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Original Article

Liver Cirrhosis Predisposes One to Complicated Deep Neck Infection: Retrospective Analysis of 161 Cases

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Introduction: Without appropriate and prompt diagnosis and treatment, life-threatening complications may occur in patients with deep neck infection. Liver cirrhosis occurs more common in Asians and few studies mention if it predisposes to complicated deep neck infection. We aimed to identify predisposing factors of complications to reduce morbidity and mortality.
Materials and Methods: A retrospective analysis of 161 patients with deep neck infection at emergency department of Kaohsiung Chang Gung Memorial Hospital between 2010 and 2012 was performed. We also analyzed the differences between patients with complicated and non-complicated deep neck infection.
Results: One hundred and twenty-two patients were men (75.8%). The most common past medical history was diabetes mellitus, followed by liver cirrhosis, which occurs more commonly in Asians. The most common site of involvement was the peritonsillar space (42.9%). The most common pathogen was *Streptococcus viridans* (23.1%). Fourteen patients (8.7%) had complications and six (3.7%) died during hospitalization. Complicated cases had significantly lower heart rate and mean arterial pressure but higher blood sugar level. They also had higher opportunity to have liver cirrhosis, multiple sites, and mediastinum involvement, resulting in longer duration of hospitalization and higher mortality rate. Logistic regression analysis determined that liver cirrhosis was the only predisposing factor for life-threatening complications.
Conclusion: People with liver cirrhosis have higher occurrence of complication if they suffered from deep neck infection. Adequate treatment including airway maintenance, appropriate antibiotics, intravenous fluid support, and surgical intervention should be provided as soon as possible to decrease complications and mortality.

Key words: *deep neck infection, liver cirrhosis, predisposing factor, complications*

Introduction

Deep neck infection is defined that infection originates from potential spaces and fascial plane of the neck which includes peritonsillar, submandibular, parapharyngeal, retropharyngeal, prevertebral, submental, parotid spaces, and posterior cervical spaces.[1] Ludwig's angina was defined while the infection involving bilateral submandibular, submental and sublingual spaces and easily caused airway compression which classified as the category of deep neck infection.[2] It can be caused by dental problems, acute tonsillitis, sialoadenitis, or cervical lymphadenitis and is associated with poor oral hygiene.[2] Current administration of antibiotics and improvement for modern dental care have significantly decreased its occurrence and progression. However, without appropriate and prompt diagnosis and treatment, the infection progresses rapidly and life-threatening complications

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such as descending necrotizing mediastinitis, septic shock, airway obstruction, pleural empyema, pericardial effusion, and jugular vein thrombosis, may occur and associate with high morbidity and mortality.[3] If any of these conditions occur, the prognosis is often poor. The mortality rate can be 40–50% in cases with descending necrotizing mediastinitis or septic shock.[3]

Liver cirrhosis occurs rarely in Westerners but is more common in Asians due to the idiosyncrasy of difference races and higher morbidity of hepatitis B or hepatitis C viral infection. The clinical course and complications of deep neck infection have been well described in the literature and through many large population studies, but few studies mention whether liver cirrhosis is the predisposing factor for complicated deep neck infection. The purpose of this study was to identify the predisposing factors for life-threatening complications in deep neck infection. Appropriate treatment can be provided as soon as possible to reduce the morbidity and mortality of these cases.

Methods

This was a retrospective analysis of 161 patients with deep neck infection diagnosed at emergency department (ED) of Kaohsiung Chang Gung Memorial Hospital and then was admission between January 2010 and December 2012.

All the data was collected when the patients visited ED and included demography (age, sex, and body weight), vital signs (body temperature, heart rate, respiratory rate, and mean arterial pressure), past medical history (diabetes mellitus, cerebral vascular accident, coronary artery disease, chronic kidney disease, and liver cirrhosis), and laboratory examination results (white blood count, blood sugar, blood creatinine, and C-reactive protein).

Other information included bacteriological results, presence or absence of surgical intervention and complications, duration of stay in the ED, duration of hospital stay, and mortality rate.

