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Review Article

Anthrax: A Looming Public Health Concern in Nigeria

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Abstract

Anthrax, a zoonotic infectious disease caused by the bacterium Bacillus anthracis, remains a persistent public health concern in Nigeria. This article delves into the multifaceted aspects of anthrax, exploring its transmission, etiology, clinical manifestations, diagnosis, management, and proposing future recommendations for effective control. Transmission of anthrax primarily occurs through contact with contaminated animal products or spores, often linked to livestock handling and consumption. The etiology section elucidates the unique characteristics of Bacillus anthracis, emphasizing its spore-forming capability, which enables survival in harsh environments and contributes to its virulence. Clinical manifestations of anthrax vary based on the route of exposure, encompassing cutaneous, inhalation, and gastrointestinal forms. Early diagnosis is essential for the right management intervention. The article discusses various diagnostic methods, including laboratory tests and imaging techniques, aiming to improve accuracy and timely intervention. Effective management of anthrax necessitates a multi-faceted approach involving antimicrobial therapy, supportive care, and preventive measures. However, the article underscores the challenges associated with limited resources, inadequate surveillance, and suboptimal healthcare infrastructure in Nigeria. These factors hinder the optimal management of anthrax cases and contribute to its persistence. Looking ahead, this article presents strategic recommendations for addressing anthrax in Nigeria's context. Enhancing public awareness campaigns, strengthening veterinary surveillance, and promoting research collaboration are highlighted as pivotal measures to mitigate the threat of anthrax. By integrating interdisciplinary efforts, health authorities can foster a comprehensive approach to anthrax prevention, diagnosis, and treatment. In conclusion, anthrax remains a formidable public health challenge in Nigeria, driven by its intricate transmission dynamics, diverse clinical presentations, and healthcare system limitations. By addressing these complexities head-on and implementing proactive measures, Nigeria can curtail the impact of anthrax, safeguarding both human and animal populations and paving the way for a healthier future.

Keywords: Anthrax; Health; Concern; Nigeria

Introduction

The meaning of the word “anthrax” can be traced back to its Greek origin, “anthrakites,” denoting a coal-like quality, which aptly captures the characteristic black eschar formation observed in cases of cutaneous anthrax manifestation. This disease, caused by the bacterium Bacillus anthracis (B. anthracis), transcends geographical boundaries as a zoonotic infection with a worldwide distribution. Possessing the dual attributes of fatality potential and heightened transmissibility, anthrax stands as a strong concern. The causative agent, B. anthracis, instills a sense of urgency due to its propensity for long periods of survival in the environment. Spores produced by this bacterium are hardy and can survive for decades in the environment. Herbivorous animals (possibly due to their grazing activity) are the natural host of the disease and all warm-blooded animals are susceptible [7].

Anthrax is a re-emerging zoonotic infection caused by gram-positive spore-forming bacteria known as Bacillus anthracis, which can be found in soil that has been contaminated [4]. This infection is characterized by its acute nature and sometimes leads to deadly outcomes. The spores of this organism exist in the soil as part of its natural habitat and are consumed by herbivorous animals, including cattle, sheep, goats, horses, and wild herbivores. Anthrax cases in Nigeria have been documented since the 1960s, with intermittent outbreaks observed across different geographical areas. The occurrence of anthrax epidemics in Nigeria has been associated with many circumstances, including the ingestion of meat that has been contaminated, direct contact with animals that are diseased, and occupational exposure within sectors such as leather tanning. The affliction impacts both human beings and livestock, hence bearing implications for the domains of public health and agriculture. On the 16th of July, a case of Anthrax was officially confirmed in Suleja, located in Niger state. The incident occurred within the premises of a mixed cattle farm. The present instance is the initial occurrence of an animal case documented in Nigeria subsequent to the commencement of the West Africa outbreak, which originated in Ghana in June 2023. On July 13, 2023, the Federal Ministry of Agriculture and Rural Development (FMARD) reported a case of unexpected livestock mortality in a specific farm. The incident involved the death of eight animals, which exhibited bleeding from exterior orifices without any evidence of blood clotting [10]. There is a suspected association between the aforementioned occurrence and the outbreak of the disease in West Africa that has been ongoing since June 2023.

