Clinical Presentations of Human Anthrax

Subjects: Infectious Diseases

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Anthrax is one of the most important zoonotic diseases which primarily infects herbivores and occasionally humans. The etiological agent is *Bacillus anthracis* which is a Gram-positive, aerobic, spore-forming, nonmotile, rod-shaped bacillus. The spores are resistant to environmental conditions and remain viable for a long time in contaminated soil, which is the main reservoir for wild and domestic mammals. Infections still occur in low-income countries where they cause suffering and economic hardship. Humans are infected by contact with ill or dead animals, contaminated animal products, directly exposed to the spores in the environment or spores released as a consequence of a bioterrorist event. Three classical clinical forms of the disease, cutaneous, gastrointestinal and inhalation, are seen, all of which can potentially lead to sepsis or meningitis.

anthrax epidemiology clinical features

1. Introduction

Anthrax is an ancient zoonotic disease which primarily infects herbivores with humans occasionally being infected. While naturally occurring, it remains a health problem in low- and middle-income countries; its potential misuse as a biological weapon puts all communities at risk [1][2][3][4][5]. Although the human form of the disease is rarely seen in western countries, human cases have been reported. The most notable being the anthrax postal attack in the United States of America in 2001 [6], and the outbreak of injectional anthrax associated with spore-contaminated heroin in 2009–2010 [7].

The causative agent of anthrax is a bacteria called *Bacillus anthracis*, which belongs to the genus Bacillus. The organism infects herbivores through contact with contaminated soils and/or water. Humans become infected through contact with ill or dead animals and their contaminated products. *B. anthracis* is an aerobic, Gram-positive, spore-forming, non-motile, rod-shaped bacillus. The bacteria are easily grown at 37 °C on blood or nutrient agar. The organism exists in two physical forms, the biologically active vegetative form and the biologically inert spore form. It is the vegetative form which is seen in the tissue of infected individuals and is responsible for the pathology associated with the disease. As the animal succumbs to infection the vegetative form converts into inert, resistant spores which provide a lifeboat for the organism until it is able to infect a new host. The relative resistance of *B. anthracis* spores to environmental conditions such as drought, heat, rain, cold, radiation and disinfectants is one of the reasons why this organism has been be explored as a potential biowarfare agent [1][8]. **Figure 1** summarizes the natural life cycle of *B. anthracis*.