All patients with deep neck infection underwent computed tomography survey to identify the sites of involvement. We also investigated whether there was involvement of multiple sites or even the mediastinum. Once diagnosis of deep neck infection was confirmed, adequate treatment including airway maintenance (oxygen supply, endotracheal tube insertion, or tracheostomy with mechanical ventilator support), appropriate antibiotics, intravenous fluid support, and surgical intervention was provided immediately. Patients who were confirmed infective sites by computed tomography which involved peritonsillar, submandibular, parapharyngeal, retropharyngeal, prevertebral, submental, parotid, posterior cervical spaces, or Ludwig's angina were included in this study. Patients who were aged under 18 year-old or pregnant were excluded from this study. Complicated deep neck infection was defined if the patients had descending necrotizing mediastinitis, septic shock, airway obstruction, pleural empyema, pericardial effusion, and jugular vein thrombosis during the ED stay.

All statistical analyses were performed using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were compared by the independent sample t test and expressed as mean ± standard deviation. The χ^2 test was used to compare categorical variables. Logistic regression with dummy variables was established to determine whether they were predisposing factors of complicated deep neck infection. Patients with complications attributed to deep neck infection were analyzed. All *p*-values were two-tailed; $p < 0.05$ was considered statistically significant. The Research Ethics Committee approved the project with the protocol number 101-4260B.

Results

Demographics and Characteristics of Patients With Deep Neck Infection

We included 161 patients with deep neck infection in our study. There were 122 men and 39 women; the mean age was 48.4 ± 16.0 years. While arriving at our ED, the mean body temperature was 36.7 ± 0.7°C, mean heart rate was 84.9 ± 16.4 beats per minute (bpm), mean respiratory rate was 18.2 ± 2.4 bpm, and mean arterial pressure was 95.5 ± 13.9 mmHg.

The patients underwent initial laboratory exams at our ED and the mean white blood count was 11,568.3 ± 6,457.8 cells/μL, mean blood sugar was 139.8 ± 73.7 mg/dL, mean blood creatinine was 1.2 ± 1.9 mg/dL, mean C-reactive protein was 80.9 ± 88.8 mg/L and there was positive wound culture result for 88 cases (54.7%).

Past medical history revealed that 34 cases (21.1%) had diabetes mellitus, five (3.1%) had cerebral vascular accident, one (0.6%) had coronary artery disease, seven (4.3%) had chronic kidney disease, and 13 (8.1%) had liver cirrhosis.

During hospitalization, 72 cases (44.7%) received surgical intervention including debridement, incision and drainage, fasciectomy or fasciotomy and tracheostomy. Complications such as descending necrotizing mediastinitis, septic shock, or upper airway obstruction occurred in 14 cases (8.7%). The mean duration of stay in ED was 22.1 ± 33.5 h and mean duration of stay in hospital was 11.8 ± 10.8 d. Six patients died during admission (Table 1).

Sites of Involvement of Deep Neck Infection

The sites of involvement overlapped and most common being the peritonsillar space (42.9%) and submandibular space (37.9%), followed by the parapharyngeal space (14.3%), retropharyngeal space (5.1%), and prevertebral space (4.3%). Seventeen cases (10.6%) involved two sites or above (Fig. 1).

Pathogens Isolated From Deep Neck Infection

Wound culture was positive in 88 cases (54.7%). The most common pathogen was *Streptococcus viridans* (*S. viridans*) (23.1%), followed by *Peptostreptococcus* species (spp.) (13.6%), *Neisseria* spp. (8.7%), *Klebsiella pneumoniae* (*K. pneumoniae*) (8.7%), *Prevotella* spp. (8.1%), and *Pseudomonas aeruginosa* (6.8%). The other pathogens were listed in Table 2. No growth of wound culture after seven days was noted in 73 cases (45.3%).

Comparison of Demographics and Characteristics of Patients With Complicated and Non-Complicated Deep Neck Infection

Fourteen patients with complicated deep neck infection were compared with 147 patients with non-complicated deep neck infection. There were no significant differences in age and sex. When arriving at our ED, complicated cases had lower mean heart rate (76.7 ± 19.9 bpm vs. 85.7 ± 15.9 bpm) and mean arterial pressure (89.1 ± 10.1 mmHg vs. 96.0 ± 14.1 mmHg) than non-complicated cases did, but no significant differences in mean body temperature and respiratory rate were observed. Compared with initial laboratory examination reports from the ED, complicated cases had higher mean blood sugar level (171.3 ± 71.1 mg/dL vs. 136.7 ± 73.5 mg/dL). No significant differences between white blood count, blood creatinine, C-reactive protein, and positive wound culture rate. Past medical history of the patients included diabetes mellitus, cerebral vascular accident, coronary artery disease, chronic kidney disease, and liver cirrhosis and only liver cirrhosis had a significant influence on the occurrence of complications. Moreover, complicated cases had higher likelihood of multiple sites and mediastinum involvement, higher mortality rate and longer duration of stay in hospital. There was no significant difference between duration of stay in ED (Table 1).