The presence of anthrax in Nigeria is a matter of considerable importance in the field of public health, as it is a zoonotic disease that can be transmitted from animals to humans. Instances of Anthrax are commonly observed in rural and semi-rural environments characterized by the close coexistence of animals and humans. According to current data, the rural population of Nigeria was predicted to be approximately 46.48% in the year 2022. Nigeria is situated in the western region of the African continent and holds the distinction of being the most populous nation on the continent. Based on data provided by the Ministry of Agriculture and Rural Development in Nigeria, the livestock population in Nigeria comprises of 22,378,374 cattle, 53,061,143 sheep, 99,879,799 goats, and 9,299,563 pigs. These animals are distributed across the six Geopolitical Zones of the country and are predominantly reared by a significant number of Nigerians, particularly in rural and semi-rural areas. Livestock production holds substantial economic importance, particularly among the rural and semi-rural regions of the nation. Anthrax is recognized as one of the Neglected Zoonotic Diseases by the World Health Organization, sometimes referred to as Diseases of the poor. It often goes undetected among individuals residing in rural settlements. Anthrax poses a significant public health concern on a global scale, with a particular impact on the least developed nations. In these regions, the management of anthrax is hindered by insufficient infrastructure, limited resources, and inadequate vaccination measures.

This article seeks to examine the history, causes and transmission, clinical manifestations, and future prospects within the Nigerian context.

Brief history of anthrax

Anthrax is a highly contagious zoonotic disease that has the potential to be fatal. The transmission of anthrax can occur by inter-animal or zoonotic routes, including the transfer of the pathogen from one animal to another or from animals to humans, respectively. There is currently no confirmed evidence of transmission occurring between individuals. This sickness has been extensively documented in ancient times and holds significant historical importance. This particular ailment is widely recognized as the initial disease affecting both humans and animals that has been conclusively attributed to a microbe. The earliest record indicative of Anthrax is considered to be in the Bible (Exodus, chapters 7 to 9) which is in reference to the fifth and sixth plagues of Egypt. The emergence of written records has led to the existence of texts that claim to trace the origins of Anthrax to ancient Mesopotamia and northern Africa. There have been scholarly assertions positing that the renowned plaque of Athens, dating back to the period of 430-427 BCE, might have been an outbreak of inhalational anthrax. Anthrax has significantly influenced the field of medicine throughout its historical trajectory [1]. The discovery and practical application of bacterial vaccines were first demonstrated in the context of this particular disease. The renowned Koch's hypothesis was empirically demonstrated in 1877 using the pathogen Anthrax. Anthrax is distributed globally, with notable concentrations observed in the continents of Europe, Africa, and Asia [3].

In Europe

The 17th century witnessed a notable epidemic of anthrax in Europe, resulting in the decimation of approximately half of the sheep population and the unfortunate demise of over 60,000 individuals. Inhalational anthrax came to be recognized in Victorian England under the name "Woolsorters' disease." The reason behind this phenomenon can be attributed to the high incidence of infection among mill workers who were exposed to animal fibers that were infected with B. anthracis spores. However, it is important to note

that the term "wool sorter's disease" is somewhat misleading, as infection was found to occur more frequently due to contact with goat hair or alpaca fibres rather than wool [7].

Incidence in the USA

Between the months of October and November in the year 2001, a total of 22 instances of proven or suspected inhalational and cutaneous anthrax were documented. These cases were directly linked to the deliberate dissemination of the anthrax bacterium within the United States. In March of 2002, there was an occurrence of more cases of cutaneous illness. Prior to this time period, the United States experienced an annual average of 127 cases of Anthrax between 1916 and 1925, 44 cases between 1948 and 1957, 0.9 cases between 1978 and 1987, and 0.25 cases between 1988 and 2000 [4]. The notable decrease might be attributed to the implementation of immunization initiatives inside the nation.

Incidence in the soviet union

In 1979, an outbreak of anthrax occurred among cattle in the vicinity of a Soviet Microbiology Facility located in Sverdlovsk. As a result, a portion of the local people experienced cases of gastrointestinal anthrax following the consumption of contaminated meat, while others contracted cutaneous anthrax through direct contact with infected animals. The outbreak resulted in a total of 96 reported cases of human anthrax, with 79 instances classified as gastrointestinal, of which 64 were deadly, while the other cases were categorized as cutaneous. The aforementioned epidemic stands as the most extensive recorded occurrence of human anthrax breakout in history [8].

Incidence in Nigeria

Anthrax cases in Nigeria have been documented since the 1960s, and have been shown to manifest as periodic epidemics throughout different locations. Two cases of Anthrax were documented in Ibadan, Nigeria, over the period of June 20 to 22, 1974. The incident took place in two captives Gennets, and there were suspicions that the animals caught the disease from the meat that was provided as food for the Carnivores. Two other carnivorous animals, which were likely given the same meat, did not exhibit signs of the disease. However, the presence of Anthrax bacilli was detected in the faeces collected from adjacent cages [8].

