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ORIGINAL ARTICLE

Diffuse descending necrotizing mediastinitis: surgical therapy and outcome in a single-centre series

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Abstract

OBJECTIVES: Descending necrotizing mediastinitis (DNM) is a rare but rapidly progressing disease with a potentially fatal outcome, originating from odontogenical or cervical infections. The aim of this article was to give an up-to-date overview on this still underestimated disease, to draw the clinician's attention and particularly to highlight the need for rapid diagnosis and adequate surgical treatment.

METHODS: We present a retrospective analysis of 17 patients diagnosed and treated for advanced DNM between 1999 and 2011 in a tertiary referral medical centre. Hence, this is one of the largest single-centre studies in recent years concerning the diffuse form (i.e. extending into the lower mediastinum) of DNM. Subsequently, we analysed and compared the international literature with our data, with the focus on surgical management and outcome.

RESULTS: In our series of 17 adult patients, 16 were surgically treated by median sternotomy ($n = 8$) or the clamshell ($n = 8$) approach for diffuse DNM. One patient, referred with septic shock, died 2 days after surgery. The median interval from diagnosis of DNM by cervicothoracic computed tomography scan and thoracic surgery was 6 h (range 1–24 h) in all but the one patient with fatal outcome (48 h). Concomitant cervicotomy was performed in 11 patients (65%) and tracheotomy in 9 (53%). The median duration of hospitalization was 16 days (range 4–50 days), including an intensive care unit stay of 4 days (range 1–50 days).

CONCLUSIONS: For DNM limited to the upper part of the mediastinum, which applies to the majority of cases, a transcervical approach and drainage may be sufficient. In advanced disease, extending below the tracheal carina, an immediate and more aggressive surgical approach is required to combat a much higher morbidity and mortality in this subset of patients. A timely situational approach via median sternotomy or a clamshell incision allowed us to maintain a very low morbidity, mortality and rate of reoperations, without major complications due to the surgical approach itself.

Keywords: Descending necrotizing mediastinitis • Necrotizing fasciitis • Cervicotomy • Clamshell • Median sternotomy

INTRODUCTION

Acute mediastinitis is a life-threatening infection of the connective mediastinal tissue filling the interpleural spaces and surrounding the median thoracic organs. Most cases of mediastinitis develop after sternotomy for cardiac surgery (incidence rate 1–2.65% [1]) or due to oesophageal perforation, commonly iatrogenic, but also due to trauma, foreign body ingestion or neoplasm. Descending necrotizing mediastinitis (DNM) is distinguished from the aforementioned types of mediastinitis, which primarily originates from structures in the mediastinum. The term DNM, first described by Pearse [2], implies the infection starting from a head and neck source, most commonly an oropharyngeal or odontogenic focus, which then spreads in the fascial spaces of the head and neck and descends downward into the mediastinum. The most common origins of DNM infection include peritonsillar, dental or odontogenic abscesses. Deu-Martín *et al.* [3] calculated an annual incidence of DNM of 5.1 cases per million inhabitants for the region of Barcelona, Spain. In general, the mortality rate is high, with reports ranging from 11 to 40% [4, 5] as mediastinal infection rapidly leads to sepsis and multiorgan failure if not treated early and appropriately.

The criteria for diagnosis of DNM established by Estrera *et al.* [5] include: (1) clinical manifestations of severe infection; (2) demonstration of characteristic roentgenographic features; (3) documentation of the necrotizing mediastinal infection at operation or post-mortem examination, or both; (4) establishment of the relationship of oropharyngeal or cervical infection, with the development of the necrotizing mediastinal process.

Endo *et al.* [6] classified DNM according to the anatomical extent of infection to suggest differential surgical management according to this classification: Type I, infection above the carina (localized form); and Type II, infection below the tracheal bifurcation (diffuse form). Type II is further subdivided into Type IIA (lower anterior mediastinum) and Type IIB (lower anterior and posterior mediastinum).

