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Gas Gangrene: A Deadly Lethal Disease due to *Clostridium perfringens*

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ABSTRACT

Clostridia gas gangrene is a long-recognized complication of trauma and penetration of intra-abdominal wounds. Some of the common symptoms for a person infected with gas gangrene can be reasonably more sweating with higher rate of heart beat (tachycardia) and relatively high fever. Severity of this catastrophic disease cannot be ignored as once infected the body starts deteriorating rapidly initiating the death of the person. On detailed examination of cases one can observe large blisters beneath the skin, damage of body cells and tissues, swelling around the wound. Thus, once Clostridium perfringens is detected in a case of gas gangrene it is recommended to undergo immediate surgery to prevent death, and remove the damaged or infected tissues from the body. Most clostridial soft-tissue infections, including gangrene, are caused by Clostridium perfringens. The criticality of this disease is that once infected it can develop in few hours or even in a day, but the fact is often it is seen to appear after several days. Puncture wounds and surgical wounds, especially GI surgeries done on the biliary tract or intestinal surgeries, are causes of clostridial infections due to inadvertent inoculation of the surgical wound with gut bacteria. In case the disease spreads to a few more regions/area of the body then there might be chances of survival following surgical removal of an arm or leg or the infected area to control the spread of infection in the body.

Key words: *Clostridium perfringens*, Toxin, Bacteremia, Necrotizing enterocolitis, Enteritis necroticans, Gangrenous appendicitis

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INTRODUCTION

Clostridium perfringens (formerly known as Bacillus welchii, or Clostridium welchii) is a bacterial agent which leads to development of the disease gas gangrene. These anaerobic bacteria are rod-shaped and have thick cell walls of the genus Costridium [1]. However, among all, fulminant necrotizing infections that affects humans the most. *Clostridium perfringens* steers to gas gangrene which is by far the most lethal. The deadliness of this disease is such that just 6 to 8 hours is enough for it to get well established in the body. This disease spreads contiguously to involve its nearby regions by several inches in just an hour [2].

Some common indications to detect if one is infected by gas gangrene is swelling, blisters and jaundice [3]. Most importantly this gas gangrene can lead to severe tissue death, damage to blood vessels and cells as it occurs inside the human body typically at the site of trauma or recent surgical wound forming gas and toxins that act as catalyst to cause above mentioned damages to the body [4]. Around 80 - 90% of gas gangrene case is due to the bacteria named "*Clostridium perfringens*".

History and genetic analysis

In the past Clostridial my necrosis or Gas Gangrene was known to be as a common war wound infection. There is a 5% occurrence of this condition from war related wounds. However, with improvements in wound care methods has resulted in a significant drop in infection rates. It was noticed during the Vietnamese war epoch that that the use of antisepsis and antibiotics have led to incidences falling down to 0.1% [5,6].

The GC content in *clostridium perfringens* is about 27-28%. Around 2500-3600 number of anticipated genes with varying size range of 3.0-4.1Mb is present in each genome. The first completed genome sequence of the bacteria was recorded in the early 2002. However, the first known strain of this kind was found in 1939. A recent study revealed a diverse pan genome with only 12.6% core genes. This research involved the investigation of over 56 *Clostridium perfringens* strains, to encapsulate the largest numbers of genomic strains [7].

Epidemiology

Myonecrosis in the United Stated is assumed to be around a thousand cases in a calendar year. Countries with lack of healthcare and other medical facilities are seen to face the disease frequently and in higher number. Whereas, provided with advanced medical technologically equipment, early detection and quick treatment, the mortality rate is marked down as 20 - 30% while few researches also claim to be even below 10%. However, as discussed earlier, the fatality rate can be 100% due to timely non-treatment of this disease. Patients with weaker immunity systems having diabetes mellitus and gets frequent infections are tend to have 67% or higher mortality rate. Upon detailed investigation if abdominal soft tissue or chest wall are detected due to gas gangrene then it will be challenging to take quick actions and the mortality rate can reach 60% [8].