Causes and transmission

Causative organism

Bacillus anthracis is the etiological agent responsible for the development of anthrax. The organism in question is a substantial, aerobic, Gram-positive rod, belonging to the Bacillus cereus genus of Bacilli. Mucoid colonies are observed upon cultivation on conventional blood or nutrient agar. Endospores are observed in cultures that are 2 to 3 days old. Bacillus anthracis has a lack of motility and does not induce hemolysis when cultured on blood agar. In an in-vitro environment, the organism persists either as a single entity or in short chains, whereas it tends to form longer chains in-vivo. The organism is capable of generating spores that exhibit resilience against various environmental variables. The spores of this organism are found in the soil and are naturally consumed by herbivorous animals, including cattle, sheep, goats, horses, and wild herbivores. The significance of the disease is heightened due to its potential as a bioterrorism threat [7].

Pathogenicity

Bacillus anthracis possesses two prominent virulence factors, both of which are encoded on distinct plasmids. Plasmid X01 encodes three distinct proteins, namely protective antigen (PA), edema factor (EF), and lethal factor (LF), which collectively constitute two exotoxins. Phosphatidic acid (PA) serves as the pivotal constituent in the composition of both poisons. The binding of PA to receptors on target cells facilitates the cellular uptake of EF and LF. The combination of protective antigen (PA) and edema factor (EF) constitutes the formation of edema toxin, while the combination of PA and lethal factor (LF) results in the creation of lethal toxin. The action of edema toxin results in the depletion of chloride ions and water from the cell, leading to the development of extensive edema in the surrounding tissue. The secondary function of edema toxin involves the inhibition of phagocytic and oxidative burst activities in neutrophils. LF is classified as a zinc metalloprotease. The phenomenon leads to heightened production of tumor necrosis factor (TNF) and interleukin-1 (IL-1) among macrophages. As a result, it induces macrophage lysis, leading to the release of inflammatory mediators. The primary factor leading to mortality in both animals and humans infected with the lethal toxin is the release of TNF and IL-1 [8].

Transmission

Anthrax is an acute bacterial disease caused by the pathogen Bacillus anthracis, which is derived from animals. The portal of entry is either through skin abrasions, inhalation, or ingestion. Therefore, three distinct manifestations of the disease can be observed: cutaneous, respiratory, and gastrointestinal, with the cutaneous type being the most prevalent. The cutaneous manifestation of anthrax initially presents as a painful skin ulcer. Subsequently, the ulcer undergoes healing, resulting in the formation of a dark, coal-black plug known as an eschar. This particular term, "anthrax," originates from the Greek word for coal. If left untreated with antibiotics, cutaneous anthrax has the potential to develop into sys-

temic illness in around 10 percent of patients. The respiratory manifestation first presents as an upper respiratory tract infection and rapidly progresses to septicaemia and toxic shock syndrome. The gastrointestinal manifestation typically presents with severe abdominal discomfort and bloody diarrhoea. Septicaemia, also known as blood infection, is the primary cause of death across various contexts, while meningitis is a less frequent cause. The fatality rate of the respiratory and gastrointestinal manifestations of the disease is notably high. Anthrax is a pathological condition that affects herbivorous animals who come into contact with or inhale spores of the bacterium Bacillus anthracis during their feeding activities. Animals who are in the terminal stages of illness have been observed to release bacilli through their blood and bodily fluids [3].

When the bacilli are exposed to the external environment, they generate resilient spores, which serve as a survival mechanism for the agent and can maintain their activity for extended durations. The primary mode of transmission for cutaneous disease in humans is by exposure to animal hides or other materials that contain spores, inhalation of strongly contaminated air carrying spores, or consumption of goods that have been contaminated. Anthrax mostly affects individuals employed in the agricultural sector and poses a significant occupational risk to those working in the tanning industry. Interventions aimed at combating anthrax encompass a spectrum of approaches, spanning from preventative measures such as operator education and dust control, to therapeutic interventions involving the administration of penicillin, disinfection protocols, and the isolation of individuals suspected of being afflicted with the disease [3].

