Clinical Characteristics of Actinomyces viscosus Bacteremia

Yi-Chun Hsiao 1,†, Yi-Hsuan Lee 2,†, Chun-Mei Ho 1, Chien-Hao Tseng 1 and Jui-Hsing Wang 3,4*

1 Department of Internal Medicine, Division of Infectious Diseases, Taichung Veterans General Hospital, Taichung 40705, Taiwan; hetairoiyig@gmail.com (Y.-C.H.); wenily@vghtc.gov.tw (C.-M.H.); tedi3tedi3@vghtc.gov.tw (C.-H.T.)
2 Department of Post-Baccalaureate Veterinary Medicine, Asia University, Taichung 41354, Taiwan; joyce0936@gmail.com
3 Department of Internal Medicine, Division of Infectious Disease, Taichung Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Taichung 40705, Taiwan
4 Department of Internal Medicine, School of Medicine, Buddhist Tzu Chi Medical Foundation Taichung Tzu Chi Hospital, Taichung 427213, Taiwan
* Correspondence: liujohnson518@gmail.com
† This author contributed equally to the first author.

Abstract: Background and Objectives: Actinomyces species are part of the normal flora of humans and rarely cause disease. It is an uncommon cause of disease in humans. The clinical features of actinomycosis have been described, and various anatomical sites (such as face, bones and joints, respiratory tract, genitourinary tract, digestive tract, central nervous system, skin, and soft tissue structures) can be affected. It is not easy to identify actinomycosis because it sometimes mimics cancer due to under-recognition. As new diagnostic methods have been applied, Actinomyces can now more easily be identified at the species level. Recent studies have also highlighted differences among Actinomyces species. We report a case of Actinomyces viscosus bacteremia with cutaneous actinomycosis.

Materials and Methods: A 66 years old male developed fever for a day with progressive right lower-leg erythematous swelling. Blood culture isolates yielded Actinomyces species, which was identified as Actinomyces viscosus by sequencing of the 16S rRNA gene. In addition, we searched for the term Actinomyces or actinomycosis cross-referenced with bacteremia or “blood culture” or “blood stream” from January 2010 to July 2020. The infectious diseases caused by species of A. viscosus from January 1977 to July 2020 were also reviewed.

Results: The patient recovered well after intravenous ampicillin treatment. Poor oral hygiene was confirmed by dental examination. There were no disease relapses during the following period. Most cases of actinomycosis can be treated with penicillin. However, clinical alertness, risk factor evaluation, and identification of Actinomyces species can prevent inappropriate antibiotic or intervention. We also compiled a total of 18 cases of Actinomyces bacteremia after conducting an online database search.

Conclusions: In summary, we describe a case of fever and progressive cellulitis. Actinomyces species was isolated from blood culture, which was further identified as Actinomyces viscosus by 16S rRNA sequencing. The cellulitis improved after pathogen-directed antibiotics. Evaluation of risk factors in patients with Actinomyces bacteremia and further identification of the Actinomyces species are recommended for successful treatment.

Keywords: Actinomyces viscosus; Actinomyces; actinomycosis; cellulitis; bacteremia; gingivitis; sequence analysis

1. Introduction

The first case of actinomycosis was described in cattle by a pathologist in 1877 [1]. Then, shortly afterward in 1890, Actinomyces israelii was discovered in humans [2]. These bacteria are Gram-positive, filamentous, and rod-shaped. They are mostly facultative anaerobic organisms, which normally colonize the oral cavity, gastrointestinal tract, colon,
Medicina 2021, 57, 1064

2 of 14

and vagina [3,4]. However, only a handful of species are known to be associated with human infections such as A. israelii, A. meyeri, A. neuii, and A. turicensis [3,4]. Odontomyces viscosus was first found in the periodontal plaque of hamsters in 1958. The species was classified and named “Actinomyces viscosus” [5,6]. The two closely related species A. viscosus and A. naeslundii showed high phenotypic and serological relatedness and could be isolated from dental plaque and mucosa samples [7]. A. naeslundii Serotype II was renamed “Actinomyces oris” in 2009 [8], and human strains which have been assigned to A. viscosus are likely members of A. oris [9]. Despite being a commensal bacterium in the majority of human adults with teeth, A. viscosus has rarely been reported to cause disease [10].

