症例報告

島根県中病医誌 48
79頁 ～ 85頁

Clinical Characteristics of Cervical Infection and Cervical Inflammation: A Retrospective Cohort Study

Shohei FUMITA[1)] Tsukasa NAKAMURA[2)3)] Toshihiro IMADA[1)]
Hiroshi HIGUCHI[4)] and Takeshi MORIMOTO[3)5)]

Abstract： **Background:** Cervical spine infectious diseases such as pyogenic spondylitis and epidural abscess can be fatal if diagnosis is delayed; however, it is difficult to distinguish them from non-infectious inflammatory diseases, especially from pseudogout. This study aim to identify clinical indicator facilitate the swift diagnosis of pseudogout.

Methods: Patients diagnosed with cervical spine infectious diseases and cervical spine non-infectious inflammatory diseases between January 1, 2000, and December 31, 2020, at Shimane Central Hospital were included. Data on patient's characteristics, vital signs, physical examination findings, underlying diseases, laboratory tests, medication history, lifestyle history, and imaging tests were extracted from the integrated information system; multivariate analysis was performed using descriptive statistics, univariate analysis, and logistic analysis.

Results: The study included 265 participants; of them, 147（56%）were male, the mean age was 73±16 years, and 84（32%）had infectious diseases. In the univariate analysis, infectious diseases were prevalent in male, younger patients, and those with a history of alcohol consumption, patients with smoking history, patients with paralysis, patients who experienced numbness, and patients who used psychotropic medication. Dyslipidemia was potentially associated with non-infectious diseases. In the multivariate analysis of infectious diseases, the odds ratios were higher for paralysis（odds ratio［95% confidence interval］: 5.5［2.4–12.5］）and psychotropic medication use（3.2［1.4–7.2］）and lower for older age（0.9［0.9–0.95］）and dyslipidemia（0.2［0.1–0.6］）.

Conclusion: Paralysis, psychotropic medication use, age, and dyslipidemia are important factors in differentiating cervical spine infectious diseases.

Key words：cervical infection, cervical inflammation, logistic regression

頸椎の炎症性疾患と感染性疾患の臨床的特徴について

文田 昌平[1)] 中村 嗣[2)3)] 今田 敏宏[1)] 樋口 大[4)] 森本 剛[3)5)]

概 要：はじめに 化膿性脊椎炎や硬膜外膿瘍などの頸椎感染性疾患は，診断が遅れると致命的となるが，非感染性の炎症性疾患，特に偽痛風との鑑別が困難である．本研究では，偽痛風の迅速診断に役立つ臨床所見を検討することを目的とした．

1）島根県立中央病院 総合診療科
2）島根県立中央病院 感染症科
3）島根県立中央病院 臨床教育・研修支援センター
4）島根県立中央病院 地域総合医育成科
5）兵庫医科大学 臨床疫学

1）Department of General Medicine, Shimane Prefectural Central Hospital, Izumo, Japan
2）Department of Infectious Diseases, Shimane Prefectural Central Hospital, Izumo, Japan
3）Clinical Education and Research Center, Shimane prefectural Central Hospital, Izumo, Japan
4）Department of Human Resources Development for General Practitioner, Shimane Prefectural Central Hospital
5）Department of Clinical Epidemiology, Hyogo College of Medicine, Nishinomiya, Japan

方法　2000年１月１日から2020年12月31日までに島根県立中央病院で頸椎感染性疾患および頸椎非感染性炎症性疾患と診断された患者を対象とした．患者情報，バイタルサイン，身体所見，基礎疾患，臨床検査，薬歴，生活歴，画像検査などのデータを統合情報システムから抽出し，記述統計，単変量解析，ロジスティック解析を用いて多変量解析を行った．

