Original Article

A new classification of descending necrotizing mediastinitis and surgical strategies

Xin Guan[1], Xiang Liang[1], Xi Liang[1], Feng Wang[1], Wentao Qian[2], Weijie Zhang[2]

[1]Department of Thoracic Surgery, Shanghai Jiao Tong University School of Medicine, Shanghai, China; [2]Department of Oral Surgery, Shanghai Ninth People's Hospital, College of Clinical Medicine, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Contributions: (I) Conception and design: X Guan; (II) Administrative support: W Zhang; (III) Provision of study materials or patients: X Liang, W Qian; (IV) Collection and assembly of data: X Liang; (V) Data analysis and interpretation: F Wang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Xin Guan, MD. Department of Thoracic Surgery, Shanghai Ninth People's Hospital, Affiliated to Shanghai Jiao Tong University School of Medicine, 639 Zhizaoju Road, Shanghai 200011, China. Email: gxin23@163.com.

Background: Descending necrotizing mediastinitis (DNM) is an inflammation occurring in the oropharynx and descending to the deep cervical space and mediastinum, which is a serious infectious disease. The investigation of a new classification system and treatment methods for DNM is still necessary.

Methods: A total of 139 patients with DNM caused by odontogenic or pharyngeal infection were retrospectively analyzed in last 20 years in the Ninth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. The patients were divided into the traditional treatment Group T (Group T: 43 patients) and the new classification Group N (Group N: 96 patients). A new DNM classification was developed based on the progression of mediastinal infection as follows: type Ia: infection in the anterosuperior mediastinum; type I: infection in the anterior mediastinum; type II: infection in the posterior mediastinum; and type III: infection of the whole mediastinum.

Results: There were 49, 8, 10, and 29 patients classified as type Ia, I, II, and III, respectively in the Group N. The type Ia DNM patients were managed with transcervical mediastinal drainage, and the patients with types I and II DNM underwent open (thoracoscopic) surgery, 1 patient within types I died. The 29 patients with type III were managed with unilateral or bilateral open (thoracoscopic) surgery, among them, 8 patients died. The mortality rate for patients with type III DNM was 27.6%. The overall mortality rate in Group N was 9.4%. The mortality rate for patients in the Group T was 25.6%. The mortality rate of Group N was significantly lower than that of Group T ($P<0.05$).

Conclusions: We have carried out a new clinical classification of DNM, and selected the appropriate treatment method according to the classification, and achieved a better effect than the traditional treatment method.

Keywords: Descending necrotizing mediastinitis (DNM); new classification; treatment method

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Introduction

Descending necrotizing mediastinitis (DNM) is often caused by odontogenic or pharyngeal infections, which can result in complications, such as abscesses, in the submaxillary, parapharyngeal, and retropharyngeal spaces. Subsequently, infection may spread downward through the pretracheal, visceral, and prevertebral spaces to the mediastinum. The invasiveness of bacteria, the patient's constitution (with or without diabetes), and the delayed treatment of oropharyngeal infection may be the important reasons for the occurrence of deep neck space infection and DNM. Once a deep cervical space infection is present,

negative pressure during breathing and gravity promotes the spread of inflammation to the mediastinum. The pathology of DNM includes tissue edema, effusion, necrosis, and abscess, which may result in pleural and pericardial effusion. Blood vessels may also become infected, causing major bleeding. Patients may go on developing severe sepsis and septic shock, and in severe cases, multiple organ failure, due to the inflammatory reaction and toxic effects of infection. In the mid-late 20th century, the mortality rate of DNM was as high as 60–70%, but active surgical management reduced it significantly to 30–40% (1-3). However, Sarna *et al*. in 2012 reported that the mortality rate among DNM patients with septic shock remained extremely high (64%) (3). Delayed diagnosis and improper surgical management are the major contributing factors to the high mortality of DNM.

Estrera *et al*. summarized the diagnostic criteria for DNM in 1983 (4); however, no standardized surgical treatment for DNM currently existed, and the outcomes of patients with this condition are still unsatisfactory (4-8). The clinical progression of DNM is closely related to its prognosis, which makes early diagnosis and appropriate surgical treatment critical to its management. The clinical progression of DNM was classified by Endo *et al.* (9). They defined superior mediastinal infection (above the tracheal bifurcation) as type I, infection of the superior and anteroinferior mediastinum as type IIA, and total mediastinal infection as type IIB. However, this DNM classification is not ideal. Firstly, it does not take into account infection of the posterior mediastinum alone. Sumi *et al.* summarized a 5-year history of DNM treatment in publications and pointed out that abscesses in the retropharyngeal space often spread via the prevertebral space, reaching the posterior mediastinum (10). Secondly, patients with DNM limited to the anterosuperior mediastinum usually show a good response to transcervical mediastinal drainage. Thirdly, infection of the superior mediastinum is insufficient to transcervical mediastinal drainage alone, and this type of DNM responds well to transthoracic debridement and drainage.