Actinomyces was redefined to include catalase-positive organisms in 1969 [11]. Unlike other species which are catalase-negative and indole-positive, these colonies are catalase-positive and indole-negative. Actinomyces species can be cultured on blood agar (BA) with selective nutritional requirements [12]. In the 1980s, a new standard of 16S rRNA gene sequencing for bacterial identification was introduced and also used to establish the genotypic taxonomy [13–15]. In order to identify bacteria at the genus and species level, we used 16S rRNA gene sequencing technology to quickly perform reliable identification of bacteria in this case.

Evidence of actinomycosis infection is based on accurate identification of Actinomyces species. Therefore, accuracy is a key factor in preventing unnecessary invasive intervention and facilitates the selection of proper treatment [16,17]. The most common pathogenic actinomycosis species include A. viscosus and A. meyeri [2–4,12]. According to some reviews, A. israelii and A. meyeri have been identified as frequently encountered specimens from periappendiceal abscesses and abdominal actinomycosis [12,18].

Cutaneous actinomycosis is uncommon in clinical practice [19] and is usually a secondary infectious process with an underlying focus in deeper tissues [20], or it may appear as a result of hematogenous spread from an actinomycotic lesion elsewhere in the body [4]. In cutaneous actinomycosis, the commonly found causative organisms were A. meyeri and A. viscosus according to previous reports [4,12]. Oral hygiene is a recognized risk factor for the development of cutaneous actinomycosis [21]. According to a literature review of original clinical studies on Actinomyces, this species can be a source of invasive disease when superadded by periodontal disease and poor oral hygiene, leading to the development of infections. Although oral cervicofacial actinomycosis is the common form, Actinomyces can also result in infection of the thoracic, abdominopelvic, cutaneous, musculoskeletal system, pericardium, and central nervous system, as well as in disseminated disease [3].

In the present review, we report a case with A. viscosus bacteremia and cellulitis in a patient with poor oral hygiene, and we gathered this information to provide a comprehensive and microbiologically consistent overview of the A. viscosus bacteremia and cutaneous actinomycosis in human infections.

2. Materials and Methods

2.1. Case Presentation

A 66 years old male with hypertension and bipolar disease under treatment with lithium, fludiazepam, and seroquel came to our emergency department due to fever up to 38.9 °C (102 °F) without chills for a day. The patient complained of an erythematous painful swelling over the right lower leg, which developed gradually during the previous week. The patient also mentioned nausea with vomiting for 2 days, which did not seem to be related to meals. Otherwise, no other symptoms were mentioned. There was no traumatic history, no bug bite, and no exposure to livestock. On physical examination, blood pressure was 131/66 mmHg, heart rate was 91/min, respiratory rate was 18/min, and body temperature was 38.9 °C. Erythematous change measuring around 10 × 20cm over the anterior tibial region with tenderness was found, but there were no excoriated skin lesions
in this region. Laboratory tests showed notable leukocytosis with neutrophil predominance. C-reactive protein level was 17.9 mg/dL, procalcitonin level was 14.5 ng/mL, serum creatinine level was 1.55 mg/dL, and ClCr level was 51 mL/min. Two sets of blood cultures were obtained and yielded Actinomyces sp. Further sensitivity tests showed susceptibility to clindamycin, penicillin, ampicillin–sulbactam, cefoxitin, cefmetazole, and carbapenem, but resistance to metronidazole. Clindamycin 600 mg Q8H was administered for Actinomyces bacteremia and cellulitis. The erythematous swelling of the right lower leg improved gradually, and antibiotic treatment was shifted to sole intravenous ampicillin 2 g every 6 h on admission day 10 due to clinical improvement. There was no bacterial growth in the following blood culture.

Due to poor oral hygiene, a dentist was consulted for evaluation. Full-mouth gingivitis with plaque deposition and easy bleeding on probing was found during the dental examination. The patient then completed 7 days of intravenous ampicillin and was discharged with oral ampicillin 500 mg every 6 h. Further 16s rDNA sequencing for identification of pathogens revealed Actinomyces viscosus. The primers used for amplification of the 16S ribosomal DNA gene were 27F/1525R, 8F2/806R, and fD1modF/16S1RR-B. The amplification products obtained by PCR were sequenced, and the sequences obtained (791 bp) were compared to known 16S ribosomal DNA sequences in the GenBank database of the National Center for Biotechnology Information using the BLASTN algorithm (http://www.ncbi.nlm.nih.gov/blast accessed on 7 September 2021). The closest match was obtained with Actinomyces viscosus (GenBank accession number NR_113030; maximal score 848, E value 0.0, and maximal identity 84% (600/711)). There was no evidence of any diseases during follow-up.