結果　対象者は265名で，うち男性147名（56％），平均年齢73 ± 16歳，感染症罹患者84名（32％）であった．単変量解析では，感染症は男性，若年者，アルコール摂取者，喫煙歴のある患者，麻痺のある患者，しびれを経験した患者，向精神薬使用者に多かった．脂質異常症は非感染性疾患の可能性のある症状であった．感染症の多変量解析では，オッズ比は麻痺（オッズ比［95％信頼区間］：5.5［2.4-12.5］）と向精神薬使用（3.2［1.4-7.2］）で高く，高齢（0.9［0.9-0.95］）と脂質異常症（0.2［0.1-0.6］）で低かった．

結論　麻痺，向精神薬，年齢，脂質異常症は頸椎感染症を鑑別する上で重要な因子である．

索引用語：頸椎炎症性疾患，頸椎感染性疾患，ロジスティック解析

Introduction

Cervical spine infections, including cervical epidural abscesses, can lead to fatal outcomes, resulting in permanent neuropathy and sepsis.[1)] They typically cause midline back pain, neck pain, fever, and progressive weakness of the limbs.[2)] The white blood cell count, erythrocyte sedimentation rate, and C-reactive protein level usually increase. Treatment with rapid diagnosis and surgical drainage can minimize the risk of mortality and the incidence of neuropathy.[1)] However, cervical spine infections rarely occur and often are difficult to diagnose. The diagnosis of epidural abscess of the spine may be delayed in up to 75% of the patients.[3)]

Non-infectious cervical spine disorders such as pseudogout have similar symptoms to cervical spine infections such as fever and tenderness of the cervical spine and can be difficult to distinguish.[4)] The red flag symptoms include fever and severe back pain, which are also common in infectious and non-infectious inflammatory diseases and make differentiation difficult. Although it can be distinguished by magnetic resonance imaging（MRI）, this procedure is not easy to perform in the primary care setting.[5)] It is often difficult to differentiate fever and back pain of infectious etiology from those of non-infectious etiology.

Inflammation can often be treated with non-steroidal anti-inflammatory drugs（NSAIDs）and other drugs compared to abscesses, which require urgent treatment. In primary care, both of these conditions may be treated by sending the patient to a tertiary hospital. However, considering medical resources and patient benefit, it was not always necessary to send the patient to a tertiary hospital immediately. However, it was not always necessary to send the patient to a higher-level hospital immediately, considering the medical resources and the patient's benefit. This study aimed to examine the clinical findings that can help distinguish infectious from non-infectious cervical spine disorders, especially in the primary care setting.

Methods

Study design and patients

This cross-sectional study was conducted in patients aged >=16 years who were diagnosed with cervical infection and inflammatory disease from January 2000 to December 2020 at the Shimane Prefectural Central Hospital. We wanted to know mainly the difference between infection and inflammation, so we designed this study to address these two diseases.

The clinical data, laboratory data, and outcomes of the eligible patients were retrieved from the integrated intelligent management system, which is a unified database that stores data from the electronic medical records, images, data from the ordering system, and other hospital information. This study was approved by the Ethics Review Board of Shimane Prefectural Central Hospital（approval number: R20-067; approval date: 2023-3-23）.

Because all data were obtained as part of routine clinical practice, the requirement for obtaining informed consent was waived by the Ethics Review Board of Shimane Prefectural Central Hospital in accordance with the guidelines of the Ministry of Health, Labor and Welfare of Japan.

Measurements

Data on age, sex, history of alcohol consumption (DRINK), history of smoking (SMOKE), height, weight, vital signs, symptoms, comorbidities, medications, laboratory data, and imaging tests were retrieved. The patients' vital signs including temperature, blood pressure (systolic and diastolic), heart rate, respiratory rate and oxygen saturation were measured. Symptoms such as paralysis, numbness, and vomiting were assessed. The patients were examined for presence of comorbidities, such as valvular heart disease, tooth decay, hypertension, dyslipidemia, diabetes, and pseudogout. The medications used were also determined: steroids, NSAIDs, and psychiatric drugs. The following laboratory data were obtained: white blood cell count, hemoglobin level, platelet cell count, total protein level, albumin level, total bilirubin level, aspartate transaminase level, alanine transaminase level, lactate dehydrogenase level, γ-glutamyl transpeptidase level, blood urea nitrogen level, creatinine level, and C-reactive protein level at the time of admission. The imaging tests performed were computed tomography (CT) and MRI.

