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Descending Necrotizing Mediastinitis as a Complication of Dental Cervical Cellulitis: A Case Report and Review

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Abstract	Case Report

Descending necrotizing mediastinitis remains a serious condition with a high mortality rate due to its often fulminant clinical presentation. An early diagnosis and a well conducted multidisciplinary therapeutic management are essential to reduce morbi-mortality. Delayed diagnosis, inappropriate antibiotic therapy, non-optimal surgical drainage or lack of surveillance may increase morbidity and mortality. We report the case of a descending necrotizing mediastinitis complicating a dental cervical cellulitis in a 27 year old female patient with a successful outcome.

Keywords: Antibiotic, Cellulitis, Drainage, Mediastinitis, Prognosis, septic shock.

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INTRODUCTION

Acute mediastinitis is a rare and very serious infection with a high mortality [1]. It may be caused by an esophageal perforation (spontaneous, iatrogenic or traumatic), a deep cervical infection spread to the mediastinum or post-surgical nosocomial infection [2]. Mediastinitis secondary to pharyngeal and odontogenic infections is often called "descending necrotizing mediastinitis" (DNM) or fasciitis [1]. This extreme medico-surgical emergency with no uniform surgical procedure requires an early diagnosis, optimized and and multidisciplinarity customized therapies (anesthesiologists, resuscitators, radiologists, thoracic and otolaryngologic surgeons and microbiologists). This case report highlights the successful management of non-fatal DNM with both optimal surgery and appropriate support.

CASE PRESENTATION

A 27-year-old female patient presented to the emergency room with dental cervical cellulitis complicated by mediastinitis. She had a history of a 15day dental pain and self-medication with non-steroidal anti-inflammatory drugs. The evolution led to a cervical cellulitis complicated one week later by dyspnea, dysphagia and dysphonia. She was initially managed at the provincial hospital where she received triple antibiotic therapy: ceftriaxone, metronidazole and gentamycin, prior to her admission to our university center for specialized and multidisciplinary care. On admission, the patient was conscious, septic, with a temperature of 39.5°C, a heart rate of 140 bpm and a blood pressure of 110/50 mmHg. She was polypneic at 30 cpm with a saturation of 97 % on room air. The patient was obese (BMI at 38 kg/m²) with a short neck. Local examination revealed a short neck, a trismus and a limitation of cervical spine mobility. Several firm, painful and inflammatory bilateral cervical and submandibular swellings with the largest measuring 4 cm were noted (Figure 1). The cervico-thoracic CT scan with contrast showed multiple bilateral sub-mandibular collections fusing at the mediastinal level associated to pericardial effusion (Figure 2). Biology revealed : hemoglobin at 9.2 g / dl, hyperleukocytosis at 45 480 elements / mm³, CRP at 152 mg / 1 with metabolic acidosis and lactate level at 3.54 (Table 1). A transthoracic echocardiography was performed showing pericardial effusion surrounding the right ventricule without signs of compressions. After monitoring (peripheric, arterial, central venous and urinary catheters...) and initial resuscitation (oxygen therapy, vascular filling, noradrenaline, large spectrum antibiotic therapy based on Meropeneme + Teicoplanin + Fluconazole), the patient underwent collections drainage through cervicotomy. The procedure decision was multidisciplinary and made to be the least invasive

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(damage control). A difficult airway management was expected and risks related to procedure and tracheotomy were explained to the patient and her family. In the operating room, the otolaryngologic surgeon was ready to perform a tracheotomy before general anesthesia induction. After vascular filling with crystalloids, crush induction was performed and intubation was achieved with an Eschmann guide. The patient underwent surgical drainage of the collections and the culture of the pus sample came back negative. Evolution was characterized by clinical and biological improvement with weaning from catecholamines and mechanical ventilation respectively on the 2nd and 4th postoperative day (Table 1). On day 10, a clinicobiological deterioration has been observed (Table 1). Chest X-ray showed bilateral pleural effusion (Figure 4B) and the cervico-thoracic CT scan revealed increasing mediastinal collections and pleural effusion but regressing cervical collections (Figures 3). Drainage of mediastinal collections and pleural effusion was performed through mediastinotomy. The patient postoperative received intensive respiratory management targeting alveolar recruitment (noninvasive ventilation, respiratory physiotherapy, incentive spirometry, postural maneuvers) associated with dynamic multimodal analgesia and nutritional management. Peroperative bacteriological sampling remained negative. Antibiotherapy duration was of ten days for fluconazole and teicoplanin and three weeks for Meropeneme. The patient received