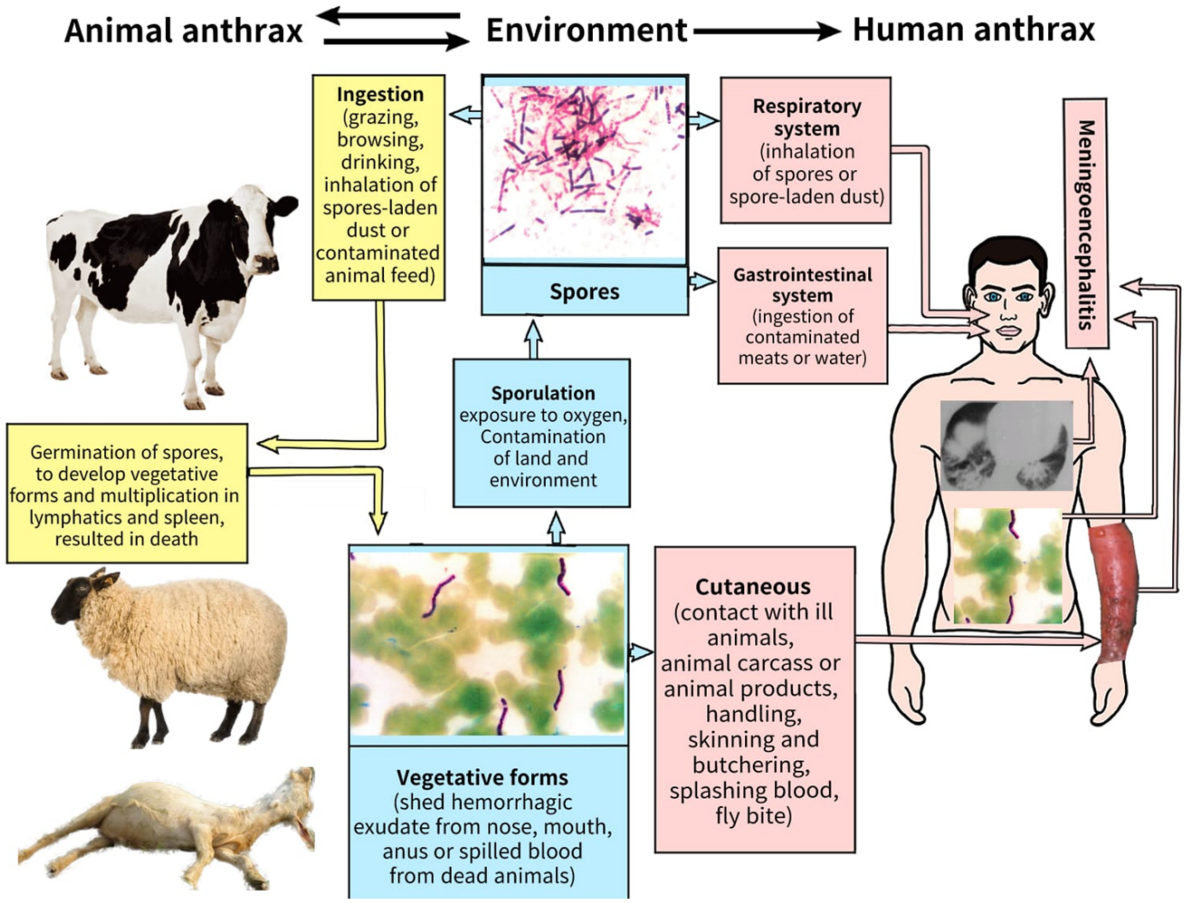

Figure 1. The life cycle of *Bacillus anthracis* in nature. Soil is the main reservoir of the pathogen and is contaminated by spores released from the carcasses of infected animals. Animals grazing on spore-contaminated land become infected resulting in a new cycle of infection, death and release of spores which can potentially contaminate a new location. Wild carnivores and scavenger birds and flies may also contribute to the spread of spores. Humans can be infected by contact with infected animals or contaminated animal products. The figure was created by Fatma Beyzanur Koyuncu, Medical student in Lokman Hekim University, Ankara).

The two principal virulence factors of *B. anthracis* are tripartite toxin and an antiphagocytic polypeptide capsule, the genes for which are carried on two plasmids designated as pX01 (182 kb) and pX02 (95 kb), respectively. Loss of either of these plasmids reduces the virulence of the organism. The tripartite toxin comprises protective antigen (PA), lethal factor (LF) and edema factor (EF). The role of PA is to transport LF and EF inside target cells where they interact with essential cellular pathways. The toxins are secreted the during multiplication of the vegetative *B. anthracis* and are responsible for the characteristic symptoms of anthrax [1][8][9].

2. Clinical Presentations

Naturally occurring anthrax is seen in one of three classical clinical forms: cutaneous, gastrointestinal and inhalational. The severity of infection depends on the innate and specific immunity of the patient, virulence and the number of infecting bacteria [1][8][9]. The majority of cases (>95%) are cutaneous in nature, with a mortality rate of

less than 3–5% due to the availability of effective antibiotics [8][10][11]. As rare complications, sepsis and meningoencephalitis can develop due to spread from the primary lesion [1][7][8][10][12]. The incidence of the other forms of infection is noted as 12% for inhalation anthrax, 5% for gastrointestinal anthrax and 4% for primary meningitis. Injectional anthrax is a newly described clinical form reported in heroin users as a consequence of injecting spore-contaminated heroin with a mortality of 9–33% [7][11].

