Cervical pyogenic spinal infections: are they more severe diseases than infections in other vertebral locations?

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Abstract

Purpose Cervical spine pyogenic infections are unusual compared to other vertebral segments, but they can be associated to worse clinical outcomes. We compared all patients with cervical spine pyogenic infections to those with thoracolumbar involvement in terms of epidemiology, prognostic factors and clinical outcomes.

Methods We retrospectively reviewed all patients discharged from our institution with diagnosis of pyogenic spinal infections (PSI) during a 14-year period. Patients' demographics, etiologic agent, co-morbidities, site of infection, white blood cell count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) at time of presentation, neurological impairment and mortality were registered to compare clinical outcomes of patients with PSI affecting the cervical spine and other segments.

Results We studied 102 patients with PSI. Nineteen (18.6 %) had cervical involvement; 73.7 % of them were males, with a mean age of 65.22 years. 89.7 % of them presented spondylodiscitis; 12 patients (63.2 %) exhibited a one segment involvement (C5–C6 being the most common), and 11 patients presented an epidural abscess. Thirteen patients (68.4 %) exhibited neurological deficit. Seventeen patients (89.5 %) presented elevated ESR and CRP, while 12 patients (63.2 %) exhibited leukocytosis. The causative organism was identified in 17 patients (89.5 %). Despite similar baseline characteristics, compared to PSI in other locations, patients with cervical PSI presented significantly more neurological involvement

(68.4 vs. 41 %; $p = 0.03$), they more often required surgical treatment (84.2 vs. 46.3 %; $p < 0.01$), and they had and increased mortality (21.1 % compared to 3.6 %; $p = 0.02$).

Conclusion An early diagnosis and prompt treatment should be the goal treating cervical PSI, considering the potential devastating complications and increased mortality.

Keywords Pyogenic spinal infection · Cervical infection · Clinical outcomes · Mortality · Neurological impairment

Introduction

Pyogenic spinal infections (PSI) are infrequent diseases; they represent 2–7 % of all skeletal infections, and their estimated incidence fluctuates from 1:250,000 to 1:400,000 people [1–3]. However, it has been suggested that their incidence and complexity have increased due to several factors including a change in the epidemiological characteristics of affected patients (e.g., aging population, immunosuppressive conditions, multiple and complex co-morbidities, etc.), increasing numbers of invasive procedures producing bacteraemia and the emergence of drug-resistant microorganisms [4–8].

Involvement of the cervical spine is unusual compared to other segments of the spine, with only 5–20 % of cases affecting the cervical segments [9–12]. Therefore, the literature about cervical PSI is scarce, despite these infections can lead to severe neurological and systemic complications.

Based on the experience with a large population of patients with PSI, we retrospectively reviewed all cases affecting the cervical spine in our institution, to evaluate

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possible differences relative to thoracolumbar PSI in terms of epidemiology, prognostic factors and clinical outcomes.

Patients and methods

Institutional review board was obtained to perform this study. Between January 1999 and May 2013, all patients who were discharged from a University Hospital with the diagnosis of PSI were identified. Different types of PSI were considered such as vertebral osteomyelitis, disk space infections (i.e., pyogenic discitis), epidural abscess, and septic facet arthritis. Inclusion criteria were (a) infections caused by haematogenous spread (i.e., not the result of direct inoculation) and (b) evidence of spinal column involvement on radiographs, computed tomography, or magnetic resonance imaging. Diagnostic confirmation of PSI required a compatible clinical and radiological picture plus: (a) bacterial identification in samples obtained directly from affected tissues, or (b) two or more positive blood cultures or (c) microscopic diagnosis of non-specific (i.e., with no granulomatous reaction) or pyogenic vertebral osteomyelitis [13]. All cases were discussed by a multi-disciplinary team including spine surgeons, musculoskeletal radiologists and infectious disease specialists. Patients with granulomatous, fungal and post-surgical infections and those related to decubitus ulcers were excluded from the study. A total of 102 consecutive patients with PSI met these criteria; however, patients involving the cervical spine were the main objective of this study.