Morphology and cultural characteristics of *Clostridium perfringens*

Clostridium perfringens is large in size and rectangular in shape having gram-positive bacilli with rounded or truncated ends and can grow on ordinary media. The bacteria falls in the pH range of 5.5 to 8.0 and can sustain 20°C to 50°C while the generation time is 10 minutes at 45°C. These anaerobic bacteria can be even in shape of straight or curved rods (3-8 µm X 0.4-1.2 µm) which can grow under micro-aerophilic conditions. Due to the filament lining on the body it can slide over the surface. The endospores here have longer life even in a critical environment condition and also it doesn't get affected when exposed to surrounding air. There are spores which are wider than the bacillary body, giving a swollen appearance that can approach like a spindle. The *clostridium perfringens* bacteria are heat resistant which can be capsulated, non-motile and non-flagellated having thick protective cell made up of peptidoglycan (Figure 1).

Laboratory isolation and identification

Diagnosis of *clostridial perfringens* is done in a conventional approach by isolating the organism to detect the toxin. Suitable tests like using fluorescent antibody reagents are performed on this organism to detect them. Few researchers have also adopted the polymerase chain reaction (PCR) to identify these toxin genes. Detection of clostridium species was also done by using soluble proteins, FA reagents, and cellular fatty acid. Gram stains of wounds in a patient confirm the presence of clostridia. Even isolation trial can be given to agar cultures of materials. More often culture analysis to done to study toxin and to improve recovery of toxigenic organism. It is always advisable for selective and differential agar media.

Virulence factors

The virulence factors of the disease *Clostridium perfringens* falls predominantly in two categories, viz. lethal and non-lethal. Major lethal toxins are mostly of four types. The first is alpha toxin which is the first microbial toxin leading to two enzyme activities like phospholipase C and Sphingo myelinase. While the second variety is the beta toxin which is mostly helpful in making veterinary medicines. The beta toxin increases the capillary permeability and falls in Type B and C of the *clostridium perfringens*. Unlike the beta toxin the third and fourth varieties epsilon and iota toxins also surges the permeability acting primarily on the vascular endothelium and are categorized in Type C - D and Type E respectively. Few non-lethal toxins also exists like theta, delta, kappa, mu, neuraminidase, enterotoxin and many more. The kappa toxin is a collagenase which fragments the integrity of membranes and body structures. The delta and theta toxins are principally hemolysis [10].

Clinical spectrum

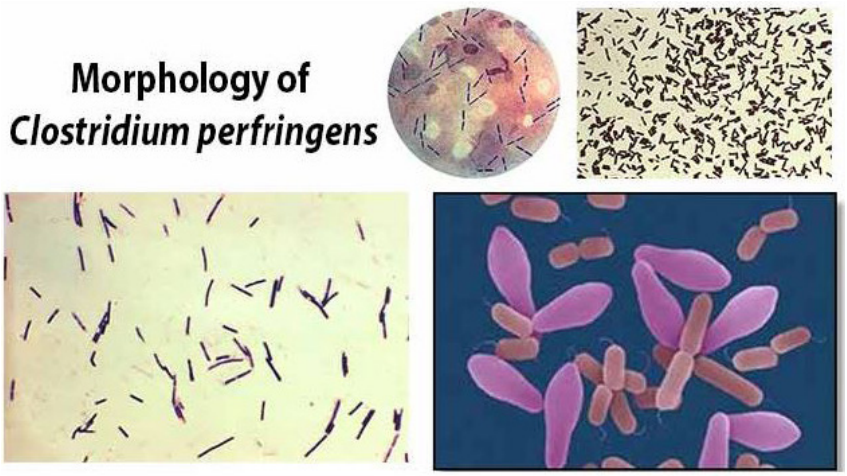
Clostridium perfringens Infections can lead to Clostridial wound infections can be further divided into anaerobic cellulitis which involves fascial plane and the other is Simple wound contamination that involves wound surface contamination.

Skin and soft tissue necrotizing infections.

Clostridial enteric infections.

Enteritis necroticans.

Figure 1: Morphology of *Clostridium perfringes* [9].



Gangrenous appendicitis.