2.1. Cutaneous Anthrax

The incubation period is between 2–7 days (range 1–19 days) with the majority of the lesions occurring on exposed areas of the body such as the hands, arms, face and neck. A lesion begins as a pruritic papule and typically progresses to a ring of vesicles surrounded by erythema and edema within 2–4 days (**Figure 2**). Some lesions may be severe and extended for some distance (**Figure 3**). Extensive edema and toxemia can be seen in cases where the lesions occur on the face and neck (**Figure 4**). The formation of the eschar its subsequent resolution can take 2–6 weeks, regardless of treatment [1][8][13][14].

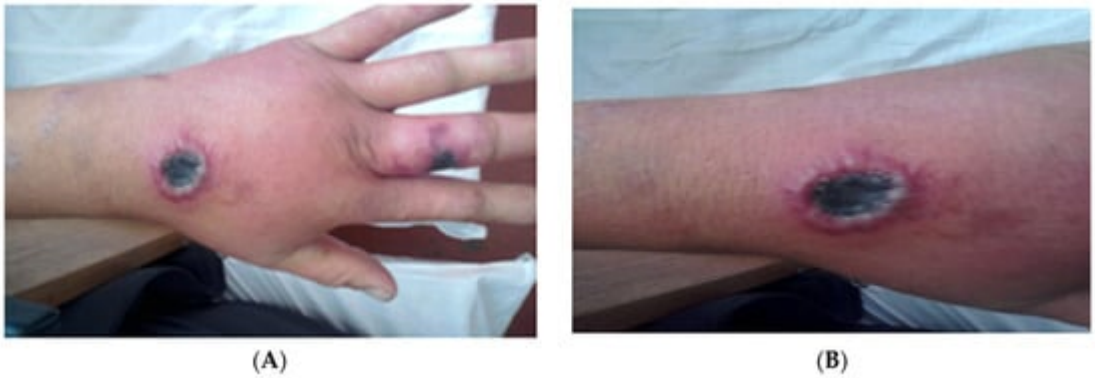

Figure 2. Typical lesions of cutaneous anthrax on the hand (**A**) and leg (anterior side) (**B**). The lesions are characterized by a central eschar with a ring of vesicles and surrounding edema that is characteristically painless. (Images supplied by Professor Ainura Kutmanova, and Dr. Saparbai Zholdoshev).