Fatima Zahra Haddari et al., Sch J Med Case Rep, Sep, 2022; 10(9): 883-888 thromboprophylaxis throughout her ICU stay. After a three-week ICU stay, clinico-biological (Table 1) and radiological improvement (Figure 4C) and antibiotic deescalation, the patient was transferred to the surgical ward and was discharged home four days later. Anatomopathology showed acute non-specific hemorrhagic and inflammatory remodelling. The patient's follow-up at the fourth month showed a good clinical, biological and radiological evolution.



Figure 1: Bilateral inflammatory cervical and submandibular swellings upon admission



Figure 2: Cervico-thoracic CT scan upon admission showing diagnosis of mediastinitis: anterior médiastinal (yellow arrows) and cervical (red arrow) collections + pericardial effusion (yellow star)



Figure 3: Control CT scan on day 10: increasing mediastinal collections (yellow arrows), decreasing cervical collections (red arrow), pleural effusion + pulmonary condensation (yellow star)



Figure 4: The course of mediastinitis through chest X-rays: A) Mediastinal enlargement with left pleural effusion on admission B) Bilateral pleural on day 10 C) Normal X-ray before ICU discharge on day 20

	Day 0 Admission	Day 2	Day 4	Day 10 Surgery	Day 13	Day 20 ICU
	Surgery 1			2		discharge
Heart rate (bpm)	140	95	82	148	120	85
Respiratory rate (cpm)	30	Mechanical ventilation	21	35	24	19
Temperature (°C)	39.5	37.8	37.2	38.6	37.5	37.1
Hemoglobin (g/dl)	9.2	7.9	7.1	9	8.3	9.5
White Blood Count (e/mm ³)	45 480	28 790	16 200	25 600	15 640	11 010
Platelets (e/mm ³)	469 000	495 000	478 000	357 000	518 000	624 000
PT (%)	55.8	44	74	62.1	68.6	67
Albumin (mg/l)	23	21	17	24	26	29
Urea (g/l)	0.2	0.25	0.21	0.07	0.37	0.11
Creatinine (mg/l)	7	6	4	4	7	5
CRP (mg/l)	152	135	37	251	120	90
Bicarbonates (mmol/l)	15	22	25	21	21	23
Arterial Lactates	3.54	1.75	1.1	-	-	-

Table 1: Clinico-biological evolution through ICU stay

DISCUSSION

DNM is a life-threatening complication of odontogenic or pharyngeal infections extending to the mediastinum along the deep fascial planes, retropharyngeal areas or peritracheal areas [3]. As with other types of mediastinitis, DNM can be categorized into Type I (localized), Type IIa (diffuse, spreading to the anterior inferior mediastinum) and Type IIb (diffuse, spreading to both the anterior and posterior inferior mediastinum) [4]. The cause is mainly odontogenic (36 % - 47 %) or pharyngeal (33 % - 45 %) and rarely cervical (15 %) or unknown (6 %) [5, 6]. Main risk factors are impaired immune function, diabetes, use of oral glucocorticoids, reduced tissue oxygenation caused by heart or respiratory failure and peripheral artery occlusive disease [7]. Our patient had no comorbidities, as reported in 13 % of patients in the literature [7]. She received non-steroidal antiinflammatory drugs (NSAIDs) prior to admission, although their implication in the occurrence of mediastinitis is controversial. The study by Petitpas et al., [8] did not reveal a relationship between NSAID use and mediastinal spread of cervical necrotizing fasciitis. However, this association has been reported in several studies [9-13], mainly retrospective and case reports.