We collected the following clinical data from patients included in this study: age, gender, site of infection, length of hospital stay, degree of neurological impairment at presentation and at hospital discharge (defined as any motor or sensory deficit from either spinal cord or nerve root dysfunction), mortality and co-morbidities including diabetes mellitus (DM), chronic liver failure (CLF) chronic renal failure (CRF), rheumatoid arthritis (RA), cardiac disease, smoking, intravenous drug abuse and chronic use of corticosteroids.

Laboratory data registered included the bacterial organism isolated by cultures or PCR analysis; white blood cell count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) at time of presentation.

Pathogen identification was intended in all cases through multiple methods, depending on the clinical scenario. Blood cultures were obtained at diagnosis. Antibiotic treatment was started if: (a) blood cultures were positive, or (b) direct tissue samples were taken from open surgery (no percutaneous CT-guided samples were obtained in patients with cervical involvement). Once samples were obtained, i.v. antibiotic treatment was initiated for a minimum of 4 weeks, followed by at least 2 months of oral antibiotics.

Initial treatment consisted generally in a combination of cefazolin and ciprofloxacin, and it was adjusted according to culture results and bacterial antibiotic susceptibility. If cultures were negative and the patient was stable with decreasing inflammatory parameters, initial antibiotic treatment was maintained for 4 weeks, followed by orally administered cefadroxil and ciprofloxacin. Universal PCR and 16S gene sequencing DNA from osteoarticular tissue were performed in 24 of 102 cases as described previously [14].

Surgical treatment was performed if there was failure of medical management, neurological deficit, in patients with an epidural abscess (with or without a neurological impairment) or in cases with vertebral compromise causing spinal instability and/or deformity.

Statistical analyses were performed using the Statistical Program for the Social Sciences (SPSS) version 18 (SPSS, Chicago, IL, USA). Continuous data were described as means and standard deviations, and categorical variables were expressed as percentages. We performed the Student *t* test to analyze continuous variables and χ^2 or Fisher exact test for categorical variables. A *p* value <0.05 was considered statistically significant.

Results

A total of 102 patients with pyogenic spinal infections met the inclusion criteria; 19 of them (18.6 %) had a PSI involving the cervical spine (Table 1). The mean age of the group was 65.22 ± 10 years, and 14 patients were men (73.7 %). Of note, 89 percent of the patients were 50 years of age or older.

A large majority of the patients presented with vertebral osteomyelitis and adjacent discitis (17 of 19, 89.7 %). Twelve patients exhibited a one segment involvement (63.2 %), C5–C6 being the most common one; five patients presented 2-segment disease and two patients had three or more segments involved. Nine patients presented an epidural abscess that occurred secondarily (Fig. 1), while two patients presented an epidural abscess without bone or disc involvement. The distribution of levels involved is shown in Table 2.

Thirteen patients (68.4 %) exhibited neurological deficit at the time of presentation. Two of these 13 patients had a complete neurological deficit (Frankel A); the description on neurological status is presented in Table 3.

Laboratory tests are shown in Table 1; 17 patients (89.5 %) presented ESR >30 mm/h and abnormal CRP (>1 mg/dl), while 12 patients (63.2 %) exhibited leukocytosis (>11,000 cells/mm³).

The causative organism was identified in 17 patients (89.5 %). In eight patients (47 %) *Staphylococcus aureus*

Table 1 Cervical versus other segment pyogenic spinal infection

	Cervical PSI (19)	Other segment PSI (83)	<i>p</i> value
Age (years)	65.2 ± 10.8	63.3 ± 16.9	0.652
Male	73.7 % (14)	55.4 % (46)	0.145
<i>Site of infection</i>			
Cervical	94.7 % (18)		
Thoracic		26.5 % (22)	
Lumbar		72.3 % (60)	
Multiple	5.3 % (1)	1.2 % (1)	
Neurological involvement at presentation	68.4 % (13)	41.0 % (34)	0.03*
Erythrocyte sedimentation rate (ESR) >30	89.5 % (17)	77.1 % (64)	0.348
C-reactive protein (CPR) >1	89.5 % (17)	88.0 % (73)	1
White blood cell (WBC) count >11,000	63.2 % (12)	50.6 % (42)	0.323
Agent identification	89.5 % (17)	74.7 % (62)	0.23
Need for operation	84.2 % (16)	46.3 % (38)	<0.01*
Co-morbidities	73.7 % (14)	78.3 % (65)	0.76
Other non-spinal infection	68.4 % (13)	38.6 % (32)	0.02*
Epidural abscess	47.4 % (9)	38.6 % (32)	0.48
Mortality	21.1 % (4)	3.6 % (3)	0.02*