As broad-spectrum antibiotics are undoubtedly one of the cornerstones of treatment, the optimal form of surgical management remains controversial, with support ranging from cervical drainage alone, to a combination of cervical drainage and thoracic approach using mediastinoscopy, thoracoscopy, thoracotomy, median sternotomy or a clamshell incision.

We report our single-centre experience and review the international literature with the objective of giving an up-to-date overview on this rare and fatal disease with the focus on the surgical approach itself and the timing of the life-saving intervention.

PATIENTS AND METHODS

This is an observational descriptive retrospective study of 17 patients with diffuse DNM Endo Type II treated at the University Hospital Bern, Switzerland, between November 1999 and October 2011. Clinical charts including imaging and bacteriological studies as well as histopathology analyses were reviewed. Diagnosis of DNM was established by clinical, radiographical and intraoperative findings. In all cases, the diagnostic criteria of DNM as defined by Estrera *et al*. [5] were fulfilled. DNM was further categorized according to Endo *et al*. [6] based on the extent of infection (radiographical and intraoperative findings).

Patients with acute mediastinitis resulting from nondescending causes and those with only localized disease (Endo Type I) were excluded from the study. Microbiological examinations included aerobic and anaerobic blood cultures as well as intraoperative swabs and surgical site samples, which were obtained in every patient. Furthermore, demographic data, comorbidity, symptoms and clinical findings at presentation, radiographical studies, primary source of infection, microbiological findings, antibiotic and surgical therapy, interval between diagnosis and operation, length of hospitalization including intensive care unit (ICU) stay and outcome were analysed. Sepsis and organ dysfunction were defined according to the updated criteria defined by the International Surviving Sepsis Campaign Guidelines [7].

To give an up-to-date overview on the topic of DNM, we analysed the international literature back to the results of Estrera *et al*. [5], who were the first to establish the diagnostic criteria of DNM and presented the first larger series in the antibiotic and surgical era. We further included the meta-analyses of Wheatley *et al*. [8] and Corsten *et al*. [9], reporting all cases of DNM in the medical literature from 1960–89 to 1983–97, respectively. Furthermore, we analysed all recent studies on DNM, in the English medical literature obtained through MEDLINE search that included at least 20 patients and at least 10 with DNM Endo Type II.

RESULTS

Seventeen patients were found to meet the criteria of DNM defined by Estrera *et al*. [5]. All of them showed involvement of the lower mediastinum (Endo Type II). Nine patients (53%) were female and eight (47%) were male. The patients' age ranged from 36 to 76 years (median: 48 years).

Clinical data

The delay between onset of symptoms of the primary infection and admission to our division ranged from 12 h to 14 days (median: 3 days). Fourteen patients were referred to us from other hospitals, whereas three were transferred from other Divisions at the University Hospital. Symptoms at admission included cervical pain ($n = 17$, 100%), odynophagia ($n = 12$, 71%), cervical swelling ($n = 5$, 29%), hoarseness ($n = 2$, 12%) and dyspnoea ($n = 2$, 12%). Stridor ($n = 1$), swelling of the face ($n = 1$), thoracic pain ($n = 1$) and shoulder pain ($n = 1$) were rarely reported. The main clinical findings were fever in all patients and swelling/redness of the pharynx/larynx ($n = 14$, 82%). Six patients (35%) were referred under ongoing treatment with vasopressor drugs or this treatment had to be installed shortly upon admission due to septic shock.

White blood cell count and C-reactive protein levels showed no clear correlation to the course or outcome of disease.

Diagnostics

All patients underwent otolaryngological examination and were promptly submitted to contrast-enhanced cervicothoracic computed tomography (CT) to confirm the clinical diagnosis and evaluate the extent of infection.

Etiology

DNM most commonly originated from cervical infections including tonsillar abscess ($n = 7$, 41%), pharyngitis ($n = 4$, 24%) and epiglottitis ($n = 3$, 18%). One patient suffered from a combined tonsillar and dental abscess and in another case, DNM resulted from a cervical phlegmon presumably originating from a central venous catheter-related infection. In one case, DNM originated directly from a suppurative thyroiditis, while in another, septic arthritis of the right sternoclavicular joint led to suppurative thyroiditis with consecutive progression to DNM.