Early diagnosis of mediastinitis is crucial for prompt initiation of antibiotic therapy and surgical intervention. Symptomatoloy is not specific and depends on underlying etiology [6]. As described in the reported cases [14], our patient presented with cervical pain and swelling, dysphagia, followed by trismus, dyspnea, dysphonia and limited cervical mobility. A systemic inflammatory response syndrome is often associated, depending on both underlying etiology and patient background [14]. This is reflected biologically by elevated white blood cell count, C-reactive protein and procalcitonin levels, as in our case. A progressive thrombocytopenia with or without disseminated intravascular coagulation signs may indicate worsening sepsis [15]. When suspected, a neck and chest contrastenhanced CT scan is the gold standard to confirm the diagnosis of mediastinitis, determine underlying cause. assess the infectious process extension and plan eventual surgical procedures. Typical CT findings include evidence of primary infection as well as collections of encapsulated fluid in the mediastinum, air in the soft tissue planes, pleural effusions, abscesses with air bubbles, and increased mediastinal fat density with loss of typical tissue planes. Magnetic resonance imaging (MRI) has rarely been used, and its utility is unknown [16].

In addition to cross-sectional imaging, the microbiological profiling of mediastinitis is crucial for targeted antimicrobial therapy. Blood cultures and either tissue or fluid samples should be obtained before starting antibiotic therapy without delaying it. This may require aspiration of deep abscess cavities or debridement of infected sternal or mediastinal tissues [17]. DNM is often polymicrobial and consisting of the usual bacterial flora of oral cavity, upper respiratory tract, ears and eyes [15]. The pathogens commonly found include Streptococcus spp., Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli and for most abscesses anaerobes such as. Peptostreptococcus spp., Fusobacterium nucleatum, Prevotella spp. and Actinomyces spp. ... Haemophilus influenzae may also be found in parapharyngeal or retropharyngeal abscesses [18-20]. Our patient bacteriological samples came back negative as in most reported cases where less than 25 % of blood and tissue cultures are positive [18]. Receiving antibiotics before admission may explain these results in our case.

Mediastinitis is a severe infection that often leads to septic shock [15]. Treatment pillars are: preventive and support treatment of sepsis and septic shock and associated organ failures, antibiotic therapy and early surgical drainage. Our patient had initial resuscitation immediately after admission, according to Surviving Sepsis Campaign recommendations [21]: monitoring, hemodynamic and arterial transport of optimization with crystalloids oxvgen filling. noradrenaline and oxygen therapy. Airway compromise should be quickly anticipated. Due to trismus and local oedema, both laryngoscopic visualization and anterior airway access may be impaired. Guidelines suggest that the airway should be managed by an expert anesthesiologist and that an alternative plan for airway control should be previously established. An early tracheostomy may be useful for both airways securing and opening the fascial planes of the neck [22]. Involvement of expert otolaryngologist and/or maxillofacial surgeon is encouraged in case of endotracheal intubation failure [23-25]. In our case, laryngoscopy was expected to be difficult due to trismus, short neck and cervical edema and anesthesia induction was performed while the team was ready to perform an urgent tracheostomy when needed. The antimicrobial treatment of mediastinitis should follow the good practice principles of empirical antimicrobial therapy in ICU patients [26, 27]. Broad-spectrum antimicrobial therapy can be initiated as long as it can be adjusted to subsequent microbiologic findings [28]. In DNM, specific data related to antimicrobial therapy are rare and recommendations are therefore based on expert opinions [15]. Empirical antimicrobial therapy should cover aerobic and anaerobic bacteria commonly associated with ear, nose and throat infections. There are no standardized schemas but the combinations of a third-generation cephalosporin with metronidazole [6] or a piperacillin/tazobactam with clindamycin [29] are

suggested. The ideal duration of antimicrobial therapy is also not well defined. A long course of parenteral therapy from 2 to 3 weeks is often necessary [6, 22], followed by maximum of 3 weeks oral monotherapy (total treatment duration of 6 weeks) [1]. CT imaging and infection markers monitoring may be useful to assess the efficiency of antibiotic therapy [30] as well as ICU organ failure scores (SOFA). In all cases, patients should be closely monitored and the dosage. duration, and regimen of antibiotic therapy should be modified if necessary [15] and management should be individualized. Our patient received ceftriaxone, metronidazole and gentamycin as empirical therapy upon admission to our center. Prior third generation cephalosporin prescription, onset of a fatal threatening septic shock and the nonavailability of piperacillin/tazobactam were behind the combination of Meropeneme, Teicoplanin and Fluconazole as initial empirical antibiotherapy. Meropeneme was maintained for three weeks without de-escalation because of a nosocomial catheter-related bacteremia complicating our case.