* Significant values

Fig. 1 Sagittal view of gadolinium-enhanced T1 image of the MRI showing C3–C4 spondylodiscitis with a secondary epidural abscess

was identified, while *Streptococcus* was identified in three patients (15.8 %), and *Staphylococcus epidermidis* was the causative agent also in three patients (15.8 %); the list of

Table 2 Distribution of levels involved

Level	No. of times involved
C1–C2	1
C2–C3	1
C3–C4	2
C4–C5	5
C5–C6	13
C6–C7	7
C7–T1	3

Table 3 Neurological status at presentation and after treatment

Neurological status	At presentation (No. of patients)	After treatment (No. of patients)
Frankel A	2	2
Frankel B	0	0
Frankel C	2	1
Frankel D	9	4
Frankel E	6	12

all identified microorganism is shown in Table 4. We could not identify the causative pathogen in two patients.

At least one co-morbidity was present in 73.7 % of the patients, the most common being type 2 DM (36.8 %) followed by chronic kidney disease (31.6 %), heart disease (31.6 %) and smoking (21.1 %); 3 patients had a history of non-spinal cancer, while one patient had CLF and one was a chronic corticosteroid user.

One patient presented a concomitant lumbar spinal infection, while 13 patients (68.4 %) presented other

Table 4 Etiologic microorganism identified

Etiological microorganism	n (%)
<i>Staphylococcus aureus</i>	8 (42.1 %)
<i>Streptococcus</i>	3 (15.8 %)
Negative coagulase <i>Staphylococcus</i>	3 (15.8 %)
<i>Escherichia coli</i>	2 (10.5 %)
<i>Pseudomonas</i>	1 (5.3 %)
More than one agent	0
No agent identified	2 (10.5 %)

Table 5 Concomitant non-spinal infections

Infection	No. of patients
Pneumonia	3
Infectious endocarditis	2
Bacteremia/septic shock	2
Urinary tract infection	1
Infected central venous catheter	1
Non-spinal musculoskeletal abscess	1
Non-spinal septic arthritis	1
Meningitis	1
Infectious cholangitis	1

concomitant, distant, non-spinal infection, as shown in Table 5.

Sixteen patients with cervical PSIs underwent surgery; surgical indications were neurological deficit at presentation in 13 cases, and the presence of an epidural abscess in the other three cases. Surgical treatment consisted in anterior corpectomy and reconstruction of the defect with bone graft and ventral instrumentation in 13 cases; 4 of these cases also required a posterior instrumented fusion. Posterior decompression with fusion was performed in one case in which a multilevel vertebral osteomyelitis and epidural abscess involved multiple spinal segments. In addition, a posterior decompression alone was performed in two patients with posterior epidural abscess without bone or disc involvement. More than 40 % of patients improved their neurological status after surgery, 50 % remained unchanged and only one patient deteriorated (7 %); of note, no patients in Frankel A improved their neurological status after surgery.

One patient had an acute anterior graft dislodgment during the first postoperative week, which required revision and delayed posterior cervical fixation. Four patients died during treatment of the PSI, three of them secondary to a concomitant non-spinal infection: two patients died secondary to respiratory failure associated to a severe pneumonia, and one case secondary to an endocarditis producing acute valve insufficiency; the last patient (who

had a CLF) died secondary to a massive upper digestive bleeding.

Compared to patients with spinal infections in other locations, patients with cervical involvement presented significantly more neurological impairment at presentation (68.4 % compared to 41 %; $p = 0.03$). Accordingly, more patients with cervical involvement required surgical intervention (84.2 % compared to 46.3 %; $p < 0.01$). In addition, the mortality rate of patients with cervical PSI was significantly higher than the mortality observed in patients with PSI in other locations. (21.1 % compared to 3.6 %; $p = 0.02$). Patients with cervical involvement also presented more concomitant non-spinal infections, however, without reaching statistical significance (Table 1).