2.2. Literature Review

A review of the English-language literature on Actinomyces bacteremia was conducted. Key search terms were Actinomyces OR actinomycosis cross-referenced with bacteremia OR “blood culture” OR “blood stream” in Pub Med/NCBI and other similar databases from January 2010 to July 2020. The infectious diseases caused by species of A. viscosus from January 1977 to July 2020 were also reviewed. All of the relevant information obtained from the literature review is presented in tables.

3. Results

We compiled a total of 18 cases of Actinomyces bacteremia from the online database search. The clinical and microbiological characteristics of these cases are summarized in Table 1.

Table 1. Characteristics and identification profile of Actinomyces bacteremia cases reported from 2010 to 2020.

| Year | Age/Sex | Nation   | Underlying Disease             | Clinical Presentation                          | Diagnosis                  | Treatment                  | Outcome   | Ref. |
|------|---------|----------|-------------------------------|-----------------------------------------------|---------------------------|----------------------------|-----------|-----|
| 2011 | 51/M    | South Korea | Alcoholic liver cirrhosis   | Fever (37.9 °C) with hematemesis             | Procedure-related bacteremia | Vancomycin ligation Cefpiramide | Death     | [22]|
| 2012 | 67/M    | South Korea | Hepatitis B virus infection | Fever, Cough, Purulent sputum, Headache       | Lung abscesses             | Ceftriaxone                | Recovered | [23]|
| 2013 | 40/F    | Belgium   | Crohn's disease              | Fever (40.7 °C), Shivering, Vomiting after IVF | Pelvic inflammatory disease with abscess | Amoxicillin–clavulanic acid    | Recovered | [24]|
| Year | Age/F | Country | History | Symptoms | Diagnosis | Treatment | Outcome |
|------|-------|---------|---------|----------|-----------|-----------|---------|
| 2014 | 31/F  | USA     | Multiparous IUD placement | Fever (38.9 °C) Pelvic pain for weeks | Tubo-ovarian abscesses | Penicillin G | Recovered [23] |
| 2014 | 26/M  | USA     | Recent right partial orchiectomy for epidermoid cyst | Fever (39.5 °C) Right testis swelling tenderness | Testicular abscess | Piperacillin/tazobactam and vancomycin IV | Recovered [25] |
| 2014 | 90/F  | Japan   | Diabetes mellitus Hypertension | Deteriorated mental status | *Actinomyces meyeri* meningitis | Ampicillin, ceftriaxone, ceftazidime, vancomycin Acyclovir | Did not regain consciousness [26] |
| 2014 | 59/M  | Croatia | Ulcerative colitis Colonoscopy (2 months ago) | Fever (39.9 °C) Vomiting Watery stools Abdominal pain | Abdominal actinomycosis | Ciprofloxacin with metronidazole Ceftriaxone | Recovered [27] |
| 2015 | 80/F  | Japan   | Bedridden Diabetes mellitus | Fever Impaired consciousness | Pyometra | Ampicillin–sulbactam | Recovered [28] |
| 2015 | 53/M  | Denmark | Recurrent skin abscesses COPD Obesity | Fever Painful swelling of right breast | Breast abscess | Dicloxacillin | Recovered [29] |
| 2016 | 47/M  | Thailand | Not mentioned | Cough and chest congestion | Aspiration pneumonia | Vancomycin and piperacillin–tazobactam | Recovered [30] |
| 2016 | 50/F  | USA     | Hypertension | Weakness Nausea Vomiting Diarrhea | Streptococcal toxic shock syndrome Pelvic actinomycosis | Clindamycin, ampicillin–sulbactam | Recovered [31] |
| 2018 | 23 weeks gestational age/F | USA | (Mother) severe HELLP syndrome Cesarean section | Prematurity | Neonatal sepsis | Ampicillin Penicillin | Discharge to another healthcare facility [32] |
| 2018 | 56/F  | USA     | Repaired TOF | Fever Epigastric pain and melena | Septic pylephlebitis | Penicillin G Ertapenem | Recovered [33] |
2019 61/M USA Endocarditis, atrial fibrillation, monoclonal gammopathy. Fever (39.4 °C), confusion, weakness, slurred speech after H/D. Infective endocarditis by *A. neuii*, aortic root abscess and presumed cerebral septic emboli. Surgery, ampicillin. Recovered [34].

