Review Article

Actinomycosis- A Compact Clinical Review

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Received Date: January 25, 2021
Publication Date: February 01, 2021

Abbreviations

A- Actinomyces
CT- Computerized Tomography
CXR- Chest X-Ray
GERD- Gastro-Esophageal Reflux Disease
IUCD- Intra-Uterine Contraceptive Devices
MALDI-TOF-Matrix-Assisted Laser Desorption Ionization Time-Of-Flight
Sep- Species Pluralis
TB- Tuberculosis

Introduction

Actinomycosis is an infrequent invasive bacterial disease that has been recognized for over a century of note, in any site, actinomycosis frequently mimics malignancy, tuberculosis (TB), or nocardiosis, as it spreads continuously and progressively, and often forms a cold abscess **(**1-4**)**.

In this review, we aim to describe:

1) The overview of the different species of Actinomyces;

2) Epidemiology;

3) Presentation with different clinical features;

4) Key elements for the diagnosis, and

5) The treatment options

Overview

Actinomycosis is a rare sub-acute to chronic infectious bacterial disease caused by actinomyces species. Actinomycetes are filamentous gram-positive, non-acid fast bacilli (AFB), anaerobic to microaerophilic bacteria mainly belonging to the human commensal flora of the oropharynx, gastrointestinal tract, and urogenital tract (1, 5).

In 1877, it was first discovered by pathologist Otto Bollinger and he described the presence of A. bovis in cattle, and very soon after that, James Israel discovered A. Israeli in humans. In 1890, the organism was isolated from the cultures of grain, grasses, and soil by Eugen Bostrom. After his discovery, a general misconception existed that actinomycosis was a mycosis that affected individuals who chewed grass or straw. The pathogen is still known as the “great masquerader" (6).

There are about 38 different species of actinomyces and the most common are A.israelli, A.bovis, A.gerencseriae, A. naeslundii, A. viscosus, A. odontolyticus, and A. Meyer, Propionibacterium propionicum, and Bifidobacterium dentium (7).

Israelii is the most prevalent species isolated in human infections and is found in most clinical forms of actinomycosis (1–4, 8, 9).

A. Viscosus and *A. Meyer* are also often reported in typical actinomycosis, although they are less common (1, 9-10), and *A. Meyer* is considered to have a great propensity for dissemination (1).

A. Israelii and *A. Gerencseriae* are responsible for about 70% of orocervicofacial infections (1, 8). Hematogenous dissemination of actinomycosis is extremely rare and has mainly been associated with *A. Meyer, A. Israelii,* and *A. Odontolyticus* (11).

Epidemiology, Etiology and Risk factors

Actinomycosis is now a rare infection, particularly in the developed world. These changes in both the disease's presentation and its incidence may be the result of improvements in oral hygiene, in the ready availability of antibiotics, and in the early initiation of treatment when the infection is suspected (12).

Disease incidence is greater in males between the ages of 20 and 60 years than in females.

Actinomyces are thought to infect deep tissues via a point of entry, such as mucosal lesions, endodontic pathways, and periodontal pockets (20-22).

Dental caries, invasive dental or maxillofacial procedures, trauma, and radionecrosis are the most common causes (20, 22-23).

The other known predisposing factors include diabetes, alcohol abuse, malnutrition, and immunosuppression (20, 23).

The pulmonary form of actinomycosis constitutes ~15% of the total burden of disease, although estimates of up to 50% have been reported (12-16).

Route of infection in pulmonary actinomycosis is mainly through aspiration of oropharyngeal secretions containing actinomycetes (5, 17).

Alcoholics and patients with severe gastroesophageal reflux disease (GERD) are at risk of having pulmonary actinomycosis.

The presentation of pulmonary actinomycosis has changed and it now appears less aggressive compared with the pre-antibiotic era (12-13).

Colonization of the female genital tract by actinomyces species pluralism (spp.) is greatly promoted by the use of intrauterine contraceptive devices (IUCD) and is associated with the duration of IUCD use (18, 19).

The use of IUCD has increased the incidence of genitourinary actinomycosis in females.

Clinical Features

In 1938, Cope classified actinomycosis infection into 3 distinct forms:

1. Cervicofacial 50%
2. Pulmonothoracic 30%
3. Abdominal-pelvic 20%

Cervicofacial actinomycosis present with nodular lesions commonly located at the angle of the jaw, which gradually increases in size with micro abscess formation and draining sinuses that opens onto the cheek or submandibular area and sulfur granules may be seen in the exudates. Typically, lymphadenopathy may be present and complicated with trismus.

