Acinetobacterlwoffii Induced Cellulitis with Allergy-like Symptoms

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Citation

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Abstract

Few reports document the misdiagnosis of Acinetobacterlwoffii skin infections for allergic reactions. In addition, A. lwoffii is frequently misidentified when applying conventional diagnostic methods. The bacterium has been reported to cause a multitude of diseases including skin and wound infections. The application of the newly established method “The Universal Method” allowed definite identification of the bacterium isolated from a leg and foot cellulitis case (Isolate QUBC mk1) that was misdiagnosed as an allergic reaction and was treated with intramuscular injections of diclofeneac sodium, anonsteroidal anti-inflammatory drug.The isolate was identified as A. lwoffii, it failed to grow on MacConkey agar, and it was sensitive to ciprofloxacin but resistant to cefazolin. The 51-year old male patient was successfully treated with intravenous administration of ciprofloxacin, doxacillin, and cefazolin. He was released in good health after ten days.This work emphasizes the importance of distinguishing between skin infections and allergies. It also stresses the importance of prompt and accurate identification of A. Lwoffii and its possible relationship to allergic reactions. Misdiagnosis isdiscussed in the context of “The Hygiene Hypothesis”.

INTRODUCTION

Efficient therapyrelies on accurate and prompt diagnosis of a disease. Misdiagnosis is a major cause of delaying therapy; serious complications to the patient may arise. Misdiagnosis is increased when different diseases share common and confusing symptoms. Our observation is that some infectious diseases mimic allergic reactions and are wrongfully treated with anti-inflammatory drugs only. Prolonged treatments or exposure to these drugs may increase the risk for heart attack or stroke[1,2]. Unfortunately, these cases fall under malpractice and are not reported in a scientific context. A large number of medical malpractice cases are due to misdiagnosis or delayed diagnosis[3].Therefore, it is difficult to draw a clear diagnostic picture of the similarities between allergy and certain infections, especially those caused by Acinetobacterlwoffi and related bacteria. A.lwoffii (formerly A.calcoaceticusvar. lwoffii) has been confused for other bacteria when using classical identification methods[4]. One study using an automated 26 system, identified ten Bordetellaholmesii isolates that were misidentified as A.lwoffii [5,6]. It has been reported that identification of A. lwoffii is problematic when applying the rapidNFT-API system which results in misidentification of certain Acinetobacterspp [7].The bacterium can be confused with other pathogens (Moraxella, Mimeae, and Bordetellaholmesii). Acinetobacter spp. belong to Neisseriaceae, they are oxidase-negative, non-motile bacteria which appear as paired Gram-negative coccobacilli. Clinically, skin infections caused by Acinitobacter spp. may be confused with allergic reactions as documented and are mistreated with anti-inflammatory drugs[8,9]. A. baumannii has been related to the modulation of the immune and cytokine responses through suppression of local Th2 response by modulating airway eosinophilia in a mouse model of allergic asthma[10].

Recent reports consider A. lwoffi to be a serious nosocomial, drug resistant, and opportunistic pathogen especially in immune compromised individuals and prosthetic valve endocarditis[6,11]. In a mouse model for gastritis, A. lwoffii induced gastritis is similar to that induced by Helicobacter pylori [12]. Healthy people harbor A. lwoffii as a commensal of skin, hands, and other sites. Some of the twenty five Acinetobacterspp. including A. lwoffii,has been reported to survive up to 21 days on dry surfaces whileA. Baumannii may survive up to 32 days.Intensive care units (ICUs) may represent high risk for Acinetobacter nosocomial infections; they include bacteremia, pneumonia, meningitis, peritonitis, endocardits, urinary tract infections, burns, and wound infection. The bacteria are ubiquitous in the environment as well[5,13-15].A. baumanni and A. lwoffii shared 96% homology

of their 16S rDNA[8].

Bacteria will continue to cause unusual infections as they seize rare opportunities. As host's internal or external environment changes creating new niches that may become colonized with opportunistic bacteria. For example, prosthetic organ implants such as heart valves and other indwelling parts such as central vascular catheter-associated bacterial infections. Diagnostic laboratories must be able to identify these opportunistic bacteria[16]. Acinetobacter spp. associated with surgical wound infections constitutes 6.2% (42/676) of which A.lwoffii contributes 2.8%(19/676)[17]. Another opportunity for infection is presented when cervical cancer is visually inspected after the application of 5% acetic acid to the cervix[18].Other reports showed that A. lwoffii had contributed 8.8% of all 690 Acinetobacter infections, ranking only second to A. baumannii (78%)[19].Viable A. lwoffii and other species were shown in the feces of experimentally infected body louse, whereas a louse strain ofA. Baumanni killed the louse within 3 day[20]. A. lwoffii may infect and cause swelling around the eye of normal healthy individuals, such infection may be confused with allergic reactions[9].