Clinical manifestation

Anthrax has been found to exhibit four distinct clinical symptoms, namely cutaneous, inhalational, gastrointestinal, and injectional. The majority of anthrax cases, namely 95%, are classified as cutaneous. These incidents are primarily concentrated in regions such as Africa, Asia, and Eastern Europe, where there are insufficient animal and worker immunization measures in place. The global annual incidence of incidents is estimated to be around 2,000. During the anthrax outbreak in the United States in 2001, it was observed that cutaneous anthrax constituted 11 out of the total 22 reported cases. Spontaneous resolution is a common occurrence in cases of cutaneous anthrax, with the death rate for untreated infections reported to range from 5% to 20% [7]. Cutaneous anthrax occurs when spores are introduced into the body through openings in the skin that are exposed to the environment. The spores undergo germination within macrophages either locally or in nearby lymph nodes, leading to the release of vegetative forms. The duration of the incubation period ranges from one to twelve days. The primary cutaneous lesion is characterized by a lack of discomfort or itching and presents as a papule accompanied by a significant degree of swelling, eventually developing into a vesicular structure of 1-2 cm in size. The presence of fever and regional lymphadenopathy may manifest. Subsequently, the vesicle undergoes rupture, leading to the formation of an ulcer accompanied by a black eschar, which eventually detaches within a period of 2 to 3 weeks. The presence of purulence is exclusively observed in cases of secondary nonanthrax infection. The presence of edema in conjunction with an infection in the face or neck region might potentially lead to a compromised airway [8].

Gastrointestinal anthrax

Gastrointestinal anthrax is commonly associated with the consumption of meat that has been contaminated with spores. While gastrointestinal anthrax is not frequently observed, its true prevalence may be underestimated as a result of the infection's non-specific symptoms. The estimated death rate ranges from 25% to 60%. While the precise rate of related shock remains unknown, available case reports indicate that severe patients often exhibit complications involving shock [8].

Inhalational anthrax

Inhalational anthrax is the result of the inhalation and subsequent deposition of spores with a diameter of less than 5 mm within the alveoli. The spores undergo phagocytosis by macrophages and are subsequently transported to nearby mediastinal lymph nodes, where they undergo germination into vegetative forms. This process involves replication and the subsequent production of hemorrhagic mediastinitis. If inadequately managed, the presence of bacteremia and toxemia can lead to the development of meningitis, gastrointestinal complications, and refractory shock. While inhalational anthrax is typically not classified as an airborne illness, histological examination during postmortem examinations occasionally reveals localized pneumonia, potentially indicating the initial point of germ penetration [7,8].

Injectional anthrax

In the year 2001, a case was reported in Norway where an individual who used heroin had a soft tissue infection caused by anthrax subsequent to a subcutaneous administration of the substance. The infection was further aggravated by the occurrence of septic shock, meningitis, and ultimately resulted in mortality despite the administration of medication. On the other hand, injectional anthrax refers to the administration of a higher concentration of bacterial inoculum to a more profound anatomical location. Prominent tissue edema, extensive capillary bleeding, and necrosis

of the superficial adipose tissue have been observed after surgical investigation of wounds in cases with injectional anthrax [8].

Diagnosis

The initial observation of Bacillus anthracis rods by microscopic examination occurred in 1838, when Professor M. Delafond, a veterinarian, noted the presence of "small rods" in the blood of animals afflicted with Anthrax. Three additional scientists independently documented the identical observation during the subsequent twenty years; yet, the importance of this observation remained unknown at that time [1]. The possibility of cutaneous anthrax should be taken into account when a painless, pruritic papule emerges, progresses into a vesicle, and afterwards exhibits a black eschar. The confirmation of the diagnosis should be conducted by the utilization of Gram's stain or the culture of vesicular fluid. The administration of antibiotics before samples are taken for diagnosis promptly renders the infected site as having negative culture results. The utilization of a biopsy material obtained from the periphery of the lesion, followed by its examination by techniques such as Gram's stain, immunohistology, and PCR testing, could potentially offer valuable insights subsequent to the initiation of antibiotic therapy.

The identification of inhalational anthrax poses challenges, particularly in instances where there is no documented exposure to an aerosol containing B anthracis. During the initial phase, the symptoms of inhalational anthrax exhibit a lack of specificity. The diagnosis can be simply established through the cultivation of blood and pleural effusions in patients that have not been treated. PCR tests of blood and pleural fluid, as well as immunohistochemistry study of pleural fluid or transbronchial biopsy specimens, may provide valuable assistance in cases that have been previously managed with antibiotics. Due to the atypical nature of primary pneumonia, sputum exams do not contribute significantly to the diagnostic process. When conducting a radiographic differential diagnosis, it is important to include histoplasmosis, sarcoidosis, TB, and lymphoma as potential conditions. Computed tomography (CT) of the chest can be utilized to identify mediastinal hemorrhagic lymphadenopathy and edema, peribronchial thickening, as well as pleural effusions. The diagnosis of gastrointestinal anthrax poses challenges due to its infrequency and resemblance to other prevalent and severe gastrointestinal disorders. The diagnosis can be inferred from an epidemiological analysis of the historical consumption of contaminated meat. Microbiological cultures are not considered confirmatory for diagnosis, unless there is evidence of bacteremia [4].