Actinomyces israelii is the most common pathogen isolated in cervicofacial actinomycosis (20, 21, 8).

Although actinomycosis can affect any structure of the cervicofacial area, it involves the mandibular area (submandibular region, ramus, and angle) in over 50% of cases (20, 23, 24).

Pulmonary actinomycosis usually presents as indolent pneumonia with fever, weight loss, cough, sputum, and chest pain. There are no specific radiographic manifestations but lesions that involve the chest wall and pleura with the destruction of adjacent bones are highly suggestive (25, 27).

The symptoms, clinical and radiological signs often mimic malignancy or TB and miliary presentations of the disease have also been reported (26, 27).

The main clinical feature of genitourinary tract actinomycosis is pelvic actinomycosis in women using an IUCD (1, 28, 29).

Symptoms of patients with pelvic IUCD-associated actinomycosis may mimic symptoms of gynecological malignant tumors, uterine myoma or adenomyosis, by presenting as a genital mass without fever (1, 29-31).

Abdominopelvic actinomycosis usually comes with antecedent abdominal surgery which presents as low-grade fever, mass in right lower quadrant firm to hard in consistency, fixed, and non-tender. The sinus tract will be formed if left untreated as peritoneocutaneous fistula.

The hematogenous spread can occur to the liver, kidneys but can also present as liver abscess and perinephric abscess (5).

There are few case reports of central nervous system involvement presenting as brain abscess due to A. meyeri have been reported. These cases could manifest as headache, increased intracranial pressure, focal seizures, hemiparesis, aphasia, ataxia, or abnormal reflexes depending on its localization.

Actinomyces of bone is not very uncommon; frequently involved bones are mandible, ribs, and spine. It results from direct extension of an adjacent soft tissue focus leading to periostitis and localized areas of bone destruction with areas surrounded by increased bone density (7).

Actinomyces causing infective endocarditis and septicemia have been reported especially following dental procedures and periodontal disease (32).

Diagnosis

Belmont et al. (21) stated that fewer than 10% of infections are accurately diagnosed on initial presentation because they are often confused with pyogenic abscesses or neoplasia.

Blood tests are usually unhelpful, however, leukocytosis may be present in some cases (20, 33). Complete blood count may reveal anemia with elevated C-reactive protein and erythrocyte sedimentation rate.

Raised Alkaline phosphatase levels and transaminitis may be observed in case of hepatic spread. Moreover, cultivating Actinomyces spp. is notoriously difficult, thus leading to a high percentage of false negative results (20).

Imaging studies: Chest X-ray, Computed Tomography (CT) scan and magnetic resonance imaging (MRI) scan be performed to locate and know the extent of disease.

Radiographic features are non-specific and may resemble any chronic inflammatory process (20, 21, 23, 34), malignancy or TB.

Although chest imaging of pulmonary actinomycosis most commonly reveals fibrotic infiltrates that are confined to a single lobe with small cavitary lesions (35) but non-specific findings are commonly observed in clinical practice (36-38).

In the context of actinomycosis diagnosis, the biopsy should remain the gold standard **(**20**).**

A gram stain of the specimen is usually more sensitive which shows non-spore-forming gram-positive rods. It is more sensitive than culture, especially if the patient had received antibiotics. Demonstration of Sulphur granules in the discharge from the sinus tracts and histopathology shows "sun ray appearance" which is diagnostic (5).

Actinomyces spp. can be cultured on chocolate blood agar media at 37°C. Growth of Actinomyces spp. is slow; it appears within at least 5 days and may take up to 15–20 days. Thus, incubation of at least 10 days is required before conclusion of a negative culture. Alternatively, other enriched media can be used for Actinomyces isolation are brain heart infusion broth and Brucella Blood Agar with hemin and vitamin K1. For selective isolation of organism additional semi-selective media (such as phenyl ethyl alcohol or mupirocin-metronidazole blood agar) can be used which may increase isolation rates by inhibiting overgrowth of concomitant organisms (39).