Statistical analyses

Continuous variables were expressed as mean and standard deviation (SD) or median and interquartile range, and categorical variables were expressed as numbers and percentages. To explore the factors associated with cervical infection, continuous variables were compared using student's t test or Wilcoxon rank-sum test. The categorical variables were compared using χ^2 test or Fisher's exact test. Then, multivariate logistic regression models were constructed using clinically important items (age, sex, DRINK, SMOKE, paralysis, hypertension, dyslipidemia, diabetes, and psychotropic drug use).

The associations were expressed as odds ratio (OR) and 95% confidence interval (CI). All reported p-values were two tailed, and a p-value of <0.05 was considered significant. All statistical analyses were performed using Stata 14 (StataCorp LLC, Texas) and JMP 12.2 (SAS Institute Inc., Cary, North California).

Results

Patients' characteristics

This study included 265 patients, and the patients' mean age was 73 years (range: 18–100 years) (Table 1). A total of 147 (55.5%) patients were male, 82 (30.9%) were DRINK patients, and 95 (35.9%) were SMOKE patients. With regard to the presenting symptoms, paralysis occurred in 47 (17.7%) patients, numbness in 16 (6.0%) patients, and vomiting in 6 (2.3%) patients. In terms of comorbidities, 138 (52.1) patients had hypertension, 60 (22.6) had dyslipidemia, 39 (14.7) had diabetes, and 34 (12.8) had a history of pseudogout. In terms of the medication history, 12 (4.5%) used steroids, 47 (17.7%) used NSAIDS, and 48 (18.1%) used psychiatric drugs. The mean body temperature was 37.2 ± 0.8℃, while the mean respiratory rate was 18 ± 5 times/minute. The mean systolic blood pressure was 135 ± 24 mmHg, while the mean diastolic blood pressure was 75 ± 15 mmHg. CT imaging was performed in 190 (71.7) patients, of whom 98 (51.6) were diagnosed with pseudogout. MRI was performed in 78 (29.4) patients, of whom 56 (71.8) were diagnosed with cervical spine infection.

Univariate analysis of cervical infection and cervical inflammation

A total of 84 patients comprised the infection group (Table 1). Infection group was younger than the non-infection group (62 [SD=16] vs. 79 [SD=13] years; $p<0.001$). The infection group had higher proportion of male patients (56 [66.7%] vs. 91 [50.3%], $p=0.012$), DRINK patients (33 [39.3%] vs. 49 [27.1%], $p=0.005$), and SMOKE patients (38 [45.2%] vs. 57 [31.5%], $p=0.03$). The mean body height was higher in the infection group (160.1 [SD 10.5] vs. 154.2 [SD 10.1] cm; $p<0.001$), but no significant differences were observed