Management

Prevention

The occurrence of Anthrax in captive carnivores in 1974 was speculated to be linked to the consumption of beef provided to the Gennets [5]. It is imperative to completely refrain from the consumption of animals that are unwell or have been discovered deceased. It is imperative to implement stringent protocols within abattoirs to mitigate the occurrence of slaughtering diseased animals or distributing unfit meat to the general population. The hides and skins of animals are regarded as delicacies in certain regions of Nigeria. Occasionally, these hides and skins are obtained from deceased animals.

Treatment

Bacillus anthracis has susceptibility to various antimicrobial agents, including penicillin, fluoroquinolones, ampicillin, erythromycin, clarithromycin, doxycycline, chloramphenicol, streptomycin, first-generation cephalosporin, vancomycin, clindamycin, and imipenem. Ciprofloxacin and other quinolones, including ofloxacin, levofloxacin, gatifloxacin, and moxifloxacin, demonstrate comparable efficacy in both the therapeutic and prophylactic management of anthrax [10]. The pathogen exhibits resistance to third-generation cephalosporin and trimethoprim-sulfamethoxazole. It is imperative to do antimicrobial susceptibility testing for all cases in order to appropriately tailor therapy. The treatment of anthrax has also involved the administration of a combination therapy consisting of antibodies targeting the protective antigen (PA) of Bacillus anthracis, together with ciprofloxacin.

Vaccination

Vaccine development history

It is noteworthy to acknowledge that the Anthrax disease has performed a significant influence in the advancement of vaccine discovery within the field of medical science. The inception of vaccine development may be traced back to the 1870s, a period during which Robert Koch successfully cultured B anthracis and made significant strides in elucidating the microbiological aetiology of infectious diseases. In the year 1881, Pasteur and Greenfield, working separately, achieved the attenuation of B anthracis and subsequently formulated efficacious vaccinations for animals.

Vaccines targeting the bacillus were successfully produced for human use during the period spanning the 1950s and 1960s. Currently, there are three commercially available vaccines, namely the Georgian/Russian, UK, and USA vaccines. It is widely believed that these vaccinations function by eliciting an immune response

against the antigens PA, LF, and EF. Anthrax vaccines have the capability to be administered through either the aerosol or cutaneous (skin) route. The latter procedure involves the removal of a fragment of the outermost layer of the skin, known as scarification, in order to facilitate the absorption of the vaccination. The comparative efficiency of vaccines has not been adequately studied due to variations in the situations under which they have been administered [6].

In the United Kingdom, vaccination is advised exclusively for individuals employed in occupations that entail a potential risk of anthrax exposure, such as employees working in tanneries engaged in the processing of wool, skins, and bone materials. In recent times, the administration of vaccinations to military personnel and essential workers has been carried out either mandatorily, as seen in the United States, or on a voluntary basis, as practised in the United Kingdom. The administration of the vaccine involves the application of four injections, each containing a volume of 0.5 ml. The intervals between the first three injections are three weeks, while the interval between the third and fourth injection is six months. An annual administration of a booster dose is recommended [6].

Prospects of readiness and concluding remarks

While anthrax infection is prevalent in West Africa, there is a significant risk of widespread outbreaks, whether they are associated with bioterrorism or the use of injectable drugs, or the consumption of contaminated meat. Its infrequency and nonspecific early symptomatology suggest that, in the event of an outbreak, many patients may present with advanced disease, which has proven difficult to treat. It is recommended that those in occupations such as veterinarians, agricultural workers, and laboratory employees who are exposed to potentially infected animals or work with B anthracis should receive vaccination. It is advisable to administer regular anthrax vaccinations to individuals employed in industrial settings where there is a likelihood of handling animal goods that may be contaminated with anthrax. These products include wool, goat hair, hides, and bones that are imported from countries where cases of animal anthrax are still prevalent. The aforementioned countries are predominantly located in the continents of Asia and Africa, with occasional inclusion of nations from South America or the Caribbean.

Implementing an effective vaccination strategy, similar to those successfully employed in the United States and the United Kingdom, holds the potential to mitigate the occurrence of additional epidemics and mitigate the profound consequences thereof. According to the research, there was a significant decrease in the average number of cases annually in 2001 when compared to preceding years, following the implementation of vaccination initiatives. Implementing measures to ensure compliance among individuals who are at a heightened risk of being exposed to Anthrax is a strategy aimed at maintaining Nigeria's Anthrax-free status.

It is imperative to further elucidate the mechanisms that underlie the progression of anthrax in its later stages, as well as to devise comprehensive management techniques that can be implemented on a wide scale.

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