Gas Gangrene:

Patients troubled with gas gangrene (myonecrosis) are prone to get high body temperature and shivering with infected area getting inflamed. The lethality of this disease is such that if not treated immediately then condition of the patient can rapidly progress to sepsis and might push him to death bed. Another visual observation can be the dishwater looking wound discharge with a musty order. The cell death due to subcutaneous fat down to the fascia can cause, which further passes into the deeper muscle. This occurs after the involvement of the vasculature supplying the large number of infected tissues. Upon careful observation towards any damage to nerve, it is found that the gravity of the pain might be less with respect to the extent of infection.

This is a non-communicable disease with the general cause of infections being traumatic wounds in addition to contamination by soil and bowel involved surgery. The inciting characteristics involve site contamination with Clostridium species and tissue devitalisation. The low oxygen concentration areas promote these infections, leading to the generation of vegetative forms from Clostridial spores. Subsequently, tissue damage and systematic manifestation occurs via α-toxin and θ-toxin. The infection successfully hampers RBCs, platelets and polymorphonuclear leukocytes (PMNs), leading to large scale damage of cell membrane and capillary walls. During the preliminary stage the infected area seems like swollen and the person might experience slightly warm and pain when touched. The affected tissues or wound portion might result in bloody discharge and with passage of time it will lead to multi-organ failure. The early diagnosis proves to be of much importance for patient management, besides aggressive resuscitation, surgical debridement, antibiotic therapy and supportive intensive care. The tissue loss and mortality maybe avoided following prompt surgical/medical intervention [11].

The incidence of gas gangrene depends on proximity with Clostridial species following wound contamination after vaccination, parturition, shearing, marking, neutering, docking, bleeding, and other traumatic interventions. The sporadic nature of disease is generally found, nevertheless outbreaks due to contaminated IV injections and needle contamination has been outlined.

The wound contaminations by spores or vegetative forms of histotoxic Clostridia primarily prompt gas gangrene initiation. The spores germinate and excite multiplying of vegetative forms of Clostridia which promote low redox potential, acidic pH and decomposing protein metabolites, which enhances anaerobicity. This leads to production of toxins signifying the gas gangrene characteristics.

Histotoxic Clostridia generates a series of enzymes to stimulate spread of the infection. These include collagenases, DNases, hyaluronidases, and neuraminidases. These lead to host defence invasion, tissue damage and nutrient acquisition, followed by spreading of infection. The toxin gains access to the blood circulation with resultant toxaemia, leading to shock and death. The Type A category of *Clostridium perfringens* can lead to intravascular haemolysis which is generated due to highly haemolytic nature of the disease.

Pathology

Severe proteinaceous oedema and haemorrhage are observed in the subcutaneous tissue (Figure 2). Vasculitis with fibrinoid necrosis and thrombosis also dwell in the same. The skin has diffuse congestion, haemorrhage, and emphysema, and in later stages, may show coagulative necrosis. Skeletal myofibers are inflated, hyper eosinophilic, and have a loss of striations, vacuolation, and hyper contraction bands (Figure 3). Intense and distinguished haemorrhage and oedema can be observed. Many degenerate leukocyte infiltrations by neutrophils have minimal to severe affected tissues [12].

Preventions

Measures to help people who are susceptible to gas gangrene and or to reduce their risk of infection include [13]:

Check frequently for cuts, sores, redness, swelling, skin breaks, or discharge on the feet.

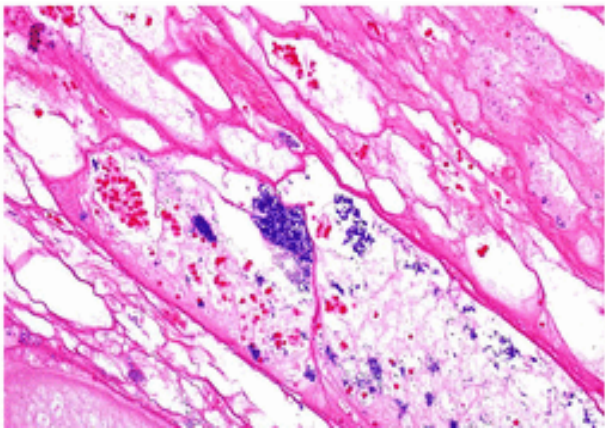


Figure 2: Severe subcutaneous edema with sparse leukocyte infiltrate and myriad intralesional rods [12].

