Case report

Thoracoabdominal actinomycosis – Chameleon through kaleidoscope

Marc Hartert a, *, Michael Wolf b, Johannes Ferber b, Martin Huertgen a

a Department of Thoracic Surgery, Katholisches Klinikum Koblenz-Montabaur, Koblenz, Germany
b Institute of Pathology, Koblenz, Germany

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ABSTRACT

Actinomyces is a gram-positive anaerobic bacterium that generally inhabits the human commensal flora of the bronchial system, the gastrointestinal and urogenital tract. In the rare case of becoming invasive under certain circumstances, the resulting Actinomycosis affects most commonly cervicofacial, thoracic, abdominal and pelvic regions. Due to its rarity and presenting with nonspecific clinical symptoms, thoracic and/or abdominal Actinomycosis in particular are highly intriguing clinical conditions that can easily be mistaken for other diseases including malignancies. Astute considerations are therefore necessary whenever we are challenged diagnostically to allow early diagnosis and thus avoiding gratuitous invasive surgery. In order to highlight different issues of this ultimate chronic disease we report a particular case of thoracoabdominal Actinomycosis.

1. Introduction

The particularity of Actinomycosis is the diversity of its clinical presentation. Heavily summarized, (1) it may affect numerous organs of the human body, (2) it may present innumerable clinical symptoms and (3) it may resemble malignancy or a variety of other diseases [1,2]. In addition, its clinical occurrence is quite unusual and its scientific evidence is rather difficult, so it’s no wonder that most clinicians are unaccustomed with this chronic infectious disease. From a microbiological point of view, Actinomycosis is caused by anaerobic or microaerophilic/capnophilic gram-positive bacteria that generally inhabit the human commensal flora of the bronchial system, the gastrointestinal and urogenital tract. In accordance with its population pattern, the most common clinical forms, inter alia, are the cervicofacial, thoracic, abdominal and pelvic [3,4]. The pathogenicity assumes damage on the mucosal membrane following dental or gastrointestinal tract procedures, aspiration, or digestive tract diseases [5]. The progressively invasive infection causes a gently continuing suppurative fibrosing inflammation, leading to florid abscess formation and chronic granulomatous lesions, developing draining sinus tracts that may discharge characteristic “sulfur granules”, and directly disseminate via contiguous tissues [6]. Due to its peculiarities (its rarity, unspecific symptoms and tendency to perform as “surrounding mass invading structure”), Actinomycosis is at least at one point of its manifestation mistaken for a malignant tumor [3,4]. The featured case is a paradigm of the Actinomycosis’ art of metamorphosis.

2. Case presentation

A 55-year-old woman without significant past history presented in July with severe pain over left hemithorax and back. She had a boarding kennel and worked as horticulturist. She solely was a chronic smoker (30 pack years) and denied persistent cough, fevers, chills, hemoptysis, dyspnea, weight or appetite changes, sick contacts, or recent travel. A myocardial infarction could be ruled out with ECG and troponin within normal limits. The initiated cortisone and analgesic therapy alleviated the symptoms temporarily. Weeks later, the pain symptomatology returned in August. Due to the localization of the pain in conjunction with leukocytosis the general practitioner suspected urinary tract infection and consequently antibioticized the patient. Continuing pain intensity in September prompted thereupon inconclusive urologic examination. In October a rheumatic disease was suspected due to modulate increase of erythrocyte sedimentation rate and persistent leukocytosis - but prednisolone still wasn’t a breakthrough. Meanwhile...

* Corresponding author. Department of Thoracic Surgery, Katholisches Klinikum Koblenz-Montabaur, Rudolf-Virchow-Str. 7-9, 56073, Koblenz, Germany.
E-mail address: m.hartert@kk-km.de (M. Hartert).
reached November, gynecological examination and esophagogastrroduodenoscopy were normal. In December plasmocytoma was suspected - and was also ruled out hemato-oncologically. Finally, a CT-scan of the thoracoabdominal region performed in January revealed a peripherally enhancing fluid-attenuation within the left lower lobe of the lung, extending to the subdiaphragmatic space, reaching spleen and left kidney, and concluded at the site of a meanwhile newly formed skin swelling at the left flank (Fig. 1A). Following transfer of the patient to our medical center, thoracic and/or abdominal malignancy could be ruled out clearing way for groundbreaking suspicion of an infection. Laboratory findings at that point in time was showing mild leukocytosis (13.0 $\times$ $10^3/\mu l$), increased C-reactive protein levels (123.3 mg/l),