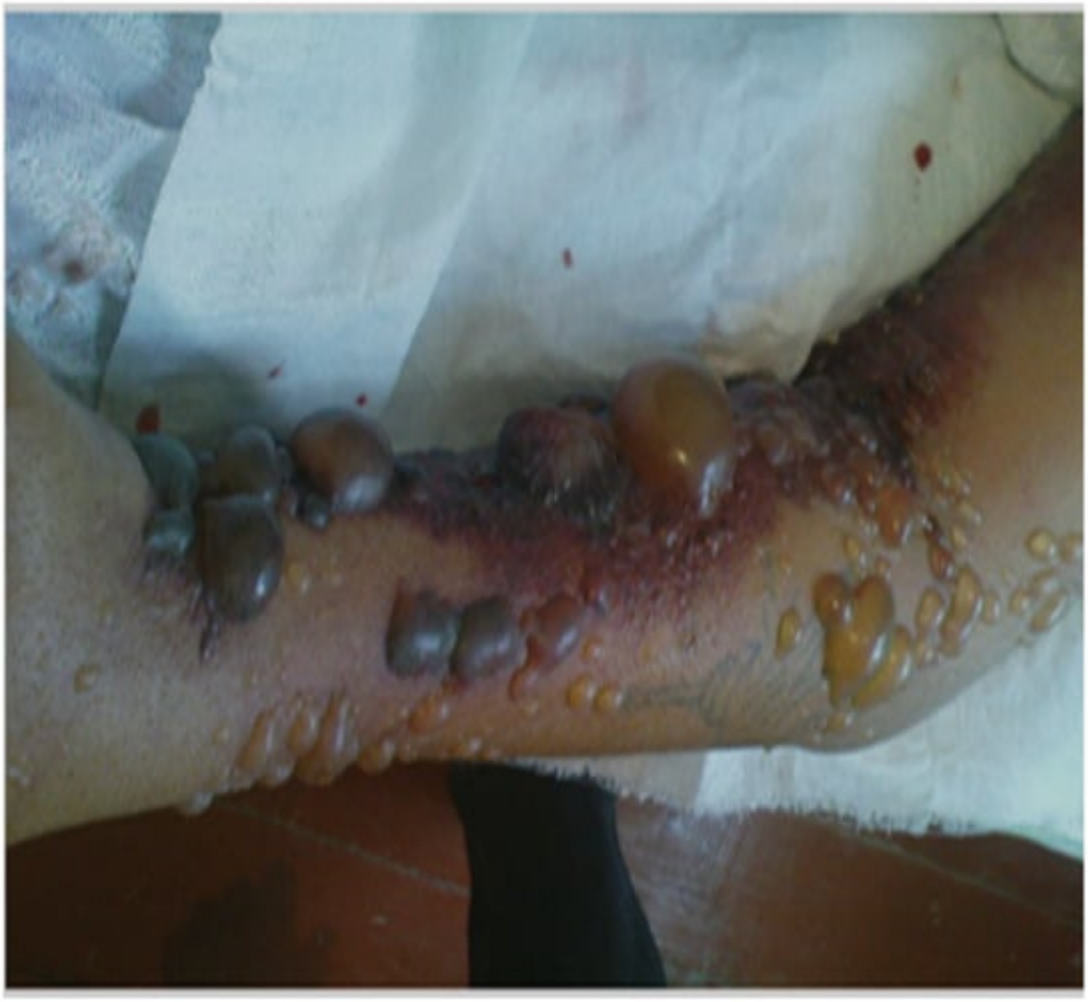

Figure 3. Typical appearance of a severe form of cutaneous anthrax lesions on the arm. Extensive erythema and oedema as well as hemorrhagic bullae can be seen (Image supplied by Professor Ainura Kutmanova and Dr. Saparbai Zholdoshev).