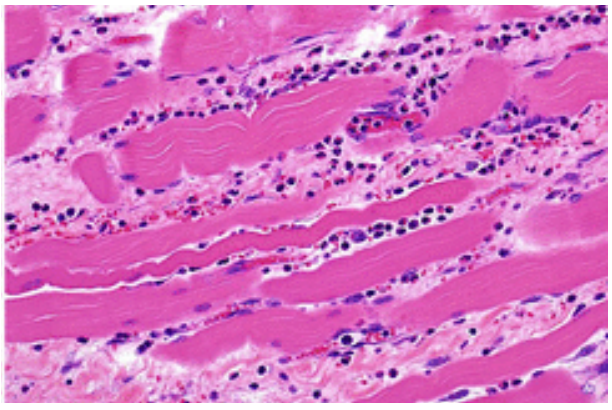


Figure 3: Interstitial muscle edema and mild neutrophilic infiltrate [12].

Having a medical foot health diagnosis annually.

Cleaning of wounds using mild soap and warm water can help in preventing spread of infection. Make sure to clean the area between toes and thus keep them clean and dry.

Avoiding home-use chemical preparations for corns, calluses, and in-growing toenails.

Obesity should be avoided. Perfect body weight must be maintained to prevent attack of diabetes, arterial disease, and obtain rapid wound healing.

Inspect for any symptoms of frostbite if exposed to prolonged cold.

Urgent medical diagnosis must be taken care of in case the skin becomes pale, hard, cold, and numb, or if any colour changes occur.

It is necessary to avoid barefoot walk and also wearing of shoes without socks should be avoided.

Perfect match footwear size can help avoid rubbing, blistering and cuts or abrasions of skin.

Diagnosing injuries if there are complications due to nerve damage in diabetes, especially in the feet.

Smoking should be strictly avoided.

Diagnosis

The patient suspected with gas gangrene should be provided with immediate initial workups including: CBC, CMP, urinalysis, PT, APTT, blood and wound cultures and further blood tests like ABG, lactic acid, and pre-calcitonin. The sepsis evaluation is frequently contemporaneous in gas gangrene and hence, finds much help and assistance from the above analysis. The x-rays, CT scan and ultrasound of the affected part of the body` are the commonly used imaging studies for the discussed case. The analyses prove to be extremely helpful in successful identification of the existence of gas in cell, detect magnitude of septicity and swelling. It should be noted that necrotic tissue removal must not be followed by the extensive lab analysis and imaging. The causal bacterium and antibiotic treatment can be determined using the aerobic and anaerobic culture of the deep wound area during removal of damaged tissue during surgical treatment [14].

Treatment of gas gangrene

The gas gangrene infection is generally observed to spread at rapid rates. Hence aggressive patient treatment is accessed by using antibiotics. The surgical consultations are also discussed in the early stages with debridement, arterial fluid revival and ICU intensive care, and high pressure gas therapy [8]. The non-delayed early surgical consultation is noted to be very important as cases for true surgical emergencies may occur, requiring exceptional response. Providers should not hold on to antibiotics to get cultures, but should begin quick treatment with antibiotics. The broad-spectrum of reasonable antibiotic medicines include Vancomycin and tazobactam. This may also include carbapenems or ceftriaxone with metronidazole. In case of suspicion for gas gangrene, they additionally suggest and induce penicillin plus clindamycin that can act as medicament to the flesh eating bacteria i.e. necrotizing fasciitis. The inhibitions in the synthesis of clostridial exotoxins can be observed following the consideration for clindamycin. This will also reduce the general effects of the toxins. It should be noted that clindamycin is bacteriostatic and not bactericidal, hence, should be used in conjunction with a second anti-microbial such as penicillin. The survival rates can be greatly improved by hyperbaric oxygen therapy along with additional typical rehabilitation of antibiotics and incision of damaged tissue. The exotoxin production by the bacteria can be controlled and minimized by the hyperbaric oxygen therapy. This in turn stimulates the initiation and movement of stem cells and polymorph nuclear cells. The improvements in bactericidal effect of the antibiotic are noted with treatment of tissue ischemia and improvement in reperfusion injury of tissue.