Table 1　Patients' characteristics and univariate analysis of infection

variables	ALL (n=265)	Cervical infection n=84	Cervical inflammation n=181	*p*-value
	no (%) or mean ± sd or median [IQR]			
Age, year	73 ± 16	62 ± 16	79 ± 13	<0.001
Male	147 (55.5)	56 (66.7)	91 (50.3)	0.012
DRINK	82 (30.9)	33 (39.3)	49 (27.1)	0.005
SMOKE	95 (35.9)	38 (45.2)	57 (31.5)	0.030
Height, cm	156.1 ± 10.6	160.1 ± 10.5	154.2 ± 10.1	<0.001
Vital signs				
Body weight, kg	54.0 ± 10.9	55.2 ± 11.7	53.4 ± 10.5	0.24
Body temperature, ℃	37.2 ± 0.8	36.9 ± 0.7	37.3 ± 0.8	<0.001
Systolic blood pressure, mmHg	135 ± 24	130 ± 21	138 ± 26	0.025
Diastolic blood pressure, mmHg	75 ± 15	76 ± 12	75 ± 16	0.58
Heart fate, /min	81 ± 15	80 ± 15	82 ± 15	0.42
Respiratory rate, /min	18 ± 5	15 ± 5	20 ± 5	<0.001
Saturation, %	96 ± 2	97 ± 2	96 ± 2	0.14
Symptom				
Paralysis	47 (17.7)	29 (34.5)	18 (9.9)	<0.001
Numbness	16 (6.0)	12 (14.3)	4 (2.2)	<0.001
Vomiting	6 (2.3)	3 (3.6)	3 (1.7)	0.39
Comorbidities				
Valvular heart disease	2 (0.8)	0 (0.0)	2 (1.1)	1.00
Tooth decay	2 (0.8)	1 (1.2)	1 (0.6)	0.53
Hypertension	138 (52.1)	36 (42.9)	102 (56.4)	0.041
Dyslipidemia	60 (22.6)	6 (7.1)	54 (29.8)	<0.001
Diabetes	39 (14.7)	13 (15.5)	26 (14.4)	0.81
History of pseudogout	34 (12.8)	34 (18.8)	0 (0.0)	<0.001
Medication				
Steroids	12 (4.5)	5 (6.0)	7 (3.9)	0.53
NSAIDs	47 (17.7)	14 (16.7)	33 (18.2)	0.76
Psychiatric drugs	48 (18.1)	23 (27.4)	25 (13.8)	0.008
Laboratory data				
White blood cell count, 10^3/μL	8,130 [6,460–10,640]	7,870 [5,650–10,070]	8,410 [6,840–10,750]	0.14
Hemoglobin, g/dL	12.1 [10.8–13.4]	12.3 [10.7–13.3]	12.1 [10.8–13.4]	0.81
Platelet count, 10^4/μL	23.1 [18.0–29.0]	26.0 [21.0–32.9]	22.3 [17.8–27.3]	<0.001
Total protein, g/dL	6.9 [6.2–7.3]	6.9 [6.7–7.4]	6.8 [6.2–7.3]	0.040
Albumin, g/dL	3.5 [2.9–3.9]	3.6 [3.2–4.1]	3.4 [2.8–3.8]	0.012
Total bilirubin, mg/dL	0.7 [0.5–1.0]	0.5 [0.4–0.7]	0.8 [0.6–1.3]	<0.001
AST, U/L	21 [16–31]	20 [15–28]	21 [16–32]	0.090
ALT, U/L	16 [11–29]	18 [13–33]	15 [11–27]	0.037
LDH, U/L	210 [178–239]	199 [164–230]	216 [184–248]	0.016
γ-GTP, U/L	28 [18–77]	52 [24–121]	23 [15–53]	<0.001
BUN, mg/dL	14.0 [11.0–19.1]	13.0 [9.9–17.3]	14.5 [11.5–22.0]	0.007
Cr, mg/dL	0.68 [0.55–0.89]	0.68 [0.52–0.87]	0.68 [0.56–0.91]	0.28
CRP, mg/dL	6.61 [2.89–12.34]	4.94 [0.69–9.71]	8.00 [4.23–12.63]	<0.001
Imaging				
CT	190 (71.7)			
Pseudogout	98 (51.6)			
MRI	78 (29.4)			
Cervical spine infection	56 (71.8)			