An early control of the infectious source and debridement of infected tissues is essential. A delay between diagnosis and surgical intervention is associated with poor outcome and should not exceed 24 hours [22]. Large cervical and mediastinal drainage combined to the underlying cause treatment are a must. The surgical approach depends on CT scan findings. patient condition and local expertise: cervicotomy for localized infections of the neck and upper mediastinum, sternotomy for anterior mediastinum median debridement, bilateral anterolateral thoracotomy to prevent subsequent sternal osteomyelitis, posterolateral thoracotomy if access to posterior mediastinum is needed. Video-assisted thoracic surgery may be interesting if available and a clamshell thoracotomy offers excellent exposure to the entire mediastinum as well as both pleural cavities if more drastic debridement is required [31]. In our case, as the patient was initially hemodynamically not stable, we opted for a two steps damage control surgery. The septic patient underwent first a less invasive procedure through a cervicotomy for drainage of the cervical and upper mediastinal collections and sampling, followed by mediastinotomy for the drainage of the mediastinal and pleural collections. Clinical or paraclinical deterioration should be early identified as it may indicate the need for surgical re-intervention [15] or inadequate antibiotherapy if surgery is not needed. Hyperbaric oxygen therapy in the treatment of a range of necrotizing soft tissue infections has been retrospectively evaluated [32], with results varying from no benefit to improved survival and tissue preservation when used in conjunction with antibiotics and conventional surgical treatment. Given the relative rarity of serious complications associated with hyperbaric oxygen therapy [32], it may represent a potentially useful addition to current management, but Fatima Zahra Haddari et al., Sch J Med Case Rep, Sep, 2022; 10(9): 883-888

probably requires more controlled studies to establish its therapeutic utility [33] and more suitable logistics for ICU patients. Several of the supportive measures associated with the treatment of mediastinitis are of particular importance. Following the recommendations of the Surviving Sepsis Campaign [21], our patient had received dynamic multimodal analgesia, pharmacological (low-molecular-weight heparin (LMWH)) and mechanical venous thromboembolism prophylaxis, stress ulcer prophylaxis with proton pump inhibitors, and nutritional management based on early enteral feeding during her ICU stay.

Mortality related to DNM remains high (15 % - 30 %) [5-7] and reported prognostic factors include: a delay in diagnosis, inadequate surgical drainage of the mediastinum [7], advanced age, high ICU severity scores and higher grade of DNM [5]. Moreover, septic shock is an independent predictor of mortality [6].

CONCLUSION

Descending necrotizing mediastinitis is a lifethreatening medicosurgical emergency. Early diagnosis and prompt multidisciplinary management are necessary for a successful outcome. The combination of an early targeted antibiotic therapy, an optimized surgical drainage and individualized organ support are key to reduce morbidity and mortality.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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REFERENCES

- Doddoli, C., Trousse, D., Avaro, J. P., Djourno, X. B., Giudicelli, R., Fuentes, P., & Thomas, P. (2010)
 Acute mediastinitis except in a context of cardiac surgery. *Revue de Pneumologie Clinique*, 66(1), 71 -80.
- Olland, A. (2015). Traitement chirurgical des médi astinites aiguës de l'adulte. *EMC - Techniques chir* urgicales – Thorax, 10(2), 1-12.
- 3. Sakai, T., Matsutani, N., Ito, K., Mochiki, M., Min eda, J., Shirai, S., ... & Kawamura, M. (2020). Dee p cervical and paratracheal drainage for descending necrotizing mediastinitis. *Asian Cardiovascular an d Thoracic Annals*, 28(1), 29-32.
- Endo, S., Murayama, F., Hasegawa, T., Yamamoto, S., Yamaguchi, T., Sohara, Y., ... & Nishino, H. (1 999). Guideline of surgical management based on d iffusion of descending necrotizing mediastinitis. *Th e Japanese Journal of Thoracic and Cardiovascula*