2019 84/F USA DM, HTN, anemia, CAD, frequent UTI due to incontinence. Severe right thigh pain. Necrotizing soft-tissue infection. Debridement, clindamycin, vancomycin, piperacillin-tazobactam. Recovered [35].

2020 60/M Denmark DM. Urinary retention, macroscopic hematuria. UTI. Mecillinam. Recovered [36].

2020 52/F Philippines UTI, vaginitis, allergic to penicillin. Lower abdominal and flank pain. Urosepsis with shock, *A. turicensis* bacteremia. Ceftriaxone. Recovered [37].

2020 8 months old/F France Metastatic neuroblastoma under chemotherapy. Fever and neutropenia. Neutropenic fever. Imipenem. Recovered [38].

Abbreviation: IVF = in vitro fertilization; IUD = intrauterine device; COPD = chronic obstructive pulmonary disease; HELLP = hemolysis, elevated liver enzymes, and low platelets; TOF = tetralogy of Fallot; ESRD = end-stage renal disease; H/D = hemodialysis; DM = diabetes mellitus; HTN = hypertension; CAD = coronary artery disease; UTI = urinary tract infection; TVOR = Trans-vaginal oocyte retrieval.

(B)

| Year | Age/Sex | Nation     | Diagnosis                                       | Isolated Species         | Identified Method | Treatment                          | Previous Invasive Procedure |
|------|---------|------------|-------------------------------------------------|--------------------------|-------------------|------------------------------------|-----------------------------|
| 2011 | 51/M    | South Korea| Procedure-related bacteremia                     | *A. graevenitzii*         | 16S rRNA          | Varice ligation                   | Yes                         |
|      |         |            |                                                  |                          |                   | Cefpiramide                        |                             |
| 2012 | 67/M    | South Korea| Lung abscesses                                   | *A. cardiffensis*         | 16S rRNA          | Ceftriaxone                        | No                          |
| 2013 | 40/F    | Belgium    | Pelvic inflammatory disease with abscess         | *A. urogenitalis*         | MALDI-TOF MS + 16S rRNA | Amoxicillin-clavulanic acid        | Yes                         |
| 2014 | 31/F    | USA        | Tubo-ovarian abscesses                           | *A. naeslundii.*          | 16S rRNA          | Penicillin G                       | Yes (IUD)                   |


| Year | Age/Gender | Location | Clinical Manifestation | Identified Species | Diagnostic Method(s) | Antimicrobial Therapy | Outcomes |
|------|------------|----------|------------------------|--------------------|----------------------|----------------------|----------|
| 2014 | 26/M USA   | Testicular abscess | *A. naeuli* (blood and abscess) | Not mentioned | Piperacillin/tazobactam Vancomycin IV | Yes |
| 2014 | 90/F Japan | Actinomycetes meyeri meningitis | *A. meyeri* | RapID ANA II | | |
| 2014 | 59/M Croatia | Abdominal actinomycosis | *P. aeruginosa* *A. naeuli* | Not mentioned | Ciprofloxacin with metronidazole Ceftriaxone | |
| 2015 | 80/F Japan | Pyometra | *A. turicensis* *Clostridium clostridioforme* | MALDI-TOF MS + 16S rRNA | Ampicillin–sulbactam | No |
| 2015 | 53/M Denmark | Breast abscess | *A. europaeus* (Blood and abscess cavity) | MALDI-TOF MS + 16S rRNA | Dicloxacillin | No |
| 2016 | 47/M Thailand | Aspiration pneumonia | *A. radicidentis* | 16S rRNA + Retrospective MALDI-TOF MS | Vancomycin Piperacillin–tazobactam | Yes (IUD) |
| 2016 | 50/F USA | Streptococcal toxic shock syndrome Pelvic actinomycosis | *A. odontolyticus* | Not mentioned | Clindamycin Ampicillin–sulbactam | No |
| 2018 | 23 weeks gestational age/F USA | Neonatal sepsis with bacteremia | *A. viscosus* | 16S rRNA | Ampicillin Penicillin | No |
| 2018 | 56/F USA | Septic pylephlebitis secondary to *Actinomyces* bacteremia | *A. meyeri* | Biochemical analysis | Penicillin G Ertapenem | No |
| 2019 | 61/M USA | Infective endocarditis by *A. naeuli* | *A. naeuli* | MALDI-TOF MS | Surgery Ampicillin | No |
| 2019 | 84/F USA | Necrotizing soft-tissue infection | *A. europaeus* *A. schaalii* | Biochemical analysis | Debridement Clindamycin Vancomycin Piperacillin–tazobactam | No |
The average age of the patients was 52.5 years, ranging widely from 23 weeks gestational age to 90 years old. Eight patients (44%) were male. Seven patients (39%) had an underlying systemic condition, which resulted in a relatively immunocompromised status (one alcoholic liver cirrhosis, four diabetes mellitus, one preterm labor, and one monoclonal gammopathy). Seven patients (39%) had previous exposure to invasive procedures or implantations (two IUD, one TVOR, one colonoscopy, one surgery, one endoscopy, and one central-line placement). Eleven (61%) patients had fever. Fifteen (83%) patients had a primary site of infection; five (33% = 5/15) of these were gynecology–genital organ infection (including testicular abscess), followed by three (20%) urinary tract infections, two (13%) pulmonary infections, two (13%) soft-tissue infections, and one case each of (7%) meningitis, abdominal infection, and endocarditis.