DRINK; history of alcohol consumption, SMOKE; history of smoking, NSAIDs; non-steroidal anti-inflammatory drugs, AST; aspartate transaminase, ALT; alanine transaminase, LDH; lactate dehydrogenase, γ-GTP; γ-glutamyl transpeptidase, BUN; blood urea nitrogen, Cr; creatinine, CRP; C-reactive protein, CT; computed tomography, MRI; magnetic resonance imaging

in the body weight (55.2 [SD 11.7] vs. 53.4 [SD 10.5] kg; p=0.24). The infection group showed lower systolic blood pressure (130 [SD 21] vs. 138 [SD 26] mmHg; p=0.025), body temperature (36.9 [SD 0.7] vs. 37.3 [SD 0.8] ℃; p<0.001), and respiratory rate (15 [SD 5] vs 20 [SD 5] bpm; p<0.001), but no significant differences were observed in the diastolic blood pressure and heart rate. With regard to the symptoms, paralysis and numbness were more prevalent in the infection group (paralysis: 29 [34.5%] vs 18 [9.9%], p<0.001, numbness: 12 [14.3%] vs 4 [2.2%], p<0.001). In terms of comorbidities, the incidence of hypertension, dyslipidemia, and history of pseudogout was relatively low (hypertension: 36 [42.9%] vs 102 [56.4%], p=0.041; dyslipidemia: 6 [7.1%] vs 54 [29.8%], p<0.001; and history of pseudogout: 34 [18.8%] vs. 0 [0.0%], p<0.001). The proportion of psychiatric drug users was higher in the infection group (23 [27.4%] vs. 25 [13.8%], p=0.008). With regard to the laboratory data, the white blood cell count, hemoglobin level, and Cr level were not significant highly.

Multivariate analysis of Infection

The multivariate logistic regression model showed that younger age (OR: 0.93, 95% CI: 0.90–0.95), paralysis (OR 5.53, 95% CI 2.38–12.8), and psychotropic drug use (OR: 3.25, 95% CI: 1.46–7.56) were independently associated with cervical infections (Table 2). Dyslipidemia (OR: 0.16, 95% CI: 0.06–0.48) was associated with non-infectious disease.

Discussion

We explored the clinical findings to distinguish between infectious and inflammatory cervical spine disorders. Paralysis and psychotropic drug use were associated with infectious cervical spine disorders (e.g., cervical abscess), while higher age and dyslipidemia were associated with non-infectious cervical spine disorders (e.g., cervical pseudogout)

In our study, the mean age of patients with cervical infections was 62 years, and male were significantly predominant in the infected group[1]. The mean age of patients with epidural abscess was 65 years,[1] while that of patients with pseudogout was 72 years.[6,7] The findings of our study were align with those of previous studies, though the age of our study's patients with non-infectious diseases was higher. This could be due to the high aging population in the area.[8] In a previous study of cervical epidural abscesses, 173 patients were analyzed, and 61.3% were men,[3] which were similar to that reports of our study.

Previous studies on epidural abscesses have identified diabetes, drug abuse, alcohol abuse, human immunodeficiency virus infection, knee osteoarthritis, and history of trauma as risks factors.[2] In our study, the incidence of diabetes mellitus and alcohol abuse were significantly higher in the infection group compared to the non-infection group according to the results of the univariate analysis, but the difference was relatively small.

Table 2 Logistic regression analysis of cervical infection

INFECTION	Odds ratio	95% Confidence Interval	p-value
Age, year	0.93	0.90–0.95	0.000
Male	0.99	0.44–2.22	0.987
DRINK	1.11	0.50–2.47	0.801
SMOKE	1.45	0.61–3.44	0.402
Paralysis	5.53	2.38–12.8	0.000
Hypertension	1.20	0.60–2.40	0.598
Dyslipidemia	0.16	0.06–0.48	0.001
Diabetes	1.56	0.59–4.14	0.373
Psychotropic drug use	3.25	1.40–7.56	0.006

DRINK; history of alcohol consumption, SMOKE; history of smoking

Non-infectious diseases, particularly pseudogout, showed an association with dyslipidemia; however, there is limited evidence to suggest a link between pseudogout and dyslipidemia.

