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Ludwig's angina: a diagnostic and surgical priority.

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Highlights

- Ludwig's angina is historically known as a rapidly and frequently fatal progressive necrotizing cellulitis of the floor of the mouth, the throat and the neck, that should not be confused with Lemierre's syndrome.
- We present four cases of severe necrotizing cervical cellulitis notably associated to concomitant self-medication with NSAIDs.
- The prognosis is directly related to early recognition leading to appropriate resuscitation measures and early surgical debridement, with a frequent second look.
- The most frequently identified micro-organisms are anaerobic bacteria and streptococci. For covering this broad bacterial spectrum, B-lactams, and more likely penicillin with β L^{ase} inhibitors, should be recommended. A combination with clindamycin could be useful.

Abstract

Ludwig's angina is known for two centuries as a rapidly and frequently fatal progressive gangrenous cellulitis or necrotizing fasciitis of the neck and the floor of the mouth.

The management of these usually young patients requires trained teams combining medical skills in surgery, antibiotic therapy and resuscitation. The prognosis is directly related to early surgical debridement and experience of the teams managing these patients.

We present four cases of severe necrotizing cervical cellulitis notably associated to concomitant self-medication with NSAIDs. Through these cases, we conclude that several surgical steps could

be required combining with broad spectrum antibiotic therapy. An optimal surgery, draining all collections and excising all necrotic tissues, seems to be a condition needed for antibiotics efficacy and finally healing.

Keywords: Ludwig's angina, septic surgery, NSAID, anaerobic bacteria

Background

Ludwig's angina was first described in 1836 by Wilhelm Friedrich von Ludwig, a German physician, as a rapidly and frequently fatal progressive gangrenous cellulitis or necrotizing fasciitis involving the neck and the floor of the mouth (1). On the historic description, the disease began by an invasion of submandibular, sublingual and submental spaces by streptococci and/or anaerobic bacteria, and could spread through mediastinum.

Usual clinical features are odynophagia, oedema and trismus. Life-threatening complications of Ludwig's angina are mainly airway obstruction and septic choc, which need resuscitation measures with a specific airway management. The overall mortality of Ludwig's angina has been reported exceeding 50% (3), decreasing to approximately 8% through appropriate management combining surgery, antibiotic therapy and resuscitation measures (2,3). Surgery is considered as the most important part of the treatment, aiming to achieve debridement of infected areas, excision of necrotic tissue and drainage of pus. A second look may be useful for debridement and drainage.

The different names, pathophysiology and clinical presentations described in the medical literature, result in a great disparity in clinical management, and it can happen that medical teams delay effective management because they have not clearly identified the syndrome and its severity quickly enough. We report our experience through four cases of cervical necrotizing cellulitis, all severe but different in terms of clinical presentation, aiming to improve clinical early recognition.

Case 1

A 35-year-old man presented to emergency for cervical pain and oedema, with a loss of voice, dysphagia, without dyspnea or trismus. The patient had no other co-morbidities, except for active ethyl and tobacco consumption. Two weeks before, he had complained of odynophagia, treated by NSAIDs (self-medication) and amoxicillin (medical order).

The patient was firstly managed in the emergency operative room, a cervicothoracic CT showed a para-pharyngeal hydroaeric collection fusing to the anterior cervical spaces and mediastinum. The initial care were based on antibiotic therapy, appropriate airway management, and surgical drainage of the para-pharyngeal collection.

The patient was then transferred to intensive care unit, and the mediastinal collection was secondarily drained through interventional radiology. Bacteriological cultures of per-operatives samples have identified *Streptococcus constellatus* and *Parvimonas micra*, leading to adapt antibiotics (amoxicillin-clavulanat and clindamycin). Moreover, dental infections were identified requiring the extraction of three mandibular teeth. At day 39, the patient had completely recovered, and was discharged.