Herein, we propose a new DNM classification method based on previous therapeutic experience and Endo classification method. Our choice of surgical modalities based on the classification of mediastinal infection should reduce mortality in patients with DNM.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-21-121).

Methods

By dividing the mediastinum, clinical classification of DNM was performed according to CT images of patients with DNM. Retrospective analysis method was used to compare the change of mortality rate of patients with DNM in different periods.

The data of 139 patients with DNM admitted to the Department of Thoracic Surgery, Ninth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine from 1999 to 2019 was collected. DNM was caused by odontogenic infection and pharyngeal infection in 99 and 40 patients, respectively. Patients were divided into two groups: the traditional treatment group (Group T) and the new classification group (Group N). In Group T, 43 patients were enrolled from 1999 to 2009, including 27 males and 16 females, with a mean age of 56.4±15.6 years (45–70 years). The Group N included 96 patients between 2010 and 2019. There were 68 males and 28 females. The mean age was 52.3±25.6 years (26–78 years).

The inclusion criteria were the following: we included patients with odontogenic and pharyngogenic DNM. We excluded patients with a traumatic mediastinitis, iatrogenic mediastinitis, and patients with concomitant tumor and cerebral infarction.

Early symptoms included toothache, sore throat, and fever, which were followed by other symptoms such as swelling and pain in the lower jaw and neck, difficulty in opening the mouth, dysphagia and dyspnea. When DNM develops to mediastinitis phase, the clinical manifestations may not be obvious, and sometimes there will be chest tightness and chest pain.

The diagnostic criteria for DNM on neck and chest computed tomography (CT) were: mandibular, parapharyngeal, retropharyngeal, or neck abscesses and/or air cavities; Soft tissue effusion containing air cavities in the mediastinum, which is the continuation of neck air cavities; non-encapsulated abscess fluid aggregation in the mediastinum with abscesses (11).

In the new classification of DNM, the anterior mediastinum was defined as the area posterior to the sternum and anterior to the trachea/pericardium. The posterior mediastinum was defined as the area between the spine and the trachea/pericardium. The mediastinum was divided into the superior and inferior mediastinum by the tracheal bifurcation. The clinical progression of DNM was classified according to CT images as follows: type Ia: infection in the anterosuperior mediastinum (*Figure 1*); type

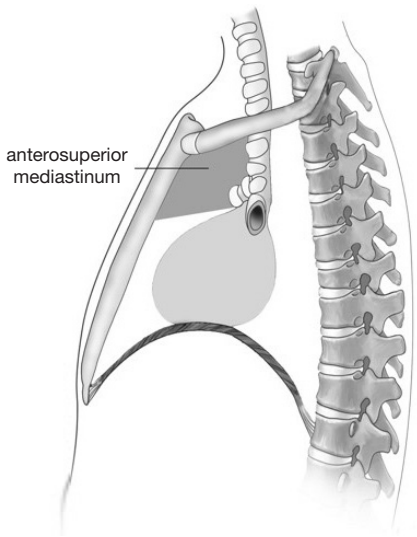

Figure 1 Type Ia: infection is confined to the anterosuperior mediastinum.

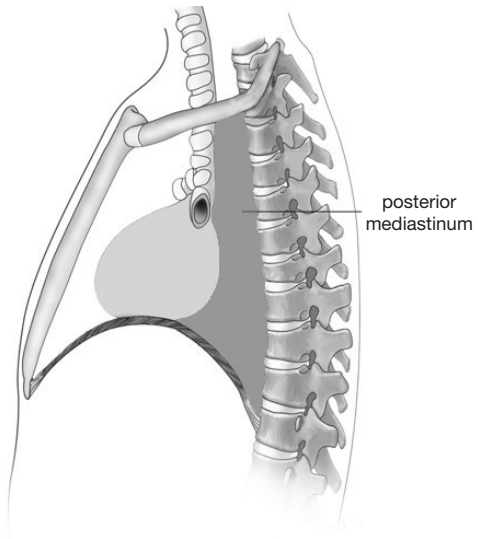

Figure 3 Type II: infection involves the posterosuperior mediastinum or the posterior mediastinum.