Most of the treatments included penicillin-based antibiotic administration. Alternative antibiotics included third-generation cephalosporin (ceftriaxone for example) or clindamycin. Broad-spectrum antibiotics, such as carbapenems, were used in severe or comorbid patients. Three patients (17%) required further surgical intervention (endocarditis, necrotizing soft-tissue infection, and pelvic inflammatory disease with abscess). Most of the patients had favorable outcomes, and only a few patients with multiple comorbidities died or suffered from morbidity.

We also reviewed previous infectious disease with the species *Actinomyces viscosus* as a causative organism from January 1977 to July 2020, using the search term “*Actinomyces viscosus*” OR “*A. viscosus*”, as shown in Table 1B. Fifteen studies were found with a total of 19 relevant human cases. The clinical and microbiological characteristics of these cases are summarized in Table 2. The 19 cases comprised 10 men and nine women. The medium age of the patients was 35 years, ranging in age from gestational age of 23 weeks to 81 years old. Six patients (32%) had a relatively immunocompromised status (multiple myeloma, alcoholism, pancreatic cancer, acute lymphoblastic leukemia under chemotherapy, and psoriatic arthritis under methotrexate). Eleven patients (57%) suffered from fever. As to the acquired specimens, in four patients (21%), *Actinomyces viscosus* was found from blood culture. Seven patients (37%) needed biopsy or tissue culture for *Actinomyces viscosus* isolation. Other specimens included pus, drainage or discharge from submandibular, neck, chest wall, and breast abscess, subdural empyema, pleural fluid, percutaneous transtracheal aspiration, and vitreous washings. Most of the specimens were diagnosed by biochemical analysis, and only two specimens were analyzed using PCR (in the year 2005) or 16s sequencing (in the year 2018). Only one patient suffered from subdural empyema, resulting in death.
Table 2. Characteristics of *Actinomyces viscosus* infection published from 1977 to 2020.