Logistic Regression Analysis of Complicated Deep Neck Infection

The variable causes of complication, for which $p < 0.05$ included heart rate, mean arterial pressure, liver cirrhosis, blood sugar, and multiple sites involvement were analyzed using logistic regression. Mediastinum involvement was excluded from analysis because mediastinitis was one of the complications in deep neck infection. Patients with liver cirrhosis had higher likelihood of experiencing complicated deep neck infection. Other variable causes were not statistically significant (Table 3).

Discussion

Deep neck infection does not occur frequently, but can be lethal even with the treatment of antibiotics. There is a high potential for severe complications and it can even cause death without proper management.[4] Deep neck infection can arise from various regions of the head and neck, including the teeth, paranasal sinuses, pharynx, and adenotonsillar tissue.[1] Dental manipulation and pharyngotonsillar infections are the major causes of deep neck infection, as identified recently in 49% and 20% of patients, respectively, by Bakir et al.[5] The origin in 32% of patients remained unknown.[6]

The mean age of patients in the literatures varies, being 38–55 years, and infection is twice as frequent in men as that in women, which is similar to our findings.[7]

While arriving at our ED, most of the patients had no fever and no shortness of breath. Their mean arterial pressure was within normal range and only mild tachycardia was noted. Laboratory analysis revealed that most of the patients had marked leukocytosis, elevated C-reactive protein, and mild renal function impairment.

We traced the past medical history of the patients. The most common systemic disease was diabetes mellitus, which was present in 21.1% of patients. This was similar to the most studies, where the incidence was

Table 1. Comparison of demographics and characteristics of patients with complicated and non-complicated deep neck infection

	Total (n = 161)		Complicated (n = 14)		Non-complicated (n = 147)		*p*
	Mean ± SD[a]	n (%)	Mean ± SD[a]	n (%)	Mean ± SD[a]	n (%)	
Demographic data							
Age (years)	48.4 ± 16.0		54.4 ± 12.1		47.8 ± 16.3		0.126
Male		122 (75.8)		9 (64.3)		113 (76.9)	0.330
Vital signs while arriving ED							
Body temperature (°C)	36.7 ± 0.7		36.6 ± 0.6		36.7 ± 0.7		0.615
Heart rate (bpm)[b]	84.9 ± 16.4		76.7 ± 19.9		85.7 ± 15.9		0.032
Respiratory rate (bpm)	18.2 ± 2.4		18.9 ± 4.6		18.1 ± 2.1		0.782
Mean arterial pressure (mmHg)[b]	95.5 ± 13.9		89.1 ± 10.1		96.0 ± 14.1		0.024
Past medical history							
Diabetes mellitus		34 (21.1)		6 (42.9)		28 (19.0)	0.078
Cerebral vascular accident		5 (3.1)		2 (14.3)		3 (2.0)	0.061
Coronary artery disease		1 (0.6)		0 (0.0)		1 (0.7)	1.000
Chronic kidney disease		7 (4.3)		2 (14.3)		5 (3.4)	0.115
Liver cirrhosis[b]		13 (8.1)		4 (28.6)		9 (6.1)	0.016
Laboratory examination							
White blood count (cells/μL)	11,568.3 ± 6,457.8		14,135.7 ± 11,598.6		11,323.8 ± 5,747.3		0.874
Blood sugar (mg/dL)[b]	139.8 ± 73.7		171.3 ± 71.1		136.7 ± 73.5		0.037
Blood creatinine (mg/dL)	1.2 ± 1.9		1.6 ± 3.1		1.2 ± 1.6		0.108
C-reactive protein (mg/L)	80.9 ± 88.8		113.1 ± 116.6		77.8 ± 85.6		0.295
Positive blood culture result		6 (3.7)		4 (28.6)		2 (1.4)	0.053
Positive wound culture result		88 (54.7)		7 (50.0)		81 (55.1)	0.783
Surgical intervention		72 (44.7)		8 (57.1)		64 (43.2)	0.403
Multiple sites involvement[b]		17 (10.5)		6 (42.9)		11 (7.5)	< 0.001
Mediastinum involvement		3 (1.9)		3 (21.4)		0 (0.0)	< 0.001
Mortality		6 (3.7)		5 (35.7)		1 (0.7)	< 0.001
Duration of stay in ED (h)	22.1 ± 33.5		27.6 ± 34.6		21.6 ± 37.5		0.304
Duration of stay in hospital (d)	11.8 ± 10.8		29.6 ± 19.5		10.1 ± 7.8		< 0.001