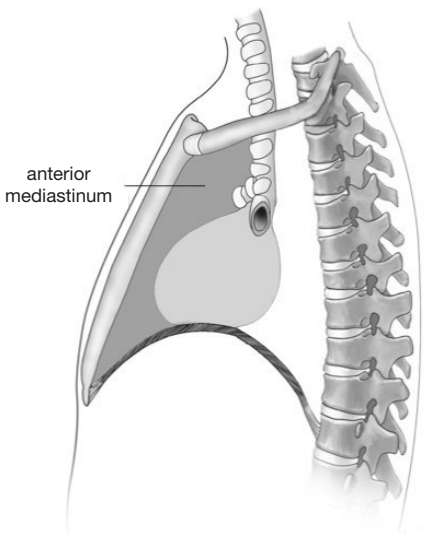

Figure 2 Type I: infection involves the entire anterior mediastinum.

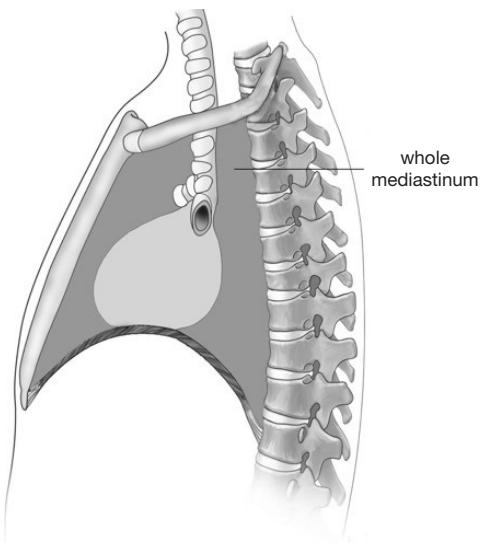

Figure 4 Type III: infection involves both the anterior and posterior mediastinum.

I: infection in the anterior mediastinum (*Figure 2*); type II: infection in the posterosuperior or posterior mediastinum (*Figure 3*); and type III: infection involving both the anterior and the posterior mediastinum (*Figure 4*).

Since the number of DNM cases is limited, we formed the idea of reclassifying DNM based on our treatment experience, and treated 96 patients with DNM according to this classification, and it is expected that the results may be better than traditional treatment methods that according to old classification. However, the number of cases was relatively small, so the study method of case-grouped control (mismatch) was adopted. All patients met the diagnostic criteria. In Group N, surgical methods were selected according to the new DNM classification. In Group T, conventional surgical methods were used according to Endo's classification. Data on all patients were

collected from hospital records containing symptoms and signs, laboratory results, imaging data (The CT scans were evaluated by an independent radiologist and the operation team), and treatment results. The study only looked at mortality rates. The bias is very low.

Statistical analyses

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS Version 26, IBM Corp., Armonk, NY, USA). The patients were divided into two groups: Group T and Group N. A Chi-square test was used to analyze categorical variables. Statistical significance was set at an alpha level of 0.05.

Ethical statement

The study was conducted in accordance with the declaration of Helsinki (as revised in 2013). The study was approved by committee of the Ninth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (No.:2016-158-T157) and informed consent was taken from all individual participants.

Results

The 96 patients with DNM in group N included 49, 8, 10, and 29 cases of type Ia, I, II, and III, respectively. The clinical manifestations included chest tightness and chest pain in 52 cases, dysphagia in 40 cases, dyspnea in 36 cases, and fever (>38 ℃) in 69 cases. Seventy-six patients had neck swelling and pain, and 28 patients had redness of the skin of the neck and chest. Bacterial culture revealed infection with Streptococcus in 41 cases (43%), Staphylococcus in 20 cases (21%), and Klebsiella pneumoniae in 12 cases (12%), while 6 cases had infections of other anaerobic bacteria. Seventeen specimens were found negative for bacterial culture. The major pathogenic bacteria species and their constitution in our patients were similar to those reported by Yuka Sumi (10).