Case 2

A 41-year-old man, known for active tobacco consumption, presented to the emergency department for submandibular edema and pain, with fever. One week before, a submandibular pain had been treated by self-medication with NSAIDs. The CT showed a left submandibular infection with abcess of masticatory space and salivary lithiasis.

Firstly, the patient was treated only with antibiotics (amoxicilline-clavulanat). At day 2, oedema increased and dyspnea appeared, leading the patient to intensive care unit for fiberoptic intubation. A surgery was conducted to drain the submandibular abcess. Bacterial cultures of peroperatives samples identified a *Streptococcus constellatus* and antibiotic was continued.

At day 4, trismus and dysphagia appeared, associated with submandibular edema. A new CT showed left para-pharyngeal and interpterygoïdal increased collections, with persistence of the known lithiasis. Patient was treated by surgical second look for debridement and drainage. The evolution was favourable, and patient was discharged at day 14. The lithiasis measured at 14 mm was finally surgically removed 6 months later.

Case 3

A previously healthy 47-year-old man presented to the emergency department for odynophagia treated since 3 days by NSAIDs (self-medication), fever, and pharyngeal swelling. A cervical CT was performed, finding a right para and retro-pharyngeal abscess causing airways compression without mediastinal extension at this time. A first surgical step was needed for flattening the abscess. Amoxicilline-clavulanat and clindamycine antibiotics combination was started, secondarily, a polymorphic flora grew on per-operative samples.

At day 6, dysphagia and bitonal voice relapsed, odynophagia increased. Many neck abscesses with a cervico-thoracic extension and mediastinitis were diagnosed on a new CT scan. A second surgery was necessary, by right cervicotomy for debridement and drainage of upper mediastinal and retropharyngeal spaces. Antibiotic therapy was modified for piperacilline-tazobactam, clindamycin and amikacine.

At Day 9, the control of CT scan showed an increased retro-pharyngeal collection with persistent extension to latero-cervical and mediastinal spaces. A third surgery was performed, with tracheotomy. Cultures of bacteriological per-operative samples remained sterile.

At day 16, the antibiotherapy was de-escalated for amoxicilline-clavulanat combined to clindamycine. Patient was discharged at day 30.

Case 4

A 27-year-old man, previously known for active consumption of cannabis and tobacco, was admitted to emergency department because of cervical edema and fever. An odynophagia,

occurring 5 days before, had been first treated by self-medication with NSAIDs, then by oral amoxicillin and steroid. The worsening of clinical situation led the patient to emergency department. Physical examination on admission confirmed the dyspnea, cervical cellulitis and fever. Respiratory failure and laryngeal stridor have been promptly managed in intensive care unit, fiberoptic support was necessary for a difficult oro-tracheal intubation. CT scan, performed just after resuscitation management, shown a large cervical abscessus with extension to mediastinum and cardiac area.

A surgery was immediately conducted for drainage of collections. Antibiotic therapy with piperacillin-tazobactam and amikacin was also started. Bacteriological culture of per-operative samples identified *Fusobacterium necrophorum*, and clindamycine was added. No evidence of jugular venous thrombosis was seen on the doppler ultrasound.

At day 5, a second surgery was needed to drain sub pectoral abscess and pericardial collection (no growth on bacteriological samples done at this time). Antibiotic therapy was finally continued with amoxicillin-clavulanat and clindamycine combination, for four weeks.

The evolution was favourable with extubation at day 15. At one month, patient was cured with normal physical examination.

Discussion

These clinical cases highlight the severity of this infectious disease, the importance of early surgical management, and appropriate resuscitation measures. The starting point of Ludwig's angina is the oral cavity and pharyngeal, dental or salivary primary involvements are illustrated here.

