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Original Article

Management of a difficult infectional disease: Descending necrotizing mediastinitis

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Abstract

Introduction: Descending Necrotizing Mediastinitis (DNM) is the fatal form of mediastinitis and mostly develops as a complication of peritonsillar abscesses or dental-odontogenic infections. The aim of this study is to evaluate clinical and surgical feature of the patients with DNM who were managed in our clinic.

Methodology: We retrospectively evaluated 13 consecutive patients with the diagnosis of DNM between February 2005 and February 2018. All of them had the typical physical appearance, history and radiological findings.

Results: Ten (77%) patients were male, 3 (23%) patients were female with a median age of 48.2 (18-76 years). All patients underwent Cervico-Mediastinal Drainage (CMD) with debridement of the necrotic and infected tissues. Other supplimantary surgical procedures were tube thoracostomy (n = 8), VATS mediastinal drainage (n = 4), tracheostomy (n = 2) and thoracatomy (n = 1). The median time to diagnosis of DNM, tube drainage (inserted after CMD) removal time, tube thoracostomy removal time, lenght of hospital stay were 1.8 (range 1-4) days, 13.6 (range 10-20), 12.6 days (range 10-27) and 21.5 days (range 15-30), respectively. Appropriate and potent antibiotics were used according to the fever-CRP response with the consultation on infectious disease specialist. Two patients were lost due to fulminant sepsis (n = 1) and massive cervical haemorrhage (n = 1). Overall mortality rate was 15%. Complications were recorded in 6 patients (46%).

Conclusions: The critical point in the management of DNM is the correct diagnosis, rapid surgical intervention with antibiotherapy and close follow-up for possible complications. We concluded that the combination of minimally invasive management as VATS-tube thoracostomy with CMD is the most appropriate surgical interventions.

Key words: infection; necrotizing; mediastinitis; fatal; developing country.

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Introduction

Mediastinitis is a severe infection of the mediastinal connective tissue, great vessels, heart and surrounding structures. Descending Necrotizing Mediastinitis (DNM) is the fatal form of mediastinitis and usually develops as a complication of peritonsillar abscesses or dental-odontogenic infections [1,2]. The delay in the treatment of a severe infection that starts in the pharynx, the tonsilla or tooth leads to the spread of the suppurative infection through the deep and superficial cervical fascial planes to the mediastinum. It is estimated that DNM can be created by the effect of gravity and negative intrathoracic pressure. In this process, the pretracheal, paraesophageal, prevertebral, retropharyngeal spaces, posterior mediastinum and pleural spaces can be affected by infection [3,4]. DNM is in most cases a mixed infection from aerobic and anaerobic species. Formed deep cervical infection leads to necrotizing cellulitis and multiple small vessel thromboses. This process causes the clinical manifestations of DNM. Although mediastinum hosts the most significant vessels of the body, it has a very suitable envirement for aerobic and anaerobic bacteria due to deep fatty tissue. Also, mediastinum has limited perfusion to antibiotics because of low microcirculation. Clinical suspicion-findings and the typical radiological results should reflect the disease. Delayed diagnosis can lead to increased morbidity and mortality [3-5]. Acute mediastinitis is observed at the rate of 0.5-5%. Primary reasons for acute mediastinitis are esophagus perforation (90%), tracheobronchial injuries and infections after cardiac surgeries. Secondary reasons include lung infection, pleural effusion and DNM(10%). DNM is common in males and young adults. The disease is classified into two types as focal and diffuse type [6,7]. DNM was first described in ten patients with mediastinitis complicating an oropharyngeal infection by Estrere at al.[8] the beginning of the 1980s.They described the diagnostic criteria in the following four titles: 1)Clinical evidence of severe oropharyngeal infection; 2) Characteristic radiographic features of mediastinitis; 3) Documentation of necrotizing mediastinal infection during operation or autopsy; 4)Establishment of the relationship between DNM and the oropharyngeal process.