The 43 patients with DNM in group T. The clinical manifestations included chest tightness and chest pain in 20 cases, dysphagia in 16 cases, dyspnea in 22 cases, and fever (>38 ℃) in 34 cases. Bacterial culture revealed infection with Streptococcus in 13 cases (30%), Staphylococcus in 8 cases (18%), and Klebsiella pneumoniae in 4 cases (10%). 18 specimens were found negative for bacterial culture.

For the infection of oropharynx and neck space, it is very important for the anesthesiologist to judge the degree of compression displacement of pharynx and throat according to CT examination. During endotracheal intubation, asphyxia due to stimulation should be avoided. Some patients have to be intubated for a longer time or have a tracheotomy. The key is to do incision drainage in the lower jaw and neck to reduce the swelling of the throat.

Infections of the oropharyngeal or neck space were treated with debridement and drainage through multiple incisions in the mandibular region or the neck. Such incisions should be large enough to allow access to the abscess cavity, especially those located on the posterior wall of the pharynx. A transverse incision was made superior to the suprasternal fossa, deep into the inflamed space, such as the pretracheal space or the perivascular spaces, and was connected to the incision in the mandibular area. Vaccum seeking drainage (VSD) is a very good drainage method. Then, the mediastinal infection was managed according to the specific type of DNM.

The characteristics and surgical treatment of type Ia DNM were as follows

Of the 49 patients with type Ia DNM, 33 had infectious lesions located superior to or beyond the left innominate vein. These patients were managed with mediastinal drainage through a suprasternal fossa incision, which was easy to perform. The patients made a quick recovery, with a mean hospital stay of 14.7 days. In the other 16 patients, air-pus cavities were observed bilateral to the trachea. Blunt dissection was carried out along the tracheal wall via the suprasternal incision, and the pus cavity in the retrosternal space was isolated. Drainage was performed using a tube or iodoform gauze or VSD. These 16 patients needed relatively longer drainage time and recovered more slowly than the above 33 patients, with a mean hospital stay of 20.4 days. Among the patients with type Ia DNM, 13 patients required tracheotomy due to dyspnea caused by swelling of the throat. All 49 patients were cured, with a mean hospital stay of 17.3 days.

The characteristics and surgical treatment of type I DNM was as follows

CT revealed mediastinal widening as well as non-encapsulated abscesses and air-pus cavity in the anterior mediastinum. The pericardial adipose tissue was swollen, with both pleural and pericardial effusion. Two of the

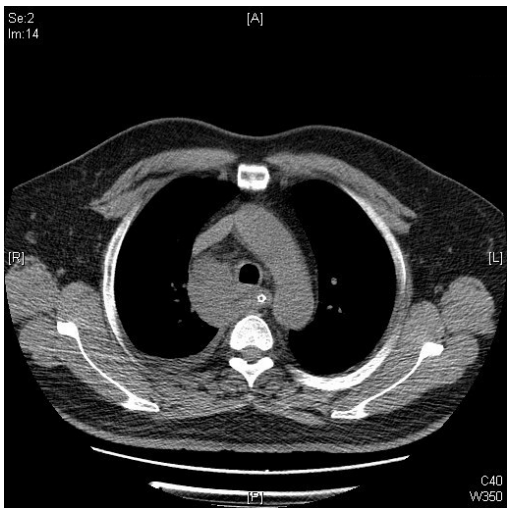

Figure 5 Chest computed tomography image showing an abscess in the posterior mediastinum of a patient.

Table 1 Comparison of mortality rates between the new DNM classification and the conventional treatment group

Group	Cases	Deaths	Mortality rate
Group N	96	9	9.40%
Group T	43	11	25.60%

χ^2=5.918, P<0.05. DNM, descending necrotizing mediastinitis.

patients suffered septic shock in 8 patients with type I DNM. Four patients were treated with debridement and drainage via thoracotomy; 2 patients underwent thoracoscopic debridement and drainage; and in the 2 remaining patients, a subxiphoid approach was taken. After pulling up the sternum, a thoracoscope was used to observe the retrosternal space. The necrotic tissue in the anterior mediastinum was debrided, and the bilateral mediastinal pleura was incised. Blunt dissection of the pus cavity beneath the sternum was performed using oval forceps, and a drainage tube was placed in the anterior mediastinum. All patients received pericardial incision and drainage. Three patients required tracheotomy postoperatively. Postoperative complications included acute respiratory distress syndrome (ARDS) in 3 patients, renal insufficiency in 3 patients, and hepatic insufficiency in 2 patients. Seven of the 8 patients were cured. The other patient developed infection involving the whole mediastinum and died due to multiple organ failure. The mean hospital stay of type I DNM patients was 32.2 days.

