanced age, which is due to a combination of factors, such as a higher incidence

Table 1. Differential diagnosis between diffuse idiopathic skeletal hyperostosis and ankylosing spondylitis according to radiological diagnostic criteria

Diffuse idiopathic skeletal hyperostosis	Ankylosing spondylitis
1. Ossification on the anterolateral surface of at least 4 vertebral bodies 2. Preservation of the intervertebral discs 3. Absence of evidence of inflammatory activity in the articular facet joints and apophyseal ankylosis 4. Absence of inflammatory changes in the sacroiliac joints	1. Erosion on the edges of the vertebral bodies (Romanus lesions) 2. Non-infectious spondylodiscitis (Andersson lesions) 3. Diffuse formation of syndesmophytes with the characteristic picture of "a spine with the appearance of a bamboo stick" 4. Ossification of intervertebral joints and apophyseal ankylosis 5. Ossification of the interspinous ligaments 6. Bilateral involvement of sacroiliac joints; 7. Bilateral involvement of hip joints 8. Involvement of the insertions of the pelvic ring ligaments, ossification of the symphysis 9. Involvement of the knee, shoulder and small joints of the hands 10. Involvement of internal organs – pulmonary fibrosis and cardiomegaly

of type II diabetes, obesity, injection drug abuse, increased life expectancy, etc. [16].

Diabetes is a common risk factor for both diseases, predisposing the spine to both spondylodiscitis through impaired immunological resistance and Forestier's disease through metabolic disturbances [17]. The combined manifestation of Forestier's disease with type II diabetes occurs in 20% of cases, and 15% of cases of spinal epidural abscess are also found to have diabetes as a comorbidity [18, 19]. In comparison, the global incidence of type II diabetes is about 6.28% [20]. These data draw attention to the potential role of type II diabetes not only as a comorbid condition and aggravating factor, but also as a predisposing factor for the occurrence of the combined manifestation of Forestier and cervical epidural empyema in the case presented.

According to the series of Ghobrial et. al. the only factor they investigated that positively influenced the recovery of motor function after surgery for cervical epidural empyema was the duration of preoperative clinical manifestation, with results favoring earlier and adequate surgical decompression [15]. A previous study by Alton et al. comparing conservative versus surgical treatment tactics in this nosology concluded failure of antibiotic therapy in 75% of cases requiring subsequent surgical treatment with poor outcomes in terms of motor function [21]. Because of the hardly predictable response to antibiotic treatment, they concluded that cases of cervical spondylodiscitis with epidural empyema are indicated for immediate surgical decompression to avoid potential irreversible neurological deficit [21]. In a comparison of different surgical techniques, Ghobrial et al. found a significant improvement in motor function with an anterior cervical approach with decompression compared with a posterior cervical approach as well as a combined anterior + posterior approach. The anterior cervical retropharyngeal approach used in the presented case is indicated in spondylodiscitis with epidural empyema occupying mainly the anterior half of the spinal canal (30% of cases according to Ghobrial) due to the better anatomical accessibility of the pathology with this technique [15]. In the remaining cases with dorsal (40%) and circumferential (27%) spread of empyema, other surgical techniques or combined approaches should be considered [15]. What favors the anterior cervical approach as the appropriate technique in this case is the combination of the inflammatory process with ossification and hypertrophy of the anterior longitudinal ligament, which cannot be reached by other means, and the possibility of surgical treatment of both pathologies in one stage with a single approach. On the other hand, the presence of diffuse idiopathic hyperostosis makes it significantly more difficult to perform anterior median corpectomy and medullary decompression. The hypotrophy and asymmetric dislocation of the musculus longus colli, the lack of opportunity to visualize the intervertebral disc and the pronounced anterior hyperostosis are responsible for the difficulty in determining the median trajectory when performing the median corpectomy and the resulting intraoperative risks - inadequate medullary decompression, risk of neural root and vertebral artery injuries. Similar to the literature data, also in the presented case early intervention with decompression of the cervical spinal cord in a patient with epidural empyema and Forestier disease, followed by vertebrodesis and postoperative antibiotic therapy according to antibiogram, resulted in good recovery of motor function and no recurrence of symptoms during the follow-up period.

Conclusion

Forestier's disease is a rare disorder, that in combination with type II diabetes may act as a predisposing factor for community-acquired S. aureus bacteremia and its resultant inflammatory complications. The combination of diffuse idiopathic skeletal hyperostosis with cervical epidural empyema requires a more complex treatment tactic - a timely surgical treatment with adequate decompression, anterior vertebrodesis, and subsequent targeted antibiotic therapy according to the antibiogram are essential for a good outcome in the management of patients with this combined pathology.

Disclaimer: *The authors declare that this material has not been published in another scientific platform or presented at a scientific event in the form of an abstract.*

Conflict of Interest: *The authors declare that there is no conflicts of interest regarding the creation process of the current material.*

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