- *r Surgery*, *47*(1), 14-19.
 Palma, D. M., Giuliano, S., Cracchiolo, A. N., Falc one, M., Ceccarelli, G., Tetamo, R., & Venditti, M. (2016). Clinical features and outcome of patients w ith descending necrotizing mediastinitis: prospectiv e analysis of 34 cases. *Infection*, *44*(1), 77-84.
- Prado–Calleros, H. M., Jiménez–Fuentes, E., & Jim énez–Escobar, I. (2016). Descending necrotizing m ediastinitis: Systematic review on its treatment in th e last 6 years, 75 years after its description. *Head & Neck*, 38(S1), E2275-E2283.
- Ridder, G. J., Maier, W., Kinzer, S., Teszler, C. B., Boedeker, C. C., & Pfeiffer, J. (2010). Descending necrotizing mediastinitis: contemporary trends in et iology, diagnosis, management, and outcome. *Anna ls of surgery*, 251(3), 528-534.
- Petitpas, F., Blancal, J. P., Mateo, J., Farhat, I., Nai ja, W., Porcher, R., ... & Mebazaa, A. (2012). Facto rs associated with the mediastinal spread of cervica l necrotizing fasciitis. *The Annals of thoracic surge* ry, 93(1), 234-238.
- Shaikh, N., Ummunissa, F., Hanssen, Y., Al Makki , H., & Shokr, H. M. (2010). Hospital epidemiolog y of emergent cervical necrotizing fasciitis. *Journal* of Emergencies, Trauma and Shock, 3(2), 123-125.
- Thiebaut, S., Duvillard, C., Romanet, P., & Folia, M. (2010). Prise en charge des cellulites cervicales avec ou sans extension médiastinale: à propos de 1 7 cas. *Revue de laryngologie, d'otologie et de rhino logie (1919), 131*(3), 187-192.
- 11. Righini, CA, Motto, E., Ferretti, G., Boubagra, K., Soriano, E., & Reyt, E. (2007, December). Extensi ve cervical cellulitis and descending necrotizing me diastinitis. In *Annals of Otolaryngology and Cervic ofacial Surgery* (Vol. 124, No. 6, pp. 292-300). Els evier Masson.
- Chaplain, A., Gouello, J. P., & Dubin, J. (1996). Ce llulites cervicales nécrosantes aigues à porte d'entré e pharyngée: role possible des anti-inflammatoires stéroidiens et non stéroidiens. A propos de 5 observ ations. *Revue de laryngologie, d'otologie et de rhin* ologie (1919), 117(5), 377-380.
- 13. Demeslay, J., De Bonnecaze, G., Vairel, B., Chaput , B., Pessey, JJ, Serrano, E., & Vergez, S. (2014). I mplications of anti-inflammatories in the complicat ions of pharyngitis. A retrospective analysis of 163 cases. *French Annals of Oto-rhino-laryngology and Cervico-facial Pathology*, 131 (5), 286-290.
- Celakovsky, P., Kalfert, D., Tucek, L., Mejzlik, J., Kotulek, M., Vrbacky, A., ... & Pasz, A. (2014). De ep neck infections: risk factors for mediastinal exte nsion. *European Archives of Oto-Rhino-Laryngolo* gy, 271(6), 1679-1683.
- 15. Pastene, B., Cassir, N., Tankel, J., Einav, S., Fourni er, P. E., Thomas, P., & Leone, M. (2020). Mediast initis in the intensive care unit patient: a narrative r eview. *Clinical Microbiology and Infection*, 26(1), 26-34.
- 16. Exarhos, D. N., Malagari, K., Tsatalou, E. G., Bena kis, S. V., Peppas, C., Kotanidou, A., ... & Roussos,

 $\ensuremath{\mathbb{O}}$ 2022 Scholars Journal of Medical Case Reports | Published by SAS Publishers, India