In this work we present evidence connecting misdiagnosis of A. lwoffi skin infection to allergic reaction, we hope this work will draw attention to considering infectious agents when allergies are suspected. This work focused on the need for prompt and accurate diagnosis of bacterial infections using "The Universal Method".

MATERIALS AND METHODS

Case Description: A 51-year-old man presented with no history of trauma, insect bite, or illness including diabetes. He was admitted to Saint Joseph Hospital with complaints of right leg and foot pain that has started 4 days earlier. Two days earlier, he was treated in a private clinic with intramuscular injection of diclofenac sodium (a nonsteroidal anti-inflammatory drug) with no improvement. As a result, a home-made remedy was applied; the patient wrapped his leg with a towel soaked in vinegar for more than 30 min, his leg and foot became worst. On admission (5 th day of initial diagnosis as allergy), he was afebrile, and his physical signs were good. Leg and foot showed redness, swelling, warmth, tenderness, postural rash, and ulcerative infection. He was diagnosed with lower extremity cellulitis and second degree burn. A swab sample was obtained from the infected ulcer for bacterial culture. The patient was started on intravenous ciprofloxacin, doxacillin, and cefazolin in addition to aseptic daily dressing. The patient was discharged in good health after ten days of treatment and care.

Bacterial Culture: A bacterial swab was cultured aerobically and anaerobically at 37˚Con chocolate agar supplemented with isovital X,blood, and MacConkey agar plates.

Bacterial Identification: The isolated bacterium was Gram stained, tested for catalase, and antibiotic susceptibility. Identification was attempted with API system (Biomatrix.Inc., France) which failed to produce a definite identification.

The Universal Method: The Universal Method for bacterial identificationwas applied to DNA extracted from the isolated bacterium[21]. Briefly, bacteria were collected from three colonies, lysed with alkaline-SDS, boiled for 10 min and diluted with sterile water and cleared by centrifugation. The supernatant was used in PCR reactions with the golden primer mixtures G5, G11, and G7 to amplify part of the 16S rRNA gene. One amplicon was sequenced then BLAST analyzed as described[21].

RESULTS

Misdiagnosis: As a result of mistaking skin infection for an allergic reaction, the 51-year old patient was treated with diclofenac for two days, since the infection did not respond to the antinflammatory drug treatment, the patient resorted to home remedy treatment; he applied bandages soaked in vinegar to the affected area which probably aggravated the infection and delayed therapy for two additional days until proper diagnosis was done after his admission to Saint Joseph Hospital.

Pathogen Isolation and Identification: Swabs collected from the infected skin showed s mall grey colonies on both chocolate and blood agar but not on MacConkey agar plates. Gram staining reviled Gram negative coccobacilli that could not be identified by the API 20 system (Biomatrix. Inc., France). The bacterium was sensitive to ciprofloxacin but resistant to cefazolin. Accordingly, The Universal Method was applied;several 16S segments were amplified including a720 bp PCR-amplicon obtained with G7 (primers QUGP Fn3 and QUGP Rn1). The 720bp amplicon was sequenced and analyzed using online-nucleotide alignment (BLAST). Alignment showed 99% homology to AcinetobacterlwoffiiFig.1&2. The identification was consistent with the fact that A. lwoffii is catalase positive, a commensal of human skin, oropharynx, and urinary mucosa[6]. It is also consistent with the fact that someA.

Lwoffii cannot grow on MacConkey agar. According toPanagopoulos et al. [6], three strains withlimited growth onMacConkey agar could neither be identifiedby routine laboratory testing nor by API 20E and API 20NE systems[3]. However, Gram-negative Vitek2 automated system (bioMerieuxInc) identified 49 A.lwoffii with 99% probability[6]. The inability of some A.lwoffii to grow on MacConkey agar (including this isolate QUBC mk1) hinders its identification. Unlike the API-20E and 20NE systems, The Universal Method was not affected by this anomaly.

Figure 1

Figure 1.Agarose gel (1.2%) with amplified 16S segments obtained with The Universal Method. The 700bp band (arrow) was purified and subjected to nucleotide sequencing (Bethlehem University).