Discussion

The cervical spine represents an infrequent site of involvement in patients with PSI, and a limited number of studies have specifically evaluated these patients; however, most authors agree that cervical PSI represent a subset of particularly serious diseases [9, 11, 12, 15]. Our study shows that patients with cervical involvement, who presented significantly more neurological compromise, were treated more frequently with surgery and had increased mortality compared to patients with PSI affecting other segments of the spine. This reaffirms prior studies suggesting that cervical compromise led to a worse neurological and overall prognosis [16].

A recent study from Shousha et al. [9] reviewed the literature available to determine the relative incidence of cervical involvement in PSI; the literature available shows that in studies including 13 to 495 patients in either location, the cervical spine represented 4–19 % of all cases [9]. The high rate of cervical involvement in our study (18.6 %) despite none of our patients was an intravenous drug abuser (which has been described to be a risk factor to develop cervical PSI [17, 18]) may be explained because our hospital is a referral center which receives patients with more severe diseases.

It is worth to mention that 68.4 % of patients with cervical involvement exhibited some degree of neurological involvement when they were diagnosed. This factor, combined with almost 50 % of cases presenting with an epidural abscess, explains the high surgical rate in our series (84.2 %). In fact, our study supports considering cervical PSI a more severe form of spinal infection, and therefore, warrants closer surveillance and perhaps, a more aggressive therapeutic approach. The patients exhibited higher frequency of neurological involvement and greater mortality rates than patients presenting with infections in the thoracic and lumbar

Fig. 2 Plain radiograph showing C5–C6 spondylodiscitis with a pathological fracture and collapse of C5

areas, even though they exhibited no demographic or comorbidity differences. Moreover, inflammatory parameters did not differ between groups, and no differences in pathogen identification were observed among patients with cervical infections and patients with infections involving other segments. The increased neurological involvement observed in patients with cervical PSI may be explained by the high prevalence of epidural abscess (57.9 %) in an area (the cervical spine) with a small cross-sectional area of the spinal canal; even though this characteristic is shared with the thoracic spine, the ribs in the thoracic area provide increased rigidity and consequently may protect this segment from further dynamic compression or pathologic fractures in contrast with the more mobile cervical spine (Fig. 2). Although it may be argued that conservative treatment could be indicated for cases with epidural abscesses and no neurological compromise, we reserve such indication only for selected cases in *cauda equina* territory (i.e., lumbar PSIs), since a vascular component may produce an irreversible neurological damage (as observed in our two patients presenting with Frankel A).

Patients with cervical PSI had an increased rate of concomitant non-spinal infections compared to PSI in other locations; this factor has already been described to be associated to neurological risk in cases with PSI [19]; this could also be a reflection of patients' overall poor medical status, representing a severity feature. Furthermore, more than one-third of patients with cervical PSI had more than

one level involved; this also suggests these patients presented a severe infectious involvement of the spine.

The literature has scant data on the mortality rate of patients with cervical PSI, mainly since most series include <5 cases, making conclusions difficult. However, larger series have exhibited 10–12 % mortality rate in these patients [9, 20]. We hypothesize that the high mortality rate in our series represents the severity of this cohort, since one of our patients died due to an acute heart failure secondary to a concomitant endocarditis and two other cases were operated in the context of a severe septic shock and neurological compromise.

Considering the impact that a cervical spinal infection represents, a high level of suspicion should be kept in patients with a potential cervical PSI, mainly as many of these cases initially seek for medical care with general physicians, internists and rheumatologists, and usually the diagnosis is delayed [15]. Patients with current or persistent sepsis and signs of neurological deficit or axial pain should prompt directed diagnostic studies, ideally through magnetic resonance imaging [12]. These infections may produce bony destruction leading to cervical spine instability; in addition, epidural abscess is common, and they may produce spinal cord compression and vascular damage to the spinal cord, with subsequent neurological involvement. Surgical treatment should include debridement of all infected tissue, drainage of any epidural abscess, decompression of the spinal canal and reconstruction of the resulting defect, with restoration of alignment and stabilization of the spine.

An early diagnosis and prompt treatment should be the goal treating this infrequent group of spinal infections. Since they appear to harbor a poorer neurological prognosis and severity as compared with PSI in other locations, an aggressive approach and early intervention should be warranted to prevent morbidity and mortality.

Conflict of interest None.

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