Multivariate analysis showed high odds ratios for paralysis and alcohol abuse in the cervical spine infectious disease group. Typical symptoms of cervical epidural abscess include back pain, fever, and paralysis. Back pain is the most common presenting symptom of epidural abscess and occurs in 70% to 100% of the patients.[2] The pain tends to be severe and localized with a duration of 1 day to 2 months.[2] Approximately 50% of the patients develop fever, while 17%–98% experience back tenderness.[2] Neurological manifestations, such as motor weakness, radiculopathy, and bladder and bowel dysfunction, have been reported in up to half of the patients. Atypical manifestations of epidural abscess, such as sudden paralysis, abdominal pain, headache, and bowel dysfunction, have also been reported.[2,9] In previous studies, epidural abscesses were associated with acquired immunodeficiency syndrome, chronic renal failure, alcoholism, cancer, epidural anesthesia, spinal surgery, and trauma.[10] The current study also emphasized the association of chronic alcohol consumption with cervical infectious disorders such as cervical suppurative spondylitis.[9]

This study has some limitations. First, the retrospective nature of this study may have introduced potential biases, affecting the data's precision. However, this study presents the real-world scenario. Second, although cervical infection and non-infection were compared in this study, other diseases should have been differentiated as well. Hence, the clinical findings of infectious and non-infectious cervical disorders should also be distinguished from those of other relevant diseases in the primary care setting.

In conclusion, in patients with neck disorders who develop fever and are admitted in the primary care setting, paralysis and psychotropic drug use are possible risk factors for cervical infectious diseases; hence, patients with these symptoms should be transferred to a higher-level medical institution.

References

1）Turner A, Zhao L, Gauthier P, et al.: Management of cervical spine epidural abscess: a systematic review. Ther Adv Infect Dis, 2019; 6: 1-17. doi: 10.1177/2049936119863940.

2）Tetsuka S, Suzuki T, Ogawa T, et al.: Spinal epidural abscess: a review highlighting early diagnosis and management. JMA J, 2020; 3(1): 29-40.

3）Davis DP, Salazar A, Chan TC, et al.: Prospective evaluation of a clinical decision guideline to diagnose spinal epidural abscess in patients who present to the emergency department with spine pain. J Neurosurg Spine, 2011; 14(6): 765-770. doi: 10.3171/2011.1.SPINE1091.

4）Younis AA: Crowned Dens Syndrome as a cause of acute neck pain: a Case Report and Review of the Literature. Mediterr J Rheumatol, 2017; 28(2): 101-105. doi: 10.31138/mjr.28.2.101.

5）Ministry of Health, Labour and Welfare: Deployment of medical equipment and safety management status. https://www.mhlw.go.jp/file/05-Shingikai-10801000-Iseikyoku-Soumuka/0000130336.pdf [2023-10-20]

6）Kohlmann R, Nefedev A, Kaase M, et al.: Community-acquired adult Escherichia coli meningitis leading to diagnosis of unrecognized retropharyngeal abscess and cervical spondylodiscitis: a case report. BMC Infect Dis, 2015; 15: 567. doi: 10.1186/s12879-015-1310-4.

7）Roddy E, Muller S, Paskins Z, et al.: Incident acute pseudogout and prior bisphosphonate use: matched case–control study in the UK-Clinical Practice Research Datalink. Medicine (Baltimore), 2017; 96(12): e6177. doi: 10.1097/MD.0000000000006177.

8）Shimane prefecture: Current and Future of the Elderly. https://www.pref.shimane.lg.jp/medical/fukushi/kourei/kourei_sien/kaigo_hoken/kaigokeikaku.data/02_genjoutosyourai.pdf?site=sp [2023-1-10]

9）Al-Hourani K, Al-Aref R, Mesfin A: Upper cervical epidural abscess in clinical practice: diagnosis and management. Glob Spine J, 2016; 6(4): 383-393. doi:

10.1055/s-0035-1565260.

10）Bond A, Manian FA: Spinal epidural abscess: a review with special emphasis on earlier diagnosis. BioMed Res Int, 2016; 2016: article ID 1614328, 6 pages. doi: 10.1155/2016/1614328.

（受付日：2023年10月24日，掲載決定日：2023年12月12日）