| Year | Age/Sex | Nation | Underlying Disease | Clinical Presentation | Specimen | Diagnosis | Treatment | Outcome | Ref. |
|------|---------|--------|--------------------|-----------------------|----------|-----------|-----------|---------|------|
| 1977 | 62/F    | USA    | Nil                | Submandibular swelling| Ductal discharge | Submandibular abscess | Flucloxacillin | Recovered | [39] |
| 1977 | 76/F    | USA    | Multiple myeloma   | Fever with crackle    | Blood     | Pneumonia | Ampicillin Cloxacillin | Recovered | [39] |
| 1978 | 8/M     | USA    | Nil                | Fever and a cervical mass | Tissue | Neck cellulitis | Phenoxymer-thyl Penicillin | Recovered | [40] |
| 1979 | 7/F     | USA    | Fall accident 6 months ago | Enlarging macular lesion on the right lower chest | Chest wall pus | Chest wall abscess with rib involvement | Rib resection Clindamycin | Recovered | [41] |
| 1979 | 18/M    | USA    | Nil                | Fever (40 °C) Chest pain Cough Hemoptysis | Percutaneous transtracheal aspiration | Pneumonia | Ticarcillin | Recovered |
| 1979 | 49/M    | USA    | Penectomy for carcinoma of the penis | Fever Cough with expectoration Night sweats Chest pain on | Transtracheal aspiration | Pneumonia | Ticarcillin Penicillin | Recovered | [42] |
| 1981 | 27/M    | USA    | Alcoholism         | Fever (38.2 °C) Cough | Biopsy | Lung abscess | Penicillin G | Recovered |
| 1981 | 21/M    | USA    | Sickle cell disease | Fever (38 °C) with cold sensation Cough | Tissue | Lung abscess | Penicillin | Recovered | [43] |
| 1984 | 60/M    | USA    | Nil                | Cough with left chest pain | Tissue | Chest wall abscess | Excision Penicillin | Recovered |
| 1998 | 55/M    | HK     | Nil                | Epigastric pain and weight loss | Biopsy | Esophageal actinomycosis | Amoxicillin–clavulanate | Recovered | [44] |
| 1998 | 81/M    | USA    | Valvular heart disease | Fever (38.5 °C) Depressed mood | Blood | Endocarditis | Ceftizoxime | Recovered | [45] |
| Year | Age | Gender | Location | Presenting Symptoms | Past Medical History | Treatment(s)          | Outcome |
|------|-----|--------|----------|---------------------|---------------------|----------------------|---------|
| 1999 | 78/M | USA    | Cataract | Suicidal ideation  | Hypertension, Gout, GERD | Penicillin | Recovered [46] |
|      |      |        |          | Anorexia            |                     |                      |         |
|      |      |        |          | Back pain           |                     |                      |         |
|      |      |        |          | Weight loss         |                     |                      |         |
| 2005 | 27/F | Italy  | Nil      | Severe right eye pain | Cataract            | Breast abscess | Recovered [47] |
|      |      |        |          |                    | Hypertension        |                      |         |
|      |      |        |          |                    | Gout                |                      |         |
|      |      |        |          |                    | GERD                |                      |         |
| 2005 | 43/F | USA    | Fever without focus 1 year before | 5 days of subjective fever | Hemoptysis          | Aortic valve repair | Recovered [48] |
|      |      |        |          |                    | Productive cough    | Vancomycin, Gentamicin, Ceftriaxone |         |
|      |      |        |          |                    | Increased dyspnea on exertion |                      |         |
|      |      |        |          |                    |                    |                      |         |
| 2007 | 35/F | India  | Nil      | Fever and throbbing type of pain of back | ALL under induction chemotherapy | Penicillin | Recovered [49] |
|      |      |        |          |                    |                    | Cotrimoxazole       |         |
|      |      |        |          |                    |                    |                      |         |
| 2008 | 17/F | India  | Nil      | Fever (39 °C) Vomiting | Lung consolidation | Empyema             | Recovered [50] |
|      |      |        |          |                    | Pleural fluid       | Imipenem–cilastatin |         |
|      |      |        |          |                    |                    |                      |         |
| 2011 | 7/F  | Tunis  | Nil      | Fever (39 °C) Vomiting | Purulent liquid from neurosurgical drainage | Ampicillin | Death [51] |
|      |      |        |          |                    | Subdural empyema    |                      |         |
|      |      |        |          |                    |                    |                      |         |
| 2018 | 74/M | USA    | COPD Smoker Psoriatic arthritis on methotrexate | Generalized weakness and difficulty to ambulate | Neck abscess | Penicillin | Recovered [10] |
|      |      |        |          |                    | Neck, lung and brain abscess |                      |         |
|      |      |        |          |                    |                    |                      |         |
| 2018 | 23 weeks gestational age/F | USA | (Mother) severe HELLP syndrome Cesarean section | Prematurity | Blood | Neonatal sepsis | Discharge to another healthcare facility [32] |

Abbreviation: GERD = gastroesophageal reflux disease; ALL = acute lymphocytic leukemia; COPD = chronic obstructive pulmonary disease; HELLP = hemolysis, elevated liver enzymes, and low platelets.
4. Discussion

*Actinomyces* species are opportunistic pathogens and capable of causing disease, which often invade the body following the disruption of mucosal barriers [4,8].

There are nine *Actinomyces* species that are commonly found in the oral cavity, namely, *A. israelii*, *A. viscosus*, *A. odontolyticus*, *A. naeslundii*, *A. georgiae*, *A. gerencseriae*, *A. meyeri*, *A. radicidentis*, and *A. graevenitzii* [52,53]. *A. israelii* is known as the most common bacterium associated with classical actinomycosis, which has been linked with dental abscesses and oral infections [12]. In this study, we reviewed cases of *Actinomyces* bacteremia in databases and found that 15 of 18 patients had at least one risk factor.