Actinomyces spp. are indole-negative bacteria. Identification was classically based on phenotypic tests (urease, catalase, fermentation of sugars, etc.) or on commercial biochemical kits but, in fact, such tests can lead to misidentification of species (40, 41). Polymerase chain reaction with specific primers can also be used for direct detection of Actinomyces in clinical material. Also matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) should be a quicker and accurate tool for actinomyces identification in the future (42).

Management

The mainstay of the treatment is prolonged courses of antibiotics.

Actinomyces infection usually discovered late with severe, extensive infection and often invasive associated with significant purulence or fistulous tracts; most commonly occurs in patients with significant underlying comorbidities.

The most preferred regimens for actinomycosis have been suggested as high-dose penicillin. Ceftriaxone and amoxicillin are reasonable alternatives. The route of administration depends on the severity of the infection (1).

For severe infections, different treatment regimens have been recommended

1.An initial course of intravenous penicillin G (10 to 20 million units daily in divided doses every four to six hours) Initial parenteral therapy is typically given for four to six weeks (43).

2.In the outpatient setting, reasonable alternative is Ceftriaxone (1 to 2 grams every 24 hours) that can also be more easily administered for treatment in the outpatient setting (44).

3. Once there is a significant improvement in the patient's condition. Parenteral penicillin can be switched to an oral regimen. The parenteral regimen is followed by oral penicillin V (2 to 4 grams per day, divided into four daily doses).

4. Oral amoxicillin is probably a good alternative and equally efficacious (7) and its generally used 1.5 to 3 grams per day, divided into three or four daily doses.

5.Tetracycline and erythromycin can replace penicillin in allergic patients, and cephalosporin's can be used in co-infection not responding to penicillin (1, 21, 23, 45).

6. The use of steroids may help treat any residual inflammatory granulomatous reaction (20, 46), however, further studies are needed to assess the validity of this treatment.

Surgical Management

The general rules for surgical indications include:

1. Extensive disease
2. Non-resolving or delayed resolution of infection with antibiotics alone
3. Relapse of the infection

In cervicofacial infections, surgery is indicated in cases of bony involvement, the presence of necrotic tissue, or in the presence of a sinus tract (20, 47-49).

Removal of the IUCD is crucial in patients with IUCD-associated actinomycosis (29, 50).

Surgical therapy may include incision and drainage of abscesses, excision of sinus tracts and recalcitrant fibrotic lesions, decompression of closed-space infections, and interventions aimed at relieving obstruction, especially in abdominal and pelvic mass (31).

Prevention

Maintenance of good oral hygiene and adequate regular dental care is important.

Patients and physicians alike should be aware of the increased risk of infection associated with the insertion of IUCD.

Conflict of interest

All authors declare no conflict of interest.

Funding

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Acknowledgment

I sincerely thank, Dr. Wisam Ghadban, A/Medical Director and Chief of Medicine, Al Khor Hospital, for encouragement and his support.

References

1. Valour F, Sénéchal A, Dupieux C, Karsenty J, Lustig S, Breton P, Gleizal A, Boussel L, Laurent F, Braun E, Chidiac C, Ader F, Ferry T. Actinomycosis: etiology, clinical features, diagnosis, treatment, and management. Infect Drug Resist. 2014 Jul 5;7:183-97. doi: 10.2147/IDR.S39601. PMID: 25045274; PMCID: PMC4094581.

2. Wong VK, Turmezei TD, Weston VC. Actinomycosis. BMJ. 2011;343:d6099.

3. Smego RA Jr, Foglia G. Actinomycosis. Clin Infect Dis. 1998;26(6):1255–1261.

4. Mandell GL, Bennett JE, Dolin R, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2010.

5. API Text book of Medicine, 9Th edition, page 1129-1130

6. Sullivan, D. C.; Chapman, S. W. (12 May 2010). "Bacteria That Masquerade as Fungi: Actinomycosis/Nocardia". *Proceedings of the American Thoracic Society*. 7(3): 216–221. doi:10.1513/pats.200907-077AL. PMID 20463251.

7. Actinomyces species (Actinomycoses) Authors: Tasaduq Fazili MD, FACP. http://www.antimicrobe.org/b73.asp

8. Pulverer G, Schütt-Gerowitt H, Schaal KP. Human cervicofacial actinomycoses: microbiological data for 1997 cases. Clin Infect Dis. 2003;37(4):490–497.

9. Eng RH, Corrado ML, Cleri D, Cherubin C, Goldstein EJ. Infections caused by Actinomyces viscosus. Am J Clin Pathol. 1981;75(1):113–116.