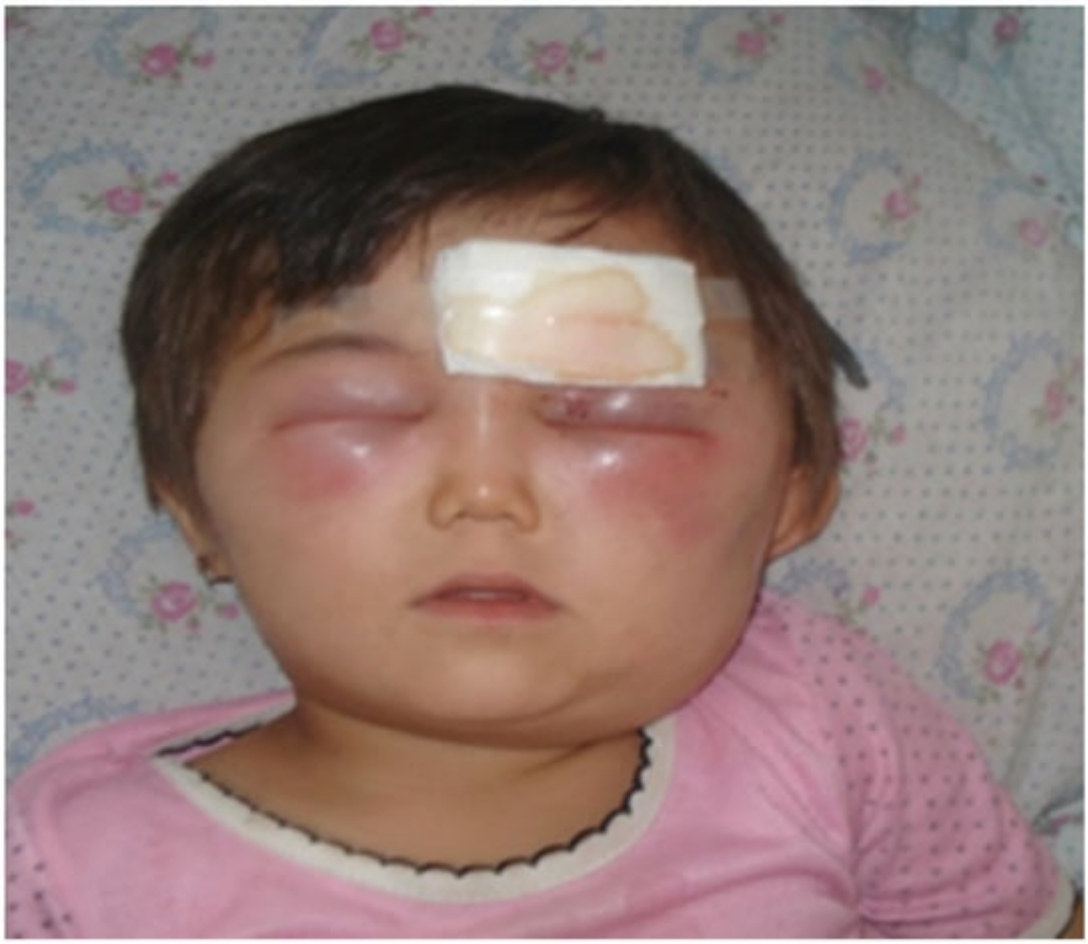

Figure 4. A severe form of cutaneous anthrax on the face. Extensive erythema and oedema can be seen (Image supplied by Professor Ainura Kutmanova and Dr. Saparbai Zholdoshev).

The differential diagnosis of cutaneous anthrax should consider staphylococcal and streptococcal skin and lymph node infections, erysipelas, orf, syphilitic chancre, cutaneous tuberculosis, ecthyma gangrenosum, ulceroglandular tularemia, plague, glanders, rickettsial infection and rat-bite fever [1][8][10][13].

2.2. Gastrointestinal Anthrax

The infection occurs within 3–7 days following the ingestion of *B. anthracis* within contaminated food or drinks. Lesions can be seen any point along the gastrointestinal tract. Two clinical forms are described in the literature: oropharyngeal and gastrointestinal [1][8][11][12].

The clinical features of oropharyngeal anthrax are fever, sore throat, dysphagia, hoarseness, painful regional lymphadenopathy, soft tissue edema and swelling in the neck. Streptococcal pharyngitis and tonsillitis, parapharyngeal abscess, Vincent angina, Ludwig angina, diphtheria and deep tissue infection as potential causes can be eliminated by the isolation of *B. anthracis* from the lesions [8][15][16].

The initial symptoms of intestinal anthrax include fever, nausea, vomiting, anorexia and diarrhea. As the infection progresses, symptoms include acute abdominal pain, hematemesis, bloody diarrhea and massive ascites followed by toxemia and shock which results in death. The lesions occur most commonly on the wall of the terminal ileum or cecum. The diagnosis should be confirmed by the isolation of *B. anthracis* from blood, ascites and the lesions [1][8][17][18].

2.3. Inhalation Anthrax

Although rare, this clinical form is mostly seen as a consequence of industrial exposure or an intentional release. The mortality is recorded at over 80% despite treatment. Following an incubation period of 1–7 days, nonspecific initial symptoms including mild fever, fatigue, malaise, myalgia, nonproductive cough and some chest or abdominal pain are seen. The disease progresses to the severe phase which is characterized by high fever, toxemia, dyspnea and cyanosis. Widening of the mediastinum is described as a typical finding of inhalation anthrax. Pleural effusion and parenchymal infiltrations can also be seen. Hypothermia and shock develop and ultimately result in death. Meningitis may develop as a complication in up to half of patients. Inhalation anthrax mimics community-acquired pneumonia and many diseases involving the pulmonary system [1][8][11].

2.4. Injectional Anthrax

This refers to a new clinical form of anthrax in which soft tissue is infected at the injectional site and leads to toxemia and sepsis. Gas gangrene, necrotizing soft tissue infections and severe cellulitis should be discounted [8][11][12].

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