According to the analysis, seven patients were relatively immunocompromised (one alcoholic liver cirrhosis, four diabetes mellitus, one preterm labor, and one monoclonal gammopathy). Seven cases had a procedure-related risk factor (two IUD, one TVOR, one colonoscopy, and one surgery), and four cases had evidence of poor oral hygiene. The diagnostic method and basic characteristics of *Actinomyces* bacteremia cases reported from 2010 January to 2020 July are summarized in Tables 1 and 2.

A phenotypic test is an easily applied, rapid, and cost-efficient tool for identification of *Actinomyces* species. The classical method is based on phenotypic tests such as gas production from glucose, urease, catalase, and acid production [8]. However, it is difficult to determine the taxon when species have the same characteristics [4]. With the low cost of 16S rRNA sequencing in recent years, it is possible to use this reliable and accurate approach currently available in clinical practice. In this study, we used 16S sequencing to confirm the pathogen, which was identified as *Actinomyces viscosus*.

In general, *Actinomyces* species are susceptible to penicillin and beta-lactam antibiotics [54]. Some studies reported that actinomycosis can be treated successfully with ceftriaxone [23,27,54], but several case reports noted that some isolates were resistant to ceftriaxone, such as *A. europaeus* and *A. graevenitzii* [12,54]. A retrospective assessment of antimicrobial susceptibility testing of isolates showed that the *Actinomyces* spp. were also susceptible to carbapenems, tetracyclines, clindamycin, and vancomycin as alternative treatments [54]. However, another interesting observation was that *Actinomyces* isolates were resistant to doxycycline [12] and clindamycin, showing a high range from 30% to 80% with poor susceptibility rates [55]. Additionally, in the present study, it was found that *A. meyeri* and *A. odontolyticus* were resistant to tetracycline and vancomycin; in most *Actinomyces* spp., isolates showed high resistance to metronidazole and quinolones as “intrinsic resistance” [55]. Therefore, the susceptibility profiles of *Actinomyces* are important as they help to inform the selection of an appropriate treatment [54]. In our study, the patient recovered well after intravenous ampicillin treatment.

A recent study on the healthy human oral microbiome showed that *Actinomyces* species are part of the oral flora in Taiwanese populations [56]. Human isolates of *Actinomyces viscosus* showed high phenotypic and serological relatedness to *A. naeslundii* [57]. Therefore, we used 16S rRNA sequencing analysis for identification of *A. viscosus*; it was also possible to differentiate it from other closely related species in the genera *Arcanobacterium* and *Actinobaculum* [58,59]. The oral cavity could be considered a causative factor in human actinomycosis [60]. The isolation of *Actinomyces* spp. from blood culture is traditionally regarded as clinically significant [61]. However, the possibility of contaminants does exist [62]. Sound clinical judgment based on the presence of risk factors is essential to interpret the results. According to the literature review of original clinical studies on *Actinomyces*, this species can become pathological when superadded by periodontal disease and poor oral hygiene, leading to the development of infections. The mucosal barrier is disrupted by triggering factors such as plaque, tooth cavities, and periodontitis in the case of oral infections [19,63,64].

In this study, our patient had poor oral hygiene and chronic periodontitis, which were considered risk factors. *A. viscosus* is an opportunistic pathogen in the oral cavity. This may have been the source of bacteremia in our patient, who had hematogenous
spreading, which led to cellulitis of the right lower leg. Furthermore, immunocompromised patients, such as those with diabetes, human immunodeficiency virus (HIV), etc., patients who have undergone a surgical or invasive procedure, and patients with local tissue damage, are also traditionally considered to be at greater risk for actinomycosis.

5. Conclusions

Actinomycosis is considered a curable disease that can be easily treated with penicillin and amoxicillin as the first-line treatment. However, chronic granulomatous clinical presentation, selective cultivation of an environment, and species differences in susceptibility profiles may result in clinical confusion, which may lead to treatment failure. In summary, we describe a case with fever and progressive cellulitis. The Actinomyces species was isolated from blood culture, which was further identified as A. viscosus by 16S rRNA sequencing. The cellulitis improved after pathogen-directed antibiotics. Evaluation of the risk factors of a patient with Actinomyces bacteremia and further identification of Actinomyces species may increase the likelihood of successful treatment.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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