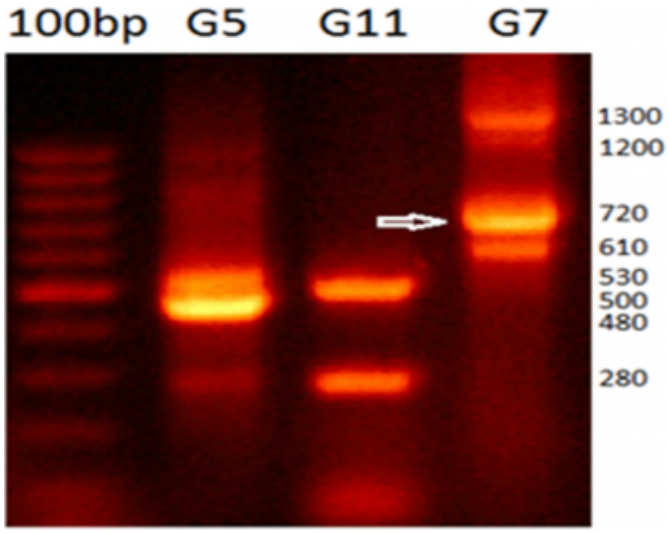
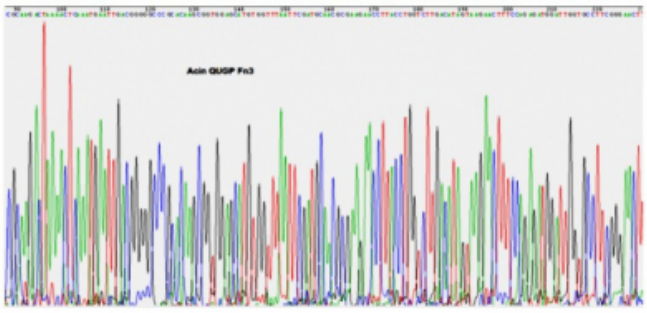


Figure 2

Figure 2: A part of the nucleotide sequence (16S gene) that was obtained with QUGP Fn3 primer, it was analyzed with BLAST which showed 99% homology to . Similar results were obtained when the amplicon was sequenced with the reverse primer (QUGP Rn1).



DISCUSSION

According to the “Hygiene Hypothesis”; the lack of early exposure to infectious and symbiotic microorganisms such as gut flora or probiotics increases susceptibility to allergic diseases by suppressing natural development of the immune system. Alternatively,a number of epidemiological studies show that exposure to farming environment during early childhood, strongly quellsthe development of allergic reactions later in life.Exposureto A. lwoffii may be an important factor in this hygiene hypothesis[23,24].

Debarry et al. [6] showed that A. lwoffi or LPS derived from A. lwoffi or Salmonella enteric can modulate human dendritic cell function leading to the proliferation of T_H1, offering possible role in protection against allergies according to the Hygiene Hypothesis, whereas LPS from Escherichia coli does not promote protection[24].

The diagnosis of skin cellulitis caused by A.lwoffii or other species, which are confused for allergic reactions leading to administering anti-inflammatory drugs to the patient.Such misdiagnosis results in delaying treatment with antibiotics for several days. In this report, diclofenac sodium (a nonsteroidal anti-inflammatory drug) was prescribed to the patientcausing a four-day delay in proper treatment and putting the patient at risk.

Therefore, it is important to keep in mind that A. lwoffi skin infections may look like an allergic reaction and should be subjected to microbial testing, sample culturing, antibiotic profiling, and pathogen identification.

For a robust, accurate, quick, inexpensive, and timeless method for the detection and identification of any bacterium, The Universal Method has been established.[21] The method proved its usefulness in this study, it was also useful in the detection and identification of bacteria from cerebrospinal fluid (CSF) taken from potential bacterial meningitis cases[22].

Skin and other infections that may appear similar to allergic reactions have been shown to be caused by bacterial infections some of which are caused by A. lwoffii and may be under reported, it may be a major cause of skin infections. Such infections may result frommicro-scratches, cuts, pulled hair, or traumas that most patients fail to remember especially as symptoms of infection are delayed for more than two days. These infections appear to be misdiagnosed as allergic reactions[8,9]. Since A. lwoffii is a member of the normal flora of the skin and is difficult to identify, in addition some strains do not grow on MacConkey agar (A.

lwoffiiQIUBCmk1), they may escape diagnosis and reporting. More efforts need to be focused on considering A. lwoffii when diagnosing skin infections, especially those appearing as diffused, afebrile, and similar to an allergic reaction in either immunocompetentorimmunocompromised individuals.

Early serotyping studies of A. calcoaceticus has shown the diversity of this complex which has been re-classified into the current Acinetobacter spp. It may be useful to correlate the described serotypesto current Acinetobacter spp. and to evaluate the serotyping approach in screening of Acinetobacter infections[15].

The application of"The Universal Method" topure bacterial sample allows identification based on 16S sequencing[21]. It is recommended that the Universal Method be applied for the accurate detection and identification of bacterial pathogens. It will also assist in monitoring emerging infectious diseases. We recommend that "The Universal Method" be applied for routine bacterial identification. The unambiguous identification of A. lwoffii illustrated in this study, emphasizes the importance of accurate pathogen identification as well as time, cost, and effort savings.

Based on the literature and the presented work regarding nosocomial infections, we recommend that efforts be made tosanitize hospital facilities. Ultra Violet, air filtration, and/or other means should be installed in hospital facilities to sanitize air and rooms; especially when closed or partially closed air circulation systems with poor fresh air aeration are utilized.

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