Comorbidity and predisposing factors

Of the 17 patients, 9 (53%) had relevant associated systemic conditions associated with reduced tissue oxygenation and/or immunodeficiency, such as diabetes ($n = 3$), severe chronic nicotine and alcohol abuse ($n = 3$). One patient was under long-term corticosteroid therapy for psoriatic arthropathy and two others were in aplasia following chemotherapy for acute myeloid leukaemia. Another patient suffered from an antibody deficiency syndrome. As possible local predisposing factors, in terms of site of entry of infection, one patient suffered from chronic tonsillitis and severe oral candidiasis and another from an intubation injury of the larynx that occurred 4 weeks previously. Five patients (30%) had no pre-existing comorbidity or predisposing anatomical condition.

Extent of disease

CT and intraoperative findings, respectively, showed DNM extending to the anteroinferior mediastinum (Endo Type IIA) in

7 patients (41%) and to the posterior lower mediastinum (Endo Type IIB) in 10 (59%).

Microbiology

Microbiological examination results were obtained from all patients and revealed that five (29%) had a polymicrobial infection with mixed aerobic and anaerobic organisms. The most common isolated aerobic bacteria were *Streptococcus* species including *milleri* ($n = 3$), *epidermidis* ($n = 3$), *pyogenes* ($n = 1$) and *pneumoniae* ($n = 1$), and *Staphylococcus aureus* ($n = 2$) as well as *Haemophilus influenza* ($n = 1$). In three patients, mixed anaerobic bacteria (*Bacteroides* spp., *Fusobacterium* spp. and *Peptostreptococcus* spp.) were present, whereas in two others, *Fusobacterium necrophorum* was the only anaerobic germ that was isolated. In one patient, *Enterobacter cloacae* was isolated in blood cultures. Only two patients revealed a multiresistant bacterial strain (methicillin-resistant *Staphylococcus epidermidis*). In four patients (23.5%), aerobic and anaerobic cultures showed no growth, which may be due to either prior antibiotic treatment or failed isolation of bacteria.

Therapy

Antibiotic therapy was started empirically with amoxicillin/clavulanic acid or a third-generation (ceftriaxon) or fourth-generation cephalosporin (cefepime) combined with metronidazole or clindamycin. Therapy was later altered according to the microbiological examinations and antibiograms if necessary.

All patients underwent surgery under general anaesthesia. The median interval between diagnosis of DNM by cervicothoracic CT scan and the thoracic surgical approach via sternotomy or clamshell incision was 6 h (range 1–24 h) in all patients except one (data not available in two patients). That patient was finally referred to us from another clinic with a delay of 48 h after DNM was confirmed by a CT scan.

Surgical management consisted of upper panendoscopy in all patients, local infection control including transoral drainage of abscess formations where needed or possible, tonsillectomy ($n = 5$) and extraction of a tooth ($n = 1$).

Further operative management included uni- ($n = 2$) or bilateral ($n = 9$) cervicotomy with cervical drainage and tracheotomy in nine patients (53%). Cervical incisions were usually left open and multiple drains (usually 1–3 on each side) were used for daily irrigation of the involved cervical spaces with saline or antiseptic solutions.

Main transthoracic procedures included opening of the main mediastinal spaces (paratracheal part and aortopulmonal window), excision of pericardial fat and thymic tissue as well as evacuation of pleural effusion and/or pleural decortications(s) with subsequent mediastinal and pleural drain placement (usually 3–5 chest drains) via median sternotomy ($n = 8$) or clamshell incision ($n = 8$). One patient was referred from another clinic with persistent/progressive disease after cervicotomy with transcervical mediastinal drainage and thus additional subxiphoidal drainage for DNM Endo Type IIA had to be performed. Midline sternotomy and clamshell incisions were regularly closed and chest drains were usually connected to an underwater seal and put to suction (10–20 cm H_2O), but no irrigation over the indwelling chest drains was performed.