bpm: beats per minute; ED: emergency department.

[a]All continuous values are expressed as mean ± standard deviation (SD) [min, max].

[b]The items are enrolled the step of logistic regression model.

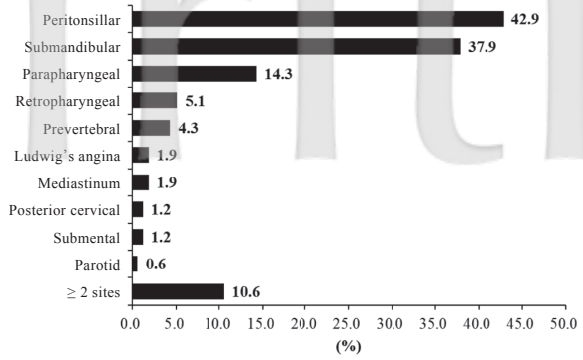

Fig. 1. Sites of involvement of 161 patients with deep neck infection.

Table 2. Pathogens isolated from 161 patients with deep neck infection

Culture result	Number of cases	%
Aerobic		
Gram-positive		
Streptococcus viridans	37	23.1
Staphylococcus aureus	3	1.9
Enterococcus spp.	1	0.6
Gram-negative		
Neisseria spp.	14	8.7
Klebsiella pneumoniae	14	8.7
Pseudomonas aeruginosa	11	6.8
Enterobacter	3	1.9
Serratia marcescens	1	0.6
Salmonella spp.	1	0.6
Anaerobic		
Peptostreptococcus spp.	21	13.6
Prevotella spp.	13	8.1
Veillonella spp.	8	5.1
Fusobacterium spp.	6	3.7
Others		
Acinetobacter	1	0.6
Mycobacterium tuberculosis	1	0.6
Burkholderia cepacia	1	0.6
Stomatococcus	1	0.6
Propioni acnes	1	0.6
Propionibacterium	1	0.6
No growth after 7 days	73	45.3

spp.: species.

16–20%.[7] The second most common systemic disease was liver cirrhosis, which was found in 8.1% of patients. Liver cirrhosis is more common in Asians and less in Westerners due to the idiosyncrasy of difference races and is mentioned less frequently in the literatures.

Many life-threatening complications might occur in patients with deep neck infection, including septic shock, upper airway obstruction, descending necrotizing mediastinitis, jugular vein thrombosis, pleural empyema, pericarditis, pericardial effusion and adult respiratory distress syndrome.[3,7] The rate of complication in the present study was 8.7%, which lower than the findings in previous studies ranged from 13% to 26%,[7] but was highly associated with mortality. The most frequent complication was upper airway obstruction often requiring tracheostomy, followed by septic shock and descending necrotizing mediastinitis, which is similar to the findings of Boscolo-Rizzo et al.[8]

The mortality rate in our study was 3.7% (n = 6). This was lower than the result of recent studies that reported about 5–10% incidence.[3] Five patients died due to septic shock with multiple organ dysfunction syndrome and the other from acute myocardial infarction. We analyzed these six patients who died at last and found that wound culture showed almost different pathogens. No specific pathogens related to higher mortality. Four patients involved submandibular space and three of them received tracheostomy due to airway compression and the other two patients involved parapharyngeal space and one patient received tracheostomy due to same problem.