Fig. 1. A) Pre-therapeutic CT-scan revealing a peripherally enhanced fluid-attenuation within the left lower lobe of the lung, extending to the subdiaphragmatic space, reaching spleen and left kidney, and concluded at the left flank (arrows). B) Abscess drainage revealing purulent discharge with “sulfur granules”. C) Histopathological examination I: Characteristic histological presentation of Actinomycosis with actinomycotic granules composed of radiating filaments with a dense granular core, surrounded by inflammatory cells composed of a mixture of neutrophils and eosinophils (hematoxylin and eosin (H&E) staining, magnification 100×). D) Histopathological examination II: Periodic Acid-Schiff (PAS) reaction confirms consistency with Actinomyces colonies (‘sulfur granules’; magnification 100×). E) Histopathological examination III: A cluster of Actinomyces visualized by Grocott-Gomori Methenamine Silver stain (GMS; magnification 100×). F) Post-therapeutic MRI after one month (arrows indicating the lesion). G) Post-therapeutic MRI after three month (arrows indicating the shrinking lesion). H) Post-therapeutic MRI after six month (absent arrows reflecting the vanished lesion).
thrombocytosis (495 × 10^9/µl), and elevated erythrocyte sedimentation rate (80 mm/h). We consciously decided on an abscess incision at the swollen left flank only in order to avoid an unnecessarily outsized surgical procedure. The abscess drainage revealed a purulent discharge with sulfur granules (Fig. 1B). Histopathological examination demonstrated Actinomycosis-typical luminous strangles ubiquitously (Fig. 1C-E). Additionally initiated microbiological investigation (including introduced 16S rRNA gene sequencing) remained negative in the meantime – in retrospect possibly as a consequence of either prolonged transport time to laboratory or storage in suboptimal media. As a result of the circumstantial evidence of Actinomycosis the patient was treated with high dose Penicillin G (intravenous therapy for 6 weeks, followed by 6 months of oral therapy). Follow-up examinations with a time range of one, three and six month showed a complete resolution of the lesion (Fig. 1F-H).

3. Discussion

Actinomycosis is typically being paraphrased by words like rare, infrequent, and uncommon. This is based on rather outdated epidemiological data, where the reported annual incidence was 1/300,000 persons - data dating as far back as the 1970s [7]. But there is still reason to believe that this data is more or less up-to-date. One reason for this is the global socioeconomic distribution pattern of the disease: due to a lack of knowledge about health issues and deprived access to qualified healthcare providers in developing countries and rural communities, the frequency of Actinomycosis is there tenfold higher than in highly-developed urban areas [8]. The risk factors remain the same during the past half century - only the longitude and latitude of its most frequent occurrence has changed. In simple terms, the impression of rarity and infrequency and uncommonness is linked to the socioeconomic environment in which he or she lives. And as human nature makes you think first of the most common than of the most infrequent (remember: hearing clippy-clop makes you rather think of horses than of zebras, and vice versa), Actinomycosis is hardly recognized at first sight, gaining him a master of disguise status.

In contrast to the rarity of its occurrence, the different aspects of Actinomycosis are widely investigated (Tables 1&2) [1-4]. In addition to this prosaic data we would like to highlight on some of the manifold aspects in a snapshot manner. The highest incidence rate meets middle-aged adults, with males slightly more often affected than women (3:1 ratio) [8,9]. Pre-existing conditions favor an increased susceptibility for an infection due to a weakening of the immune system [2,3,10,11]. The usual course of appearance of symptoms and correct diagnosis is ranged from one to twelve months [12]. In the present case we have to assume that the onset of the disease originates from the respiratory tract. The patient led - apart from being a nicotine addict - a healthy life and did not display any pulmonary Actinomycosis favoring conditions. Whether the living environment with intensified contacts to animals and plants in combination with the immunosuppressive property of smoking was beneficial to the development of the disease is rather vague and remains a matter of speculation. From a microbiological view, the etiology of Actinomycosis is multilayered