Mortality, outcome

The 30-day mortality rate was 5.9% ($n = 1$). The patient who died was referred 48 h after initial presentation in a state of septic shock due to confirmed DNM, and finally died of multiple organ failure (MOF) 48 h after mediastinal debridement through clamshell incision.

Another patient, presenting with DNM Endo Type IIB and treated via clamshell incision with a diagnostic–therapeutic delay of 24 h, who underwent several reoperations (redo clamshell) on postoperative days 8, 11 and 14, due to recurrent bilateral pleural empyema and pericardial empyema formation, respectively, died 4 months later after a history of recurrent severe pulmonary infections and adult respiratory distress syndrome. At autopsy, the main cause of death was respiratory failure; no signs of phrenic nerve injury or sternal osteomyelitis were present.

Apart from 1 case of early death, the remaining 16 patients were hospitalized after thoracic surgery for a duration of 8–50 days (median: 16 days) including an ICU stay of 2–50 days (median: 4 days). Seven patients were discharged home, four to a rehabilitation centre and another five were transferred to another clinic for further treatment.

As mentioned before, only one patient (5.9%) underwent a thoracic reoperation. Another patient needed non-thoracic surgery, which consisted of coverage of the larynx and neck with a musculocutaneous latissimus dorsi muscle flap on postoperative day 26, because of extensive soft tissue necrosis.

Significant risk factors for morbidity and mortality were identified through meta-analysis of the literature data (Table 2) and analysis of our results (Table 3).

Complications

Complications of DNM were recorded in 12 patients (70.6%) and included multiple organ dysfunction syndrome (MODS) in 6 (35%), of whom 5 initially presented in a state of septic shock. MODS involved lung and renal dysfunction ($n = 2$), lung/renal/liver ($n = 1$), lung/gastrointestinal ($n = 1$), lung/renal/liver/cardiac dysfunction and disseminated intravascular coagulation ($n = 1$) and MOF in another patient, resulting in imminent death. Other encountered complications in the postoperative course were pneumonia ($n = 3$), critical illness polyneuropathy ($n = 2$), atrial fibrillation ($n = 3$), cerebral venous sinus thrombosis ($n = 1$) and Lemierre syndrome ($n = 1$).

Surgery-related complications occurred in two patients (12%) and included left recurrent laryngeal nerve paresis in one and surgical site infection of the clamshell incision, which healed uneventfully under vacuseal treatment, in another.

Literature review and meta-analysis

A comparison of the collected literature data (described in the section Patients and Methods) with our results is presented in Table 1. The table illustrates an increase in patients' age over time, as well as a shift from mainly odontogenic sources of infection in the past to predominantly pharyngeal causes in recent studies. Meta-analysis of the collected literature data is presented in Table 2, and further clarifies that the extent of infection directly affects the mortality rate, which was 9.8% (range 6–25%)

Table 1: A literature review and comparison with own results

	Estrera *et al.* [5]	Wheatley *et al.* [8] Meta-analysis	Corsten *et al.* [9] Meta-analysis	Misthos *et al.* [17]	Roccia *et al.* [10]	Ridder *et al.* [4]	Own data
Time frame	1975–81	1960–89	1983–97	1985–2002	1996–2005	1997–2008	1999–2011
No. (patients)	10	43	80	27	23	45	17
Mean age	28	32	37.6	nd	49	52	47.4
Source of infection							
Pharyngeal	5 (50%)	8 (18.6%)	nd	10 (37%)	14 (60.9%)	21 (46.7%)	14 (82.3%)
Odontogenic	5 (50%)	25 (58.1%)	nd	17 (63%)	9 (39.1%)	5 (11.1%)	1 (5.9%)
Endo classification							
Type I (localized)	2 (20%)	nd	nd	–	8 (34.8%)	33 (73.3%)	–
Type II (diffuse)	8 (80%)	nd	nd	27 (100%)	15 (65.2%)	12 (26.7%)	17 (100%)
Surgical approach							
Transcervical only	2 (20%)	22 (51.2%)	30 (37.5%)	3[b] (11.1%)	8 (34.8%)	39 (97.5%)	–
Thoracotomy	8 (80%)	12 (27.9%)	42 (52.5%)	19[b] (70.4%)	15 (65.2%)	5 (12.5%)	–
Sternotomy	–	–	–	–	–	–	8 (47%)[a]
Clamshell incision	–	–	–	–	–	–	8 (47%)[a]
Mortality rate							
Overall	40%	34.9%	31%	33%	30.4%	11.1%	5.9%
In Endo Type I	0%	nd	nd	–	2 (25%)	2 (6.1%)	–
In Endo Type II	4 (40%)	nd	nd	9 (33%)	5 (33.3%)	3 (25%)	1 (5.9%)