Predisposing factors were frequently reported (3), such as poor dental hygiene, diabetes mellitus, obesity, denutrition, alcoholism... NSAID, and/or self-medication, seems to be determining factors in oropharyngeal infections. A link between peritonsillar abscesses and self-medication with anti-inflammatory drugs was recently reported (4–7). The hypothesis that NSAIDs facilitate progression

to abscessing is also supported by experimental data (8). Another hypothesis is the decrease of clinical signs and a subsequent delay in consultation and treatment (9), due to NSAIDs intake. The natural course of this infection is extending rapidly in contiguous area, fatty and cellular tissue of cervical spaces. According to some authors (10) the use of an ultrasound may help to identify cellulitis and abscess at early stage. Severe sepsis and obstruction of the upper airway could occurred, needing appropriate resuscitation management. Facing this acute and diffuse cellulitis, the surgical management should be performed as early as possible. The prognosis is directly related to surgical delay and quality. The spread of infection to mediastinum is a frequent complication of those cervical necrotizing cellulitis (11).

Surgery for debridement and drainage, and effective antibiotics are the crucial part of the treatment. The most frequently identified micro-organisms are anaerobic bacteria (12–14) including *Bacteroides sp.*, *Micrococcus sp.*, *Fusobacterium sp.*, or *Peptostreptococcus sp.* Among aerobic bacteria, streptococci are the most frequent, including for only 7% of cases (15) the β -hemolytic streptococcus group A. The recommended antibiotic therapy, covering a broad spectrum, is based on B-lactams, more likely penicillin (+/- penicillinase inhibitors). A combination with clindamycin may be useful in our experience.

Since this infection involved the throat and the mouth, and is frequently due to anaerobics bacteria, it might be mistaken for Lemierre's syndrome (16). Although the comparison is right for the location, as well as bacterial characteristics and recommended antibiotics, it has to be said that the pathophysiology and the importance of surgery are dramatically different (Table). For Lemierre's syndrome, the treatment is primarily medical, mainly based on an appropriate antibiotic therapy and the management of septic thrombosis. As opposite, the treatment of Ludwig's angina is mainly based on surgery. The comparison with Fournier's gangrene (17–20), involving an opposite anatomical location, appears more appropriate regarding pathophysiology, medical management and importance of surgery.

Conclusion

Ludwig's angina is a serious acute cellulitis involving visceral neck areas that requires urgent multidisciplinary approach including surgery and intensive care. The prognosis depends on clinical early recognition, celerity of the surgical procedure and experience of the teams managing these patients.

The severity of this infection is often directly linked to comorbidities and probably concomitant medication with NSAIDs. These four cases show that several surgical steps are generally required for drainage, debridement and excision of necrotic tissues. To ensure antibiotics efficacy, a useful broad spectrum including Gram-positive and anaerobic bacteria should be taken into account. The management of these usually young patients requires trained teams and is focused on three main areas: surgery, antibiotherapy and resuscitation measures.

Ethical Approval

Not required

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Conflict of Interest Statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Table : What could be confusing about anaerobics soft tissue infections?

	Ludwig's angina	Lemierre's syndrom	Fournier's gangrene
Initial presentation	oral infection	tonsillitis or endometritis	perineal infection
Extension and spread of infection	Cervical necrotizing cellulitis, mediastinal extension, suppurative complication. Venous thrombosis is possible	Septic venous thrombosis, origin of haematogenous dissemination	Perineal necrotizing cellulitis, extension to external genitalia and abdominal wall, suppurative complications. Venous thrombosis is possible
Bloodstream infection with secondary location	Possible but uncommon	Constant diffusion mechanism	Possible but uncommon
Surgery	Main part of the treatment	Rarely needed (exceptionally drainage of pulmonary abscesses, or septic arthritis for example)	Main part of the treatment
Microbiology	Streptococci and anaerobic bacteria are the most frequent pathogens involved in both infections, possibly polymicrobial		Polymicrobial : Streptococci and anaerobes are frequently involved, with a part for Staphylococci and gram negative bacilli
Antibiotherapy	B-Lactams (more likely penicillins, such as amoxicillin, with β L ^{ase} inhibitors) + Clindamycin +/- aminoglycoside		