The characteristics and surgical treatment of type II DNM were as follows

In most cases, the retropharyngeal abscess spreads downward along the prevertebral space to the posterior mediastinum, resulting in an abscess above the azygous vein (*Figure 5*). Of the 10 patients with type II DNM, 7 were treated with debridement and drainage via thoracotomy, and 3 were treated with thoracoscopic debridement and drainage. After the posterior mediastinal pleura and the abscess wall were opened, the pus cavity was dissected in front of the spine and upward to the neck space. The anterior mediastinal pleura still needed to be opened, regardless of whether there was an abnormality in the anterior mediastinum. Two patients required postoperative tracheotomy. Postoperative complications included 2, 3, and 3 cases of ARDS, renal insufficiency, and hepatic insufficiency, respectively. One patient suffered superior vena cava rupture on day 7 postoperatively and received emergent thoracotomy for vessel repair. All 10 patients were cured, and the mean hospital stay was 30.2 days.

The characteristics and surgical treatment of type III DNM were as follows

Chest CT found abscesses and air-containing exudate in both the anterior and posterior mediastinum. All 29 patients with type III DNM had severe sepsis, including septic shock in 12 cases. Twenty patients were managed with unilateral thoracotomy (including thoracoscopic surgery in 8 cases), and 9 patients were managed with bilateral thoracotomy (including thoracoscopic surgery in 4 cases). All patients underwent bilateral closed thoracic drainage and pericardial incision and drainage. Thirteen patients received tracheotomy. Twenty-five patients had ARDS, hepatic, and kidney dysfunction to different extents. Twenty-one patients were cured, and the mean hospital stay was 48.6 days. Eight patients died from septic shock and multiple organ failure. The mortality rate for type III DNM was 27.6%.

A total of 9 patients in the study died, representing an overall mortality rate of 9.4%. Follow-up of the discharged patients found mild to moderate ventilation restriction in 6 patients. All surviving patients returned to their normal life.

According to the data collected, 11 of 43 patients in the traditional treatment group died, with a mortality rate of 25.6%. The mortality rate of 96 patients in Group N was 9.4%, and the P value between the two groups was below

0.05 (*Table 1*).

Discussion

Prevent oral cavity, larynx department infection, the infection should be applied to antibiotics, when there is abscess, it should be timely incision drainage. Attention should be paid to cervical space infection, and transverse incision drainage at the supra sternal fossa can stop the spread of inflammation to the mediastinum. However, once DNM occurs, the selection of appropriate treatment should be able to reduce the mortality.

Although antibiotic therapy selected on the basis of bacterial culture and antibiotic resistance testing is critical in the treatment of DNM, surgical debridement and drainage are also essential. Until the 1980s, transcervical mediastinal drainage was still the most important treatment method for DNM, at which time the mortality rate exceeded 40% (4). In the early 1990s, Wheatly *et al.* concluded that transcervical mediastinal drainage was insufficient for the treatment of DNM (12). Later, Marty-Ane *et al.* showed that the survival rate of patients treated with thoracotomy debridement and drainage was significantly higher than that of patients who received only transcervical mediastinal drainage (7,13), which implies that the difference in survival rate with the different approaches led to a change in treatment ideas and methods for DNM. This is important for the surgeon to change treatment idea and method of DNM. Nevertheless, transcervical mediastinal drainage remains an effective treatment method for anterosuperior mediastinal infection (14,15).

Therefore, determining the location of the mediastinal infection is the key to selecting the appropriate treatment (15-17).

In the past, mediastinal division was of great value in the evaluation of the origin and nature of mediastinal tumors, but it was unsuitable for the classification of DNM. In this study, we proposed a new method for mediastinal division, which classifies DNM into type Ia, type I, type II, and type III. In our classification, superior mediastinal classification in Endo classification is reclassified as total mediastinal infection (type III). This is because superior mediastinal infection involves both the anterior mediastinum and the posterior mediastinum, and may spread rapidly to the lower mediastinum if the infection progresses fast. Furthermore, simple transcervical mediastinal drainage is insufficient for the treatment of superior mediastinal infection. At this time, if an abscess or downward spread of the infection is detected on CT, then a secondary surgery is required. Posterior mediastinal infection caused by the downward spread of retropharyngeal abscesses along the prevertebral space is usually confined, and typically CT image forms an abscess posterolateral to the trachea and superior to the azygous vein. Abscess s often shown as an isolated lesion on CT images and during surgery, with no involvement of the anterior mediastinum; thus, Posterior mediastinal infection is classified as type II.