nd: Not defined.
[a]One patient was treated with combined transcervical and subxiphoidal drainage.
[b]Eight of 11 patients with an initial transcervical approach ultimately needed thoracotomy.

Table 2: Mortality and extent of infection, meta-analysis of literature data of Table 1

	Survival (*n*)	Death (*n*)	*P*-value*	Odds ratio (OR); 95% confidence interval (CI)
Extent of infection ($n = 105$)				
Endo Type I	39	4	**0.005**	OR: 4.99; CI: 1.44–19
Endo Type II	41	21		

*Fisher exact test, two-tailed *P*-value.
Statistically significant values ($P < 0.05$) are printed in bold.

Table 3: Risk factors for morbidity and mortality, analysis of own data

Analysis of own data	No/mild complications	MODS	Death	*P*-value*	OR; 95% CI
Diagnostic–therapeutic delay[a]					
<15 h ($n = 12$)	9	3	–	**0.044**	OR: infinite; CI: 0.76–infinite
>15 h ($n = 3$)	–	2	1		
Septic shock at time of diagnosis					
Yes ($n = 6$)	2	3	1	0.109	OR: 4.5; CI: 0.4–61.6
No ($n = 11$)	9	2	–		

[a]No data available in two patients.
*Fisher exact test, two-tailed *P*-values.
Statistically significant values ($P < 0.05$) are printed in bold.

in localized (Endo Type I) and 31.5% (range 25–33%) in diffuse disease (Endo Type II), and thus shows a comparatively rather favourable outcome in our series with a 30-day mortality rate of 5.9% ($n = 1$).

Statistical analysis of our results showed that a diagnostic–therapeutic delay was another significant predictor of morbidity and mortality and that septic shock at the time of diagnosis shows a tendency towards a higher morbidity rate (Table 3).

DISCUSSION

DNM results from infections of usually polymicrobial origin (most commonly *Streptococcus* spp. and *Bacteroides* spp. [3]), reflecting the process of oral bacteria entering through disruptions of mucosal and tissue barriers and spreading from a head or neck source, along the deep fascial planes, downward into the mediastinum. The different anatomic neck spaces from which infection spreads to the mediastinum are well described in the literature [2, 9–12]: The pretracheal space, that ends inferiorly at the pericardium and parietal pleura at carinal height, represents a possible pathway in ∼8% of cases of DNM for infections of the airways, i.e. epiglottitis/laryngitis and the thyroidea to the anterior and middle mediastinum. Odontogenic infections tend to spread posteriorly towards the vascular space (Fig. 1) and from there, in ∼12% of cases of DNM, further to the anterior mediastinum (Fig. 2). The retropharyngeal space (Fig. 3) drains directly into the posterior mediastinum and is, with an estimated incidence of 70%, one of the main spreading routes for especially oropharyngeal infections in DNM [2, 13]. However, as each of these potential spaces contains loose areolar tissue that lacks defence cells and is poorly vascularized, and therefore allows the unresisted spread of any cervical infection along and across them, any cervical infection can potentially involve the entire