Descending necrotizing mediastinitis is the worst complication of deep neck infection. It may rapidly progress to septic shock and is related to poor prognosis with 40–50% mortality.[7]

Prompt recognition and treatment of deep neck infection are very important for improving the prognosis.[7] Contrast-enhanced computed tomography scanning is the most important imaging examination and is more effective for determining the sites of involvement in comparison with surgical findings and clinical symptoms, which according to a clinical study in São Paulo, Brazil, may easily underestimate the extension of the area.[9] It can also detect abscess formation earlier in patients with deep neck infection, thus enabling the immediate administration of adequate surgical intervention that includes debridement, incision and drainage, fasciectomy or fasciotomy, and tracheostomy for better treatment and prognosis.[10]

The most common site of involvement that we

Table 3. Logistic regression analysis of variable causes of complication

	RR	*p*	95% CI
Heart rate (bpm)	1.0	0.146	0.91–1.01
Mean arterial pressure (mmHg)	0.9	0.081	0.86–1.01
Liver cirrhosis	17.6	0.003	2.61–118.60
Blood sugar (mg/dL)	1.0	0.167	1.00–1.02
Multiple sites involvement	2.8	0.284	0.43–18.54

bpm: beats per minute; CI: confidence interval; RR: relative risk.

detected was the peritonsillar space, and was often due to acute tonsillitis. The submandibular space and parapharyngeal space were also frequently involved and only secondary to the peritonsillar space. These findings were quite similar to the results of a recent study.[8] The medical history of our patients revealed that only some of them underwent dental manipulation recently. The origins of deep neck infection in the other patients remain unknown.

Lee et al. demonstrated that *K. pneumoniae* was the most common pathogen among positive cultures, followed by *S. viridans*.[3] This differed from the results of recent studies and ours, which reported that *S. viridans* was the most common pathogen.[2,8,11] In our study, *Peptostreptococcus* spp. was present in 13.6% of patients and was the most common pathogen in some studies.[6,10] In addition, the negative culture rate in this study was 45.4%, higher than the most studies, which reported 27–40% incidence.[7]

Comparing complicated and non-complicated deep neck infection, we found that complicated cases had significantly lower heart rate, lower mean arterial pressure, and higher blood sugar level. This corresponded to a previous study that stated that control of blood sugar, especially in patients with diabetes mellitus, was important for controlling the infection.[11] Further analysis of the patients' past medical history revealed that complicated patients had significantly higher liver cirrhosis morbidity. This is not mentioned frequently in the previous literatures. There was no significant difference in diabetes mellitus between two groups. This was different from the findings of previous studies.[10,11] We also found that complicated cases had significantly higher likelihood of multiple sites involvement and mediastinum involvement, resulting in longer duration of stay in hospital and higher mortality that was similar to the findings of Boscolo-Rizzo et al.[8]

Logistic regression with variable causes of complication revealed that liver cirrhosis was the only predisposing factor for life-threatening complications in patients with deep neck infection. Liver cirrhosis predisposes patients to serious bacterial infections with an incidence that is five to seven times higher than patients without liver cirrhosis according to the previous literatures.[12] This increased incidence is due to multiple immune system defects and increased risk of bacterial translocation from gastrointestinal mucosa.[13] Organisms can gain access to the gastrointestinal tract and escape phagocytosis of the hepatic reticuloendothelial system due to the portal-systemic shunting circulation in cirrhotic patients and establishes systemic bacteremia. The bacteria in the bloodstream may seed in the soft tissue and cause severe soft tissue infections or primary septicemia. Multiple sites involvement was the predisposing factor in many previous studies, but not in ours.[2,6,8] This was probably due to the fewer case numbers in our study (n = 3). More care must be provided to patients with liver cirrhosis, and adequate treatment including airway maintenance (oxygen supply, endotracheal tube insertion or tracheostomy with mechanical ventilator support), appropriate antibiotics, intravenous fluid support, and surgical intervention including debridement, incision and drainage, fasciectomy or fasciotomy and tracheostomy should be provided as soon as possible to reduce complications and mortality.[3]

One limitation to our study was the much difference in number of complicated (n = 14) and non-complicated cases (n = 147). Having a similar number of cases in the two groups would yield more accurate findings. Another limitation was the small number of complicated and mortality cases. Future study designs should include more cases so that they may contain more complicated and mortality cases for further analysis.

Conclusions

People with liver cirrhosis have higher occurrence of complication if they suffered from deep neck infection. Adequate treatment including airway maintenance, appropriate antibiotics, intravenous fluid support, and surgical intervention should be provided as soon as possible to decrease complications and mortality.

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