C. (2005). Acute mediastinitis: spectrum of comput ed tomography findings. *European radiology*, *15*(8), 1569-1574.

- Gottlieb, G. S., Fowler Jr, V. G., Kong, L. K., McC lelland, R. S., Gopal, A. K., Marr, K. A., ... & Core y, G. R. (2000). Staphylococcus aureus bacteremia in the surgical patient: a prospective analysis of 73 postoperative patients who developed Staphylococc us aureus bacteremia at a tertiary care facility. *Jour nal of the American College of Surgeons*, *190*(1), 5 0-57.
- Qu, L., Liang, X., Jiang, B., Qian, W., Zhang, W., & Cai, X. (2018). Risk factors affecting the progno sis of descending necrotizing mediastinitis from od ontogenic infection. *Journal of Oral and Maxillofa cial Surgery*, 76(6), 1207-1215.
- Brook, I. (2004). Microbiology and management of peritonsillar, retropharyngeal, and parapharyngeal a bscesses. *Journal of oral and maxillofacial surgery* , 62(12), 1545-1550.
- Laulajainen-Hongisto, A., Aarnisalo, A. A., Lempi nen, L., Saat, R., Markkola, A., Leskinen, K., ... & Jero, J. (2017). Otogenic intracranial abscesses, our experience over the last four decades. *The journal o f international advanced otology*, *13*(1), 40.
- Rhodes, A., Evans, L. E., Alhazzani, W., Levy, M. M., Antonelli, M., Ferrer, R., ... & Dellinger, R. P. (2017). Surviving sepsis campaign: international gu idelines for management of sepsis and septic shock: 2016. *Intensive care medicine*, 43(3), 304-377.
- 22. Abu-Omar, Y., Kocher, G. J., Bosco, P., Barbero, C., Waller, D., Gudbjartsson, T., ... & Cardillo, G. (2017). European Association for Cardio-Thoracic S urgery expert consensus statement on the preventio n and management of mediastinitis. *European jour nal of cardio-thoracic surgery*, *51*(1), 10-29.
- 23. Updated by the Committee on Standards and Practic ce Parameters, Apfelbaum, J. L., Hagberg, C. A., C aplan, R. A., Blitt, C. D., Connis, R. T., ... & Ovass apian, A. (2013). Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesi ology*, *118*(2), 251-270.
- Frerk, C., Mitchell, V. S., McNarry, A. F., Mendon ca, C., Bhagrath, R., Patel, A., ... & Ahmad, I. (201 5). Difficult Airway Society 2015 guidelines for m

- anagement of unanticipated difficult intubation in a dults. *BJA: British Journal of Anaesthesia*, 115(6), 827-848.
- Langeron, O., Bourgain, J. L., Francon, D., Amour, J., Baillard, C., Bouroche, G., ... & Nouette-Gaulai n, K. (2018). Difficult intubation and extubation in adult anaesthesia. *Anaesthesia Critical Care & Pai n Medicine*, 37(6), 639-651. https://doi.org/10.1016 /j.accpm.2018.03.013.
- Campion, M., & Scully, G. (2018). Antibiotic use i n the intensive care unit: optimization and de-escal ation. *Journal of intensive care medicine*, 33(12), 6 47-655.
- 27. Pastene, B., Duclos, G., Martin, C., & Leone, M. (2 016). Antimicrobial therapy in patients with septic shock. *La Presse Médicale*, *45*(4), e111-e117.
- McDanel, J. S., Perencevich, E. N., Diekema, D. J., Herwaldt, L. A., Smith, T. C., Chrischilles, E. A., ... & Schweizer, M. L. (2015). Comparative effectiv eness of beta-lactams versus vancomycin for treatm ent of methicillin-susceptible Staphylococcus aureu s bloodstream infections among 122 hospitals. *Clin ical Infectious Diseases*, *61*(3), 361-367.
- Gunaratne, D. A., Tseros, E. A., Hasan, Z., Kudpaj e, A. S., Suruliraj, A., Smith, M. C., ... & Palme, C. E. (2018). Cervical necrotizing fasciitis: systematic review and analysis of 1235 reported cases from th e literature. *Head & Neck*, 40(9), 2094-2102.
- Zhang, T., Wang, Y., Yang, Q., & Dong, Y. (2017)
 Procalcitonin-guided antibiotic therapy in criticall y ill adults: a meta-analysis. *BMC infectious diseas es*, 17(1), 1-11.
- 31. Son, H. S., Cho, J. H., Park, S. M., Sun, K., Kim, K. T., & Lee, S. H. (2006). Management of descending necrotizing mediastinitis using minimally invasive video-assisted thoracoscopic surgery. *Surgical L aparoscopy Endoscopy & Percutaneous Technique s*, 16(6), 379-382.
- Jallali, N., Withey, S., & Butler, P. E. (2005). Hype rbaric oxygen as adjuvant therapy in the manageme nt of necrotizing fasciitis. *The American journal of surgery*, *189*(4), 462-466.
- Weaver, E., Nguyen, X., & Brooks, M. A. (2010). Descending necrotising mediastinitis: two case rep orts and review of the literature. *European Respirat* ory Review, 19(116), 141-149.