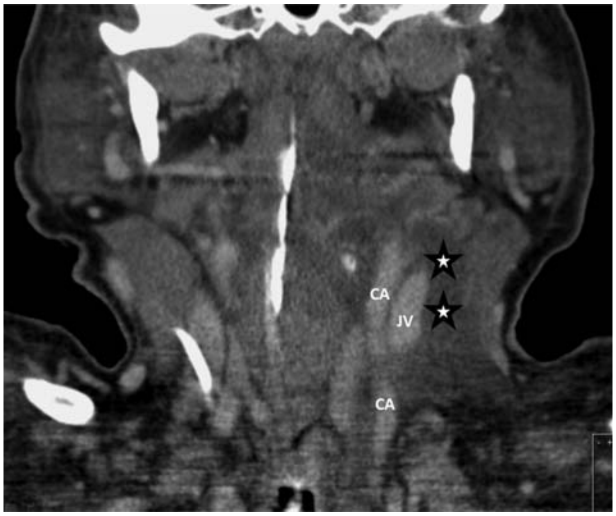

Figure 1: A CT scan revealing an abscess (stars) located in the left perivascular space adjacent to the internal jugular vein (JV) and carotid artery (CA).

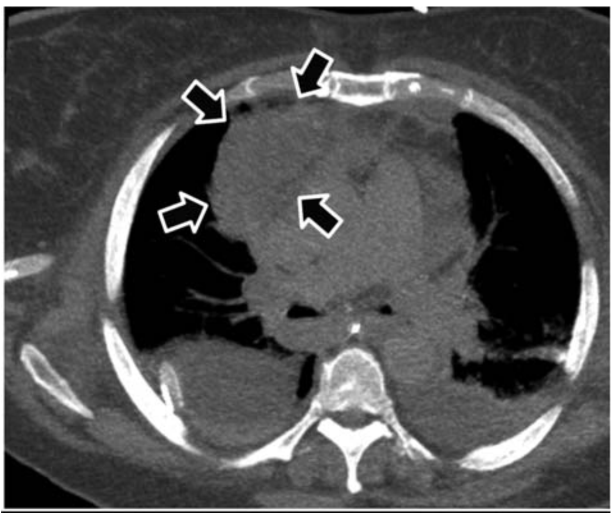

Figure 2: A thoracic CT scan (native phase) of the same patient (Fig. 1) showing a large abscess in the anteroinferior mediastinum (arrows) and bilateral pleural empyema.

mediastinum. Downward spread is additionally facilitated by gravity, breathing and negative intrathoracic pressure [5, 8, 9].

With better oral hygiene and constantly growing access to good dental treatment as well as the liberal use of antibiotics, in our degrees of latitude, the common cause of DNM has shifted from predominantly odontogenic infections in the past to mainly oropharyngeal reasons nowadays (Table 1). Other potential causes of DNM, besides dental infections and common oropharyngeal infections such as tonsillitis and epiglottitis, include pharyngitis, primary neck infections (including posttraumatic), cervical lymphadenitis, suppurative thyroiditis, parotitis [14], traumatic endotracheal intubation (with DNM usually occurring in the early postoperative period) and jugular intravenous drug use/abuse [15].

DNM appears to affect men as well as women with a mean age of around 50 as shown by our results and recent studies (Table 1), but as other authors have documented, this disease can affect patients from an age of 4 months up to the eighth decade [16].

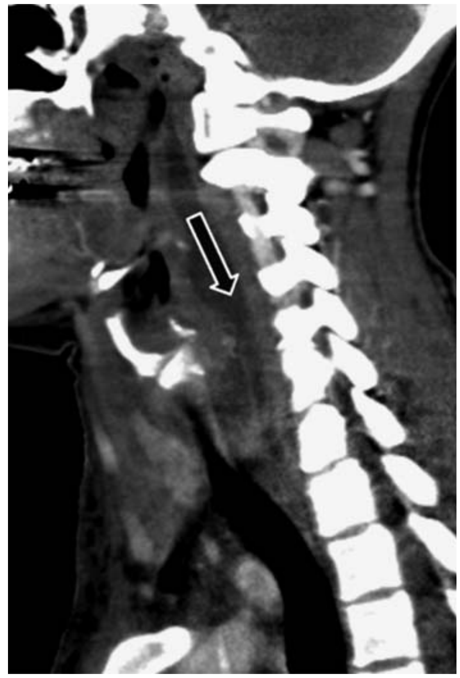

Figure 3: A CT scan showing downward spread of retropharyngeal abscess formation (arrow).