10. Fazili T, Blair D, Riddell S, Kiska D, Nagra S. Actinomyces meyeri infection: case report and review of the literature. J Infect. 2012;65(4):357–361.

11. Felz MW, Smith MR. Disseminated actinomycosis: multisystem mimicry in primary care. South Med J. 2003;96(3):294–299.

12. Mabeza GF, Macfarlane J. Pulmonary actinomycosis. Eur Respir J. 2003 Mar;21(3):545-51. doi: 10.1183/09031936.03.00089103. PMID: 12662015.

13. Russo TA.. Agents of actinomycosis In: Mandell GL, ed. Principles and Practice of Infectious Disease. 5th ednNew York, Churchill Livingstone, 1995; pp. 2645–2654

14. Holm P. Studies on the aetiology of human actinomycosis. II. The “other” microbes of actinomycosis and their importance. Acta Pathol Microbiol Scand 1951;28:391.

15. Hachitanda Y, Nakagawara A, Ikeda K. An unusual wall tumour due to actinomycosis in a child. Paediatr Radiol 1989;20:96.

16. Rose HD, Varkey B, Kutty CP. Thoracic actinomycosis caused by *Actinomyces myeri. Am Rev Respir Dis* 1982;125:251–254

17. Wolff K, Goldsmith LA, Katz S, Gilchrist BA, Paller A, Leffell DJ (2007). *Fitzpatrick's Dermatology in General Medicine* (7th ed.). McGraw Hill.

18. Al-Kadhi S, Venkiteswaran KP, Al-Ansari A, Shamsudini A, Al-Bozom I, Kiliyanni AS. Primary vesical actinomycosis: a case report and literature review. Int J Urol. 2007;14(10):969–971.

19. Westhoff C. IUDs and colonization or infection with Actinomyces. Contraception, 2007:75 (Suppl 6): S48-S50

20. Sadeghi S, Azaïs M, Ghannoum J. Actinomycosis Presenting as Macroglossia: Case Report and Review of Literature. Head Neck Pathol. 2019 Sep;13(3):327-330. doi: 10.1007/s12105-018-0966-7. Epub 2018 Sep 22. PMID: 30244331; PMCID: PMC6684727.

21. Belmont MJ, Behar PM, Wax MK. Atypical presentations of actinomycosis. Head Neck. 1999;21:264–268. doi: 10.1002/(SICI)1097-0347(199905)21:3<264::AID-HED12>3.0.CO;2-Y.

22. Reichenbach J, Lopatin U, Mahlaoui N, et al. *Actinomyces* in chronic granulomatous disease: an emerging and unanticipated pathogen. Clin Infect Dis. 2009;49:1703–1710. doi: 10.1086/647945.

23. Lancella A, Abbate G, Foscolo AM, et al. Two unusual presentations of cervicofacial actinomycosis and review of the literature. Acta Otorhinolaryngol Ital. 2008;28:89–93.

24. Gerbino G, Bernardi M, Secco F, et al. Diagnosis of actinomycosis by fine-needle aspiration. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996;81:381–382. doi: 10.1016/S1079-2104(96)80011-4.

25. Yildiz O, Doganay M. Actinomycoses and Nocardia pulmonary infections. Curr Opin Pulm Med200612228–234.

26. Fisher M. “Miliary” actinomycosis. J Can Assoc Radiologists 198031149–150.

27. Cohen RD, Bowie WR, Enns R, Flint J, Fitzgerald JM. Pulmonary actinomycosis complicating infliximab therapy for Crohn's didease. *Thorax* 2007;62(11):1013-1014

28. Lew DP, Waldvogel FA. Osteomyelitis. *Lancet*. 2004;364(9431):369–379.

29. Choi MH, Hong DG, Seong WJ, Lee YS, Park IS. Pelvic actinomycosis confirmed after surgery: single center experience. Arch Gynecol Obstet. 2010;281(4):651–656.

30. Garner JP, Macdonald M, Kumar PK. Abdominal actinomycosis. *Int J Surg*. 2007;5(6):441–448.

31. Sung HY, Lee IS, Kim SI, et al. Clinical features of abdominal actinomycosis: a 15-year experience of a single institute. *J Korean Med Sci*. 2011;26(7):932–937.