Transcervical mediastinal drainage is the best treatment option for type Ia DNM confined to the area above the left innominate vein. Ridder *et al.* summarized the 50-year experience of DNM treatment and found that in most cases, DNM was confined to the superior mediastinum at diagnosis (18). Determining whether the infection is in the anterosuperior or superior mediastinum is vital.

Type I DNM, which may quickly progress to total mediastinal infection, is relatively rare. This type of DNM can be managed through thoracotomy or thoracoscopic debridement and drainage. Thoracoscopic debridement and drainage using a subxiphoid approach is another treatment option. While there is a certain risk in guiding the drainage tube in front of the innominate vein, this method is easy to perform and is minimally invasive, with good drainage results (19).

In type II DNM, the pharyngeal abscess spreads through the prevertebral space into the posterior mediastinum, resulting in cellulitis and abscesses. Chest CT may reveal abscesses in the posterior mediastinum, mostly located above the azygous vein, or extending downward along the esophagus. The results of intraoperative exploration are usually consistent with the findings of CT, and there is usually no involvement of the anterior mediastinum. In the case of Type II DNM, abscess should be cut open and managed with debridement of the necrotic tissue near the wall of the superior vena cava followed by thorough rinsing and drainage. The aim of this approach is to control the infection and prevent blood vessel rupture.

Type III is the most severe type of DNM. Its surgical treatment requires the patient to be in a stable systemic condition. Thoracoscopy can achieve comparable treatment outcomes as thoracotomy (8). Patients with low blood volume should be monitored for intraoperative hypotension. A high proportion of patients with type III DNM go on to develop septic shock. Severe infection may also increase the risk of postoperative complications, such as ARDS, renal insufficiency, hepatic insufficiency, and major gastrointestinal bleeding. Deu-Martín *et al.* reported that septic shock is an independent predictor of mortality in DNM patients (2).

Similarly, the majority of deaths in our study occurred in patients with type III DNM and septic shock.

Traditional treatment methods do not carry out precise treatment for patients with DNM, only routine debridement and drainage. During the course of treatment, infection may spread further, systemic inflammatory response may increase, complications may increase, and deaths may increase.

Sarna *et al.* reviewed the literature published from 1995 to 2010, which showed DNM to have a mortality rate of 41% (3). In recent years, significant progress has been made with oral surgery, otolaryngology, radiology and thoracic surgery in the treatment of DNM. The multidisciplinary cooperative treatment of DNM can quickly trace the origin of infection, understand the degree of compression of edema tissue to the throat and the degree of neck and chest infection through CT examination, and make diagnosis and clinical classification, and select the surgical method. Prado-Calleros *et al.* systematically analyzed the best evidence from the 26 studies of level III published between 2009 and 2014 (20). They found that, in this period of time, the overall DNM mortality rate had dropped to 17.5%, although it remained high. Several aspects are important in reducing the mortality rate of DNM: these include early diagnosis, surgical treatment based on DNM classification, timely and effective debridement and drainage, efficient intensive care, and multiple postoperative CT examinations (18-21).

However, our study was a single-center retrospective study with a small sample size, and although the mortality rate was lower than that of the control group and that reported at the same time, it is still necessary to increase the number of cases and design a better study protocol in the follow-up work.

Conclusions

Neck infection in DNM patients can be treated with debridement and drainage via a cervical transverse incision, which can prevent the downward spread of the infection. Mediastinal infection is classified according to the mediastinal division and its clinical progression. In the new classification presented herein, DNM is classified as follows: type Ia is anterosuperior mediastinal infection; type I is anterior mediastinal infection; type II is posterior mediastinal infection; and type III is infection of the entire mediastinum. Patients with type Ia DNM respond well to transcervical mediastinal drainage, while those with type I DNM can be managed with thoracotomy, transthoracic thoracoscopy, or infra xiphoid thoracoscopy. Meanwhile, patients with type II or III DNM require thoracotomy or thoracoscopic surgery. Among the patients in this study, our new DNM classification achieved good treatment outcomes, with an overall mortality rate of only 9.4%.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/atm-21-121

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-21-121). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Committee of the Ninth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (NO.: 2016-158-T107) and informed consent was taken from all individual participants.

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