Patients usually have experienced and present with symptoms and signs of an oropharyngeal/odontogenic infection and fever to their family physician or nearby emergency department. Thus, DNM can be difficult to recognize in its early stage.

Diagnostics

Besides oropharyngeal examination, a liberal use of a contrast-enhanced cervicothoracic CT scan [11] is essential for the early detection of DNM in patients scan can also be a helpful tool in identifying any clinically suspected progression or persistence of infection in the postoperative period [12].

Therapy

Administration of IV broad-spectrum antibiotics with coverage for aerobic and anaerobic bacteria as soon as possible is mandatory regarding the high mortality rates of up to 85% in the pre-antibiotic era [2]. However, antibiotic therapy is not efficient without adequate surgical drainage of the cervical and mediastinal collections. After restoration of the pharyngeal or dental focus and airway management, prompt and adequate drainage of the neck and the mediastinum should be performed. Airway compromise due to inflammatory oedema is a common finding in DNM that should be anticipated and treated with early tracheotomy, which can serve a dual role of opening fascial planes and securing the airway.

In the past, sole transcervical drainage of the mediastinum was condemned by several authors who advocated a more aggressive management of DNM regardless of the extent of infection [8–10, 12, 15, 17, 18].

Endo *et al*. [6] suggested, on the basis of four reported cases, to determine the surgical strategy according to the expected extent of disease: for Type I disease, localized in the upper mediastinum above the tracheal carina, transcervical drainage. In Type IIA disease, extending to the lower anterior mediastinum, combined transcervical and subxiphoidal drainage with additional thoracic drainage (percutaneous) when necessary. For Type IIB, with additional spread into the posterior mediastinum, they recommended a bilateral thoracotomy (right standard and left minithoracotomy).

For Type I disease, which basically represents the beginning of a downward spread of an infectious process in the head and neck region, recent results by Ridder *et al*. [4] also showed a favourable outcome in 85% of these patients using early cervicotomy and transcervical mediastinal drainage. They furthermore stated that widespread inferior mediastinitis may even be prevented with an early cervical approach. For better visualization, mediastinoscopy-assisted drainage is also described as a treatment option in this stage of the disease [19, 20].

For further advanced disease (i.e. Endo Type II), in our experience and in agreement with other authors [8, 12, 15, 18], simple drainage is not enough and optimal treatment should include radical surgical debridement of affected tissue, i.e. pericardial fat and thymic tissue, through an open thoracic approach. Corsten *et al.* [9] were the first to identify a statistically significant difference in survival in a subsequent meta-analysis, between patients undergoing only transcervical mediastinal drainage (53%) and those receiving transthoracic mediastinal debridement (81%). Ten years later, Misthos *et al*. [17] showed that early combined transthoracic mediastinal and cervical debridement and drainage were the only favourable factor for survival compared with cervical drainage and/or transcervical mediastinal drainage alone, in 27 patients with DNM Type IIA, with an odds ratio of 9.99.

In agreement with our colleagues [17, 21], we prefer a median sternotomy approach in patients with disease Type IIA. And in our experience, midline sternotomy can also be effectively used in selected patients with Type IIB disease, demonstrated in 5 of 10 patients in our present series, without major problems or complications, i.e. no death and no recurrent disease/reoperation. Furthermore, we presented our experience with the clamshell approach as an alternative option for treatment of Type IIB disease in an earlier study from our institution [22], highlighting the excellent exposure of the whole mediastinum, and the possibility of bilateral decortications and debridement of the entire mediastinum.