32.Case Report Actinomyces naeslundii: An Uncommon Cause of Endocarditis
Case Report | Open Access Volume 2015 |Article ID 602462 | https://doi.org/10.1155/2015/602462

33. Weese WC, Smith IM. A study of 57 cases of actinomycosis over a 36-year period. A diagnostic ‘failure’ with good prognosis after treatment. Arch Intern Med. 1975;135:1562–1568. doi: 10.1001/archinte.1975.00330120040006.

34. Park JK, Lee HK, Ha HK, et al. Cervicofacial actinomycosis: CT and MR imaging findings in seven patients. AJNR Am J Neuroradiol. 2003;24:331–335.

35. Higashi Y, Nakamura S, Ashizawa N, Oshima K, Tanaka A, Miyazaki T, Izumikawa K, Yanagihara K, Yamamoto Y, Miyazaki Y, Mukae H, Kohno S. Pulmonary Actinomycosis Mimicking Pulmonary Aspergilloma and a Brief Review of the Literature. Intern Med. 2017;56(4):449-453. doi: 10.2169/internalmedicine.56.7620. Epub 2017 Feb 15. PMID: 28202870; PMCID: PMC5364201.

36. Huang CW, Lee MA, Lu RH, Peng HC, Chao HS. A case of pul- monary aspergilloma and actinomycosis. J Med Microbiol 60: 543-546, 2011.

37. Flynn MW, Felson B. The roentgen manifestations of thoracic actinomycosis. Am J Roentgenol Radium Ther Nucl Med 110: 707-716, 1970.

38. Cheon JE, Im JG, Kim MY, Lee JS, Choi GM, Yeon KM. Tho- racic actinomycosis: CT findings. Radiology 209: 229-233, 1998.

39. Lewis R, McKenzie D, Bagg J, Dickie A. Experience with a novel selective medium for isolation of Actinomyces spp. from medical and dental specimens. J Clin Microbiol. 1995;33(6):1613–1616

40. Ng LS, Sim JH, Eng LC, Menon S, Tan TY. Comparison of phenotypic methods and matrix-assisted laser desorption ionisation time-of-flight mass spectrometry for the identification of aero-tolerant Actinomyces spp. isolated from soft-tissue infections. Eur J Clin Microbiol Infect Dis. 2012;31(8):1749–1752.

41. Miller PH, Wiggs LS, Miller JM. Evaluation of API An-IDENT and RapID ANA II systems for identification of Actinomyces species from clinical specimens. J Clin Microbiol. 1995;33(2):329–330.

42. Hall V, Talbot PR, Stubbs SL, Duerden BI. Identification of clinical isolates of Actinomyces species by amplified 16S ribosomal DNA restriction analysis. J Clin Microbiol. 2001;39(10):3555–3562

43. PEABODY JW Jr, SEABURY JH. Actinomycosis and nocardiosis. A review of basic differences in therapy. Am J Med 1960; 28:99.

44.Skoutelis A, Petrochilos J, Bassaris H. Successful treatment of thoracic actinomycosis with ceftriaxone. Clin Infect Dis 1994; 19:161.

45. Moghimi M, Salentijn E, Debets-Ossenkop Y, et al. Treatment of cervicofacial actinomycosis: a report of 19 cases and review of literature. Med Oral Patol Oral Cir Bucal. 2013;18:e627–e632. doi: 10.4317/medoral.19124.

46. Bubbico L, Caratozzolo M, Nardi F, et al. Actinomycosis of submandibular gland: an unusual presentation. Acta Otorhinolaryngol Ital. 2004;24:37–39.

47. Sudhakar SS, Ross JJ. Short-term treatment of actinomycosis: two cases and a review. Clin Infect Dis. 2004;38:444–447. doi: 10.1086/381099.

48. Barabas J, Suba Z, Szabo G, et al. False diagnosis caused by Warthin tumor of the parotid gland combined with actinomycosis. J Craniofac Surg. 2003;14:46–50. doi: 10.1097/00001665-200301000-00008.

49. Oostman O, Smego RA. Cervicofacial actinomycosis: diagnosis and management. Curr Infect Dis Rep. 2005;7:170–174. doi: 10.1007/s11908-005-0030-0.

50. Bonacho I, Pita S, Gómez-Besteiro MI. The importance of the removal of the intrauterine device in genital colonization by actinomyces. *Gynecol Obstet Invest*. 2001;52(2):119–123.

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