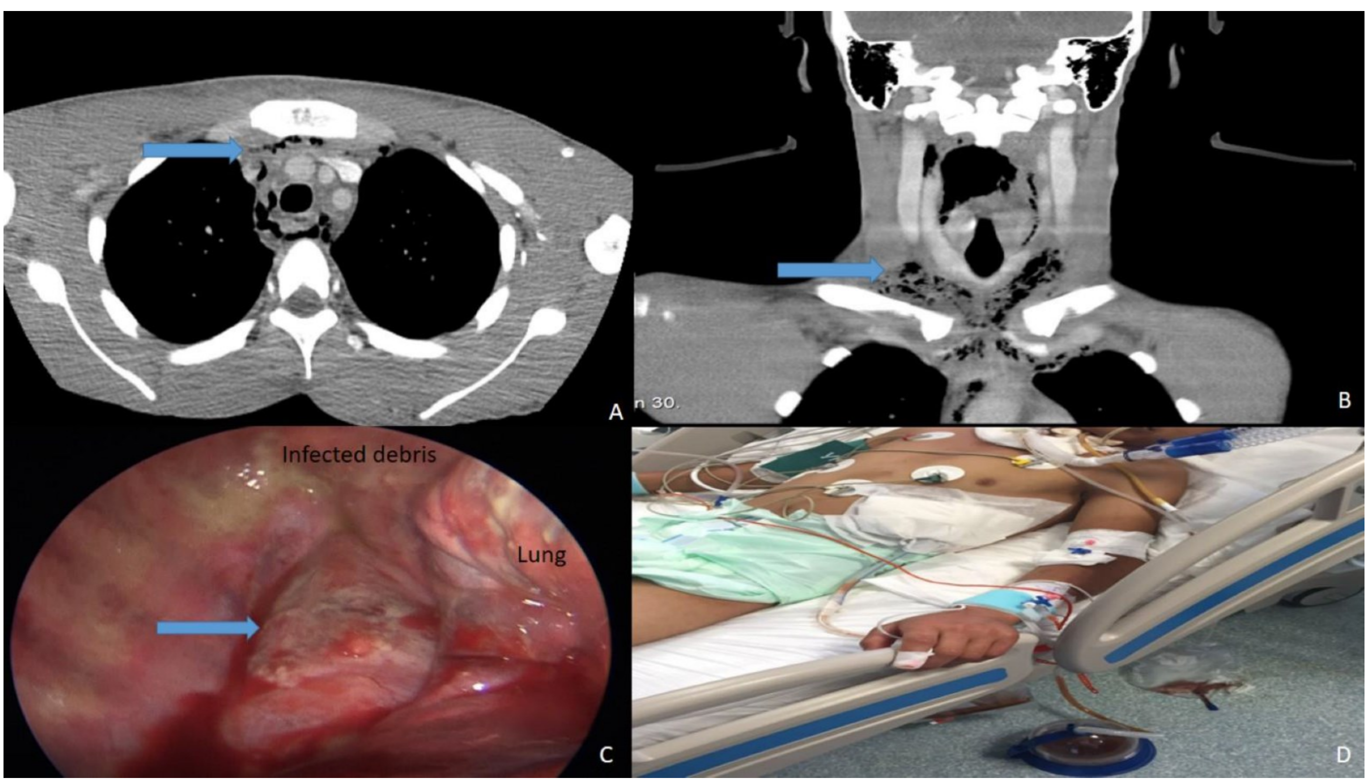
The aim of this study is to evaluate clinical and surgical features of the patients with DNM who were managed in our clinic. We tried to find out the best surgical approach-medical intervention to treat DNM, which is still a fatal problem in developing countries.

Methodology

We retrospectively evaluated a total of 13 consecutive patients with the diagnosis of DNM in our department between February 2005 and February 2018. Age, gender, the origin of infection, time to diagnosis, identified microorganisms, surgical procedure, applied treatments, complications and surgical outcomes were reviewed. We evaluated all patients with Chest X-ray, cervical-thorax Computed Tomography (CT). CT scan confirmed all the diagnoses of DNM with the findings of the complex air-fluid collection in the mediastinum extending to the neck (Figure 1 A, B). Otolaryngologist consultation and examination were requested from all patients. The diagnosis of DNM confirmed with typical anamnesis, physical examination findings and radiological results. The diagnosis was made from the physical appearance, history, physical examination and radiological studies according to the criteria that Endo *et al.* [7]. have set. The time interval between diagnosis and surgical intervention was range 1-2 days in our series.This varies from the onset of the symptoms, location, age and socioeconomic level of the patient.

Routine hemostasis, hemogram parameters and biochemical blood tests examined. C-Reactive Protein (CRP) and sedimentation values were followed. Additionally, the cardiac status of the patients was evaluated by serial serum cardiac enzyme determinations, electrocardiograms, and if needed with echocardiography. Empirically broad-spectrum antibiotics were administered to all patients until the culture results were obtained. Blood culture was performed on all patients. Oxygen saturation, arterial blood gases and blood pressure were closely monitored. Continuous nasal oxygen therapy, fluid replacement and parenteral nutrition were applied. Oral intake was stopped until drainage was achieved and dysphagia disappeared. All patients underwent Cervico-Mediastinal Drainage (CMD) for debridement of the

Figure 1. A: Image of mediastinal complex air -fluid collection on Thorax CT axial section, marked with a blue arrow. **B:** Image of mediastinal complex air -fluid collection extending to the neck on Thorax CT coronal section, marked with a blue arrow. **C:** Intraoperative VATS view of infected debris in thorax cavity and loculation under paratracheal mediastinal pleura, marked with a blue arrow. **D:** Postoperative follow up in ICU with bilateral tube thoracostomy and mediastinal drainage and tracheostomy.



necrotic and infected tissues with general anaesthesia in the operating theatre. Purulent drainage was found in every patient (Figure 2A). Additional surgical procedures were performed if needed according to Endo *et al.* [7]'s DNM type classification. Transcervical CMD for type 1, combining CMD, complete mediastinal drainage-debridement with opening the mediastinal pleura via VATS or thoracotomy for type 2A and 2B were used (Figure 1 C, D, Table 1). Tube thoracostomy was performed if pleural effusion detected assuming spontaneous mediastinal pleural drainage. The daily rifampicin+ hypertonic fluid lavage was performed from the silicone mediastinal drain placed during CMD (Figure 2B).

Data Analysis

Statistical analysis was performed using the Statically Package for the Social Science program (SPSS, 20.0) Data were expressed as mean ± SD. Frequencies and percentages were used for the certain measures.

Results

Demographic-clinical features and surgical outcomes of patients were summarised in Table 1. 10 (77%) patients were male, 3 (23%) patients were female with a median age of 48.2 (18-76 years). The first symptoms of patients were neck pain and swelling (in 30% patients), crepitus-edema on the face, neck and upper chest (in 3, 23% patients),high fever (in 3, 23% patients), dyspnea (in 2, 16% patients), dysphagia (in 1, 8% patient). In six of the patients(46%) retropharyngeal abscess, in five of them(38% peritonsillar abscess and two of them (16%) odontogenic infection was suspected for the formation of the DNM. Nine of the patients were referred to our clinic, and the other four patients were first enrolled in the otolaryngology clinic and were consulted and transferred to our clinic. All patients had elevated C-reactive protein (CRP) and leukocyte count.

According to the Endo *et al.*'s DNM classification, 10 (77%) of our patients were type 2B, 2 (15%) of them were type 2A, and only one (8%)of them was type 1 [7]. As a surgical procedure, all patients underwent CMD and also in five patients tube thoracostomy, in four patients VATS, in one patient thoracotomy was added. Only CMD operation was sufficient in 3 of the patients. Four (30%) patients required intensive care after the operation. Two patients were lost while being treated in intensive care unit. One of the deaths developed with massive cervical bleeding while the other developed fulminant sepsis. Overall mortality rate was 15%.

Table 1. Demographic-clinical features and surgical outcomes of patients.

Number of cases	Age/Gender	Origin of infection	DNM type[7]	Surgical procedures	Requirement of ICU	Outcome
1	56/M	Retropharyngeal abscess	Type 2B	CMD, right thoracotomy, left TT	No	Survived
2	30/M	Odontogenic	Type 2B	CMD, bilateral TT	Yes	Died
3	76/M	Retropharyngeal abscess	Type 2B	CMD, bilateral TT	No	Survived
4	18/M	Odontogenic	Type 2B	CMD and tracheostomy, right VATS, left TT	Yes	Died
5	65/M	Peritonsillar abscess	Type 2B	CMD, right TT	No	Survived
6	58/M	Retropharyngeal abscess	Type 2B	CMD, right TT, left pleural catheter	Yes	Survived
7	53/E	Peritonsillar abscess	Type 2B	CMD and tracheostomy, bilateral TT	Yes	Survived
8	52/F	Peritonsillar abscess	Type 2B	CMD, bilateral VATS	No	Survived
9	48/M	Retropharyngeal abscess	Type 1	CMD	No	Survived
10	38/F	Peritonsillar abscess	Type 2B	CMD, right VATS	No	Survived
11	54/M	Retropharyngeal abscess	Type 2A	CMD	No	Survived
12	21/M	Retropharyngeal abscess	Type 2A	CMD	No	Survived
13	58/F	Peritonsillar abscess	Type 2B	CMD, right VATS, left TT	No	Survived

CMD: Cervico-Mediastinal Drainage, TT: Tube Thoracostomy, VATS: Video assisted Thoracic Surgery DNM type: Descending Necrotizing Mediastinitis classification; Type 1 is localized in the upper mediastinum above the carina; type 2A is extending to the lower anterior mediastinum; and type 2B is extending to the anterior and lower posterior mediastinum.

Figure 2. A: Intraoperative view of cervicomediastinal drainage, marked with a blue arrow; **B:** View of the silicone mediastinal drain placed at the end of the operation, marked with a blue arrow.

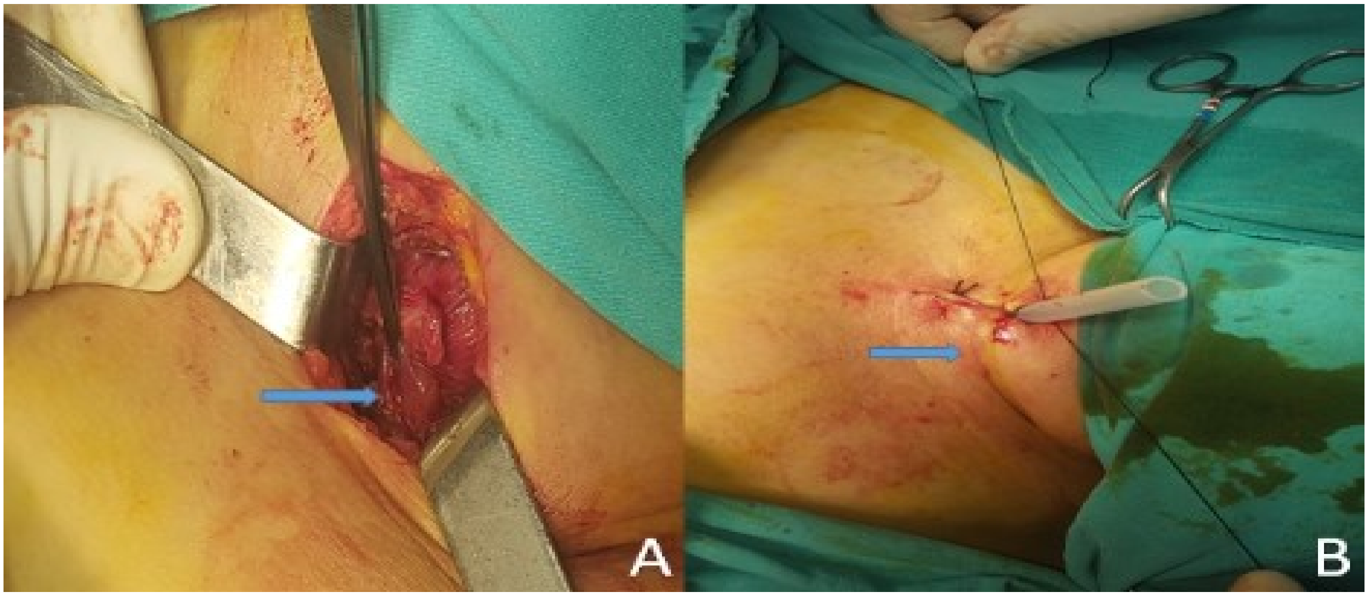


Table 2. Evaluation of clinical-microbiological outcomes.

Number of cases	Time to diagnosis (days)	Tube removal time (days)[&]	Length hospital stay (days)	Comorbidity	Identified microorganism	Antibiotherapy
1	2	12	21	DM	Unidentified	Ampicillin-Sulbactam, Ceftazidime
2	3	20	20	No	*Pseudomonas aeruginosa*	Piperacillin/Tazobactam
3	3	10	24	HT, RA, DM	*Acinetobacter baumannii*	Ampicillin-Sulbactam, Imipenem
4*	4	18	18	Drug addict	*Streptococcus İntermedius,*	Piperacillin/Tazobactam
5	1	11	21	DM	Unidentified	Ampicillin-Sulbactam, metronidazole
6	2	14	25	CAD	*Streptococcus agalactiae*	Piperacillin/Tazobactam
7	1	17	28	HT, DM	Unidentified	Ampicillin-Sulbactam, metronidazole
8	1	10	16	DM	Unidentified	Ampicillin-Sulbactam, Piperacillin/Tazobactam
9	1	12	15	No	*Streptococcus mitis*	Ampicillin-Sulbactam, Piperacillin/Tazobactam
10	2	16	22	No	Unidentified	Ampicillin-Sulbactam+ Clindamycin
11*	1	11	18	DM	*Bacteroides fragilis*	Piperacillin/Tazobactam-Clindamycin
12	2	10	22	No	Unidentified	Meropenem
13	1	17	30	HT, DM	Unidentified	Piperacillin/Tazobactam, Imipenem

*Blood culture (+); [&] Silicone tube inserted after cervico-mediastinal drainage; DM: Diabetes Mellitus, HT: Essential Hypertension, RA: Rheumatoid Arthritis use immunosuppressive medication, CAD: Coronary Artery Disease.

The median time to diagnosis of DNM, the median tube drainage (inserted after CMD) removal time, the median tube thoracostomy drainage removal time, the median length of hospital stay were 1.8 (range 1-4) days, 13.6 days (range 10-20 days), 12.6 days (range10-27 days) and 21.5 days (range 15-30 days), respectively. Also the median time interval between diagnosis and surgical intervention was 1.2 days (range 1-2 days). The most common comorbidity was type II Diabetes Mellitus (DM) (in 54% of the patients) (Table 2).

Identified microorganism and antibiotherapy was summarised in Table 2. Culture from seven patients (54%) could not be defined. Specific microorganisms were detected in six patients (46%) (Table 2). Although blood culture was studied from all patients, only two of the blood cultures was positive Streptococcus intermedius was present in the blood culture of patient no. 4 and Bacteroides fragilis in the patient no. 11. Despite extensive antibiotherapy and surgical intervention fulminant sepsis developed in patient no. 4 and the patient died in the intensive care unit on the 18th day. Whereas in the other patient no.11, CMD + antibiotherapy for 14 days was successful. Blood cultures in the other 11 patients were negative. However, necessary appropriate and potent antibiotics were used according to the fever-CRP response with the consultation on infectious disease specialist. In 8 patients (62%) pleural effusion was developed, and tube thoracostomy was performed for the drainage of this pleural effusion.

Complications were recorded in 6 patients (46%), including sepsis (n = 2), atelectasis requiring fiberoptic bronchoscopy (n = 2) and laryngeal oedema (n = 1)-tracheal aspiration (n = 1) requiring a tracheostomy.

A total of four (30%) patients underwent more than one surgical procedure for repeated drainage and debridement. A total of four patients required surgical intervention after otolaryngologist consultation. Repeated chest X-ray control or unenhanced CT scanning when necessary was performed as treatment response screening and the need for further surgical intervention. Transoral tonsillectomy was performed in two patients and transoral retropharyngeal abscess drainage in the other two during the follow-up period.

Discussion

Descending necrotizing mediastinitis is a polymicrobial acute fatal condition caused by deep cervical-dental infections. The infection is spreading to the mediastinum with the help of anatomical facial planes defined as retropharyngeal, pretracheal, and perivascular planes. Another feature of DNM is leading to connective tissue necrosis [1-3].

All of the cases that were taken to our study met all of the Estera *et al*. criteria [8]. The disease is less common in developed countries due to better oral hygiene and improved diagnostic and therapeutic interventions. It is more common in the third and fourth decades of male patients. The etiologic origin is often secondary to odontogenic infection of the second or third molar tooth or untreated retropharyngeal-peritonsillar abscess. More rarely, suppurative lymphadenitis, cervical trauma, sternal-clavicular osteomyelitis, Ludwig's angina may cause of DNM [4-9]. In our study, eight (77%) of 13 patients were male with the median age 48,2 years as concordsnce with the literature. The origin of DNM was found as a retropharyngeal abscess (46%), peritonsillar abscess (39%) and odontogenic abscess (15 %) respectively in our study

Descendant mediastinitis is usually caused by oral cavity originated aerobic and anaerobic mixed microorganisms. Streptococcus spp. are most frequently detected for aerobic and Bacteroides spp. for anaerobic [1,10]. In our study, Streptococcus spp. were most often isolated (in 3 patients). Anaerobic identification was found in only one patient as Bacteroides fragilis. No microorganisms could be identified in 7 of patients (54%). These low ratio of culture results could be due to antibiotic suppression before taking samples for culture (Table 2).

Immunosuppression should come to mind in many DNM patients. The comorbidities most commonly associated with DNM are type II DM, inadequate nutrition and poor hygiene, advanced age, chronic renal-liver failure and malignancy. However, there are a certain number of DNM patients without any comorbidities [10]. In our study, seven patients (54%) had diabetes, and four patients (31%) had no comorbidities (Table 2).

The clinicians should be prepared for laryngeal oedema and airway obstruction due to the nature of the disease. Tracheostomy may be necessary if intubation is not possible. Tracheostomy is also proposed for secretion cleaning and the prevention risk of aspiration. Adult Respiratory Distress Syndrome(ARDS) can be developed primarily when the diagnosis is delayed [11]. In our series, a total of two patients (15%) underwent tracheotomy for laryngeal oedema (n = 1) and secretion and aspiration (n = 1). ARDS was not detected in any patient.

DNM is often diagnosed late due to the lack of early clinical and radiological findings. Conventional radiology is often inadequate in the diagnosis of DNM. CT is a beneficial method of approaching the diagnosis of mediastinum and neck infections. CT also shows the surgical drainage pattern and it is very helpful in evaluating and monitoring the patient [12,13]. In our study CT was used for diagnosis, treatment evaluation and follow-up in all patients.

Wei *et al*. [14] reported that they performed transcervical drainage for all patients, and 12% of the patients were treated with additional tube thoracostomy simultaneously. Complications were recorded in 34 patients (41.5%), including sepsis (n = 22), pleural effusion or empyema (n=10), renal failure (n=10), multiple organ failures (n=8), and acute respiratory distress syndrome (n=3) in their study [14]. Despite aggressive surgery and antibiotherapy in the 1980s when the disease first described mortality rates were approximately 40 percent [8]. In recent years, the mortality rate has declined to around 10% with less invasive surgery and specific antibiotherapy [14]. There are also reports with no mortality altough patients underwent major surgery [15,16]. In our study, complications were recorded in 6 patients (46%) and our overall mortality rate was 15% with a combination of minimally invasive management as CMD and tracheotomy if necessary with VATS-tube thoracostomy + antibiotherapy.

Typically symptoms of DNM are neck pain, neck swelling, anterior neck oedema-erythema, crepitus-oedema on the face, neck and upper chest, dysphagia, anorexia, dyspnea and fever [3,9]. In our study, all of these typical symptoms were detected at the time of diagnosis or in the treatment process.

As a surgical treatment; altough before major surgeries had performed such as sternotomy and thoracotomy for mediastinal drainage, to day more minimally invasive procedures are preferred. However, the fundamental principle of surgery in both methods continues to be drainage and debridement [17]. We believe that the primary surgical principle for DNM of drainage and debridement can be achieved by minimally invasive methods like CMD with recurrent drainage + VATS-tube thoracostomy while preventing morbidity of aggressive treatment approach as sternotomy-thoracotomy. However, the surgical procedure used to treat DNM should be selected according to the location of the infection. So thoracotomy-sternotomy should not be avoided in situations where sufficent drainage and debridement can not be performed with minimally invasive methods.

Alternative treatment efforts for DNM are also available in the literature. Immunoglobulins and polymyxin B hemoperfusion treatment used successfully after surgery for a 38 years old man with septic shock from DNM [18]. One of the risk factors of DNM is IgG hypogammaglobulinemia. Although rapid diagnosis, aggressive surgical debridement and broad-spectrum antibiotic, a 58 years old female patient with a low level of endogenous IgG who lengthened in the intensive care unit identified have been reported to be treated with passive adjuvant immunotherapy. Immunological parameters should be assessed in resistant cases, and intravenous immunoglobulins (IVIG) can be tried in treatment [19]. Hyperbaric oxygen therapy may be another alternative adjunctive treatment for DNM [20].

Lemierre's syndrome is a condition characterised by thrombophlebitis of the internal jugular vein and bacteremia caused by primarily anaerobic organisms, following DNM. Neck ultrasonography, neck and chest computed tomography can be used for diagnosis. It has been reported that PET-CT may be useful in diagnosis and monitoring for a DNM complication of Lemierre’s syndrome. Treatment involves prolonged antibiotic therapy occasionally combined with anticoagulation [21]. No Lemierre’s syndrome was detected in any of our patients and PET / CT was not performed in any of the patients.

This fulminant and fatal infectional disease is still not so rare in developing countries, because of the poor economic conditions and consequent lack of medical resources for prevention and treatment of dental and oropharyngeal diseases. Delay in diagnosis is the main reason for the high mortality rate in DNM because it usually runs a fulminant course [1-4,22].

Conclusions

Descendant necrotizing mediastinitis is a rare condition in which deep cervical or odontogenic infections can spread from anatomical planes to mediastinum through gravity and respiratory mechanics, which can be severely fatal. Although, surgical drainage-debridement and antibiotherapy have reduced mortality rates in recent years; the disease is still a significant health problem especially in developing countries. We concluded that the combination of minimally invasive management as VATS-tube thoracostomy with CMD is the most appropriate surgical interventions. Specific antibiotherapy should be added. Alternative treatments such as immunotherapy and hyperbaric oxygen can be used as adjunctive therapy in resistant cases. The critical point in the management of DNM which is still a fatal common problem in developing countries should be the correct diagnosis, rapid surgical intervention with antibiotherapy and close follow-up for possible complications.

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