Midline sternotomy allows good access to the anterior mediastinum and both thoracic cavities, permitting early decortications and irrigation, and proved to be a fast and simple approach with no need for patient repositioning (especially after prior cervicotomy) and thus enables the surgeon to treat even critically ill patients with a one-stage procedure. The problem of limited access to the posterobasal mediastinum, especially on the left side, can be overcome by single-lung ventilation (double lumen tube, bronchial blocker), as well as using short-term apnoea or ventilation with small tidal volumes if single-lung ventilation is not tolerated. Often cited possible adverse events after median sternotomy or clamshell incision, such as phrenic nerve palsy, sternal dehiscence or even sternal osteomyelitis, have never occurred in any of our patients.

As posterolateral thoracotomy is described as a standard approach by some authors [12, 18, 23], others reported their experience with less-invasive approaches such as subxiphoidal drainage or video-assisted thoracic surgical (VATS) drainage [20, 24] in analogy to the management of oesophageal perforations. However, as addressed before, systematic debridement and broad opening of involved fascial spaces are essential in preventing persistent or even progressive disease, and with that, the need for reoperation and the risk of severe complications. Chen *et al*. [20], for example, used transcervical mediastinal drainage or mediastinal VATS drainage in a group of 18 patients suffering from DNM as a treatment option, reporting the need for reoperation in 4 of their patients, whereas 2 of them suffered from a fatal outcome. Marty-Ane *et al*. [18] reported the need for reoperation in 33% (3 of 9 patients) of their patients, primarily treated with unilateral thoracotomy due to persistent mediastinitis.

Cho *et al*. [24] reported their experience with 17 patients treated with video-assisted thoracoscopic surgery, but only 8 suffered from DNM, whereas the remaining 9 had mediastinitis due to oesophageal perforation. Consequently, their reported mortality rate for diffuse DNM was 25% (2 of 8).

Obviously each of these techniques offers potential advantages and disadvantages, and presumably, the surgical approach has to be carefully chosen according to the patients' condition, the extent of disease and the surgeons' experience, to maintain a low rate of complications, reoperations and mortality. In contrast to Karkas *et al*. [25], our management algorithm therefore comprises a sternal approach to inferior mediastinal involvement (anterior as well as posterior), reserving the clamshell incision for mainly bilateral posteroinferior disease.

Morbidity and mortality

Mortality rates in DNM of 40% reported in the past have likely improved secondary to the widespread use of antibiotics and improved oral hygiene, as well as with better understanding of this rare disease with the consequence of earlier diagnosis and more adequate surgical treatment. As demonstrated by our actual meta-analysis, currently one has to face mortality rates of ~9.8% in localized (Endo Type I) and 31.5% in diffuse forms of DNM (Endo Type II). Besides an advanced stage of disease, any delays in diagnosis and thus surgical therapy are the most important risk factors for high morbidity and mortality rates (Tables 2 and 3). Furthermore, we believe, in agreement with other authors [9, 17, 18, 21], that inappropriate surgical therapy is another very important factor influencing patient outcome. Deu-Martín *et al*. [3] identified septic shock, in the course of disease, i.e. in the post-operative period, to be an independent predictor of mortality, whereas in our series, septic shock at the time of diagnosis showed only a tendency vs higher morbidity rates. Comorbidities, especially of immunosuppressive character, i.e. diabetes, alcoholism, malnutrition, corticosteroid therapy and chemotherapy, might as well predispose to development of DNM and more complicated courses of the disease [4, 9, 18, 20].

CONCLUSIONS

Despite vast improvements in antibiotic treatment, critical care medicine and CT imaging in the last decade, the mortality of DNM, especially in its diffuse form, remains very high.

Early diagnosis and the avoidance of any diagnostic–therapeutic delay are crucial. Whereas transcervical drainage may be sufficient for disease localized in the upper mediastinum, we consider median sternotomy in combination with a double lumen intubation to be a fast and direct one-stage approach to diffuse DNM (Endo Types IIA and B) and patients who need operative revision after failed transcervical drainage alone. For patients with disease involving mainly the posterior lower part of the mediastinum, the clamshell incision might be more suitable. Both surgical strategies show an acceptable morbidity, with no serious complications due to the surgical approach itself, in our present series. Less-invasive approaches may be used in the early phase of the disease, and in certain conditions, but still have to prove their efficiency in larger series or clinical trials.

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