The daily or repeated surgical debridement is deemed necessary for patients with gas gangrene. This is expected to continue until the necrotizing infection is controlled. The additional reception for hyperbaric oxygen therapy, twice a day; until tissue necrosis stops and signs of tissue recovery with granulation tissue formation occur, is also suggested. The intensive care treatment will stay continued for the patient, along with the hemodialysis for suspected renal failure. The patients with severe adult respiratory distress syndrome (ARDS) may need an extracorporeal membrane oxygenation (ECMO) [15].

Postoperative and rehabilitation care

The gas gangrene affected patients once get cured; they would entail care towards the infected area. Every so often the fluid and infection needs to be drawn out to heal quickly. However, to do so a distinctive kind of dressing/bandage is applied over the wound with a nominal pressured vacuum pump being attached to it and this technique is termed as Negative Pressure Wound Therapy (NPWT). Plastic surgery remedy is also adopted to replace the unhealthy or dead tissues with skin graft or live tissues from other location of the body. Yet, most of the patients have to stay in ICUs for a protracted period of time and subsequently have to continue at the rehabilitation centers for quick survival and rejuvenate body functions. Additionally, treatments like hyperbaric oxygen therapy, restorative rehab programs with physical therapy and occupational therapies are also implemented for providing relief to infected patients.

CONCLUSIONS

More emphasis should be given to the disease gas gangrene following the involvement of traumatic wounds, which will then induce rapid, severe and extensive necrosis of the affected tissue. The major virulence factors involved are the production of four major toxins. Gram staining of *Clostridium perfringens* shows thick, stubby, boxcar-shaped, gram positive bacilli

without spore. Utilization of antibiotics like penicillin and clindamycin for around 2 weeks can be beneficial to treat gas gangrene. Hyperbaric oxygen therapy along with surgical debridement is also quintessential to kill the obligate anaerobe. The deadliness of the disease is such that if not treated early it will lead to sepsis and may result in death of the patient.

REFERENCES

1. https://en.wikipedia.org/wiki/Clostridium_perfringens
2. Barroso LA, Wang SZ, Phelps CJ, et al. Nucleotide sequence of Clostridium difficile toxin B gene. Nucleic Acids Res 1990; 18:4004.
3. Stevens DL, Bryant AE. The role of clostridial toxins in the pathogenesis of gas gangrene. Clin Infect Dis 2002; 35:93-100.
4. https://en.wikipedia.org/wiki/Gas_gangrene
5. https://medlineplus.gov/ency/article/000620.htm
6. Takehara M. Host defense against bacterial infection and bacterial toxin-induced impairment of innate immunity. J Pharm Soc Japan 2018; 138:1249-1253.
7. Stevens DL, Aldape MJ, Bryant AE. Life-threatening clostridial infections. Anaerobe 2012; 18:254-259.
8. Buboltz JB, Murphy-Lavoie HM. Gas gangrene. StatPearls 2022.
9. https://microbenotes.com/clostridium-perfringens/#pathogenesis-of-clostridium-perfringens
10. Smith LD. Virulence factors of Clostridium perfringens. Rev Infect Dis 1979; 1:254-262.
11. Kiu R, Hall LJ. An update on the human and animal enteric pathogen *clostridium perfringens*. Emerg Microbes Infect 2018: 7:1-15.
12. Junior CA, Silva RO, Lobato FC, et al. Gas gangrene in mammals: A review. J Vet Diagn Invest 2020; 32:175-183.
13. Silva RO, Uzal FA, Oliveira CA, et al. Gas gangrene (malignant edema). Clostridial Dis Animal 2016; 243-54.
14. https://www.medicalnewstoday.com/articles/158770#prevention
15. Shindo Y, Dobashi Y, Sakai T, et al. Epidemiological and pathobiological profiles of *Clostridium perfringens* infections: Review of consecutive series of 33 cases over a 13-year period. Int J Clin Exp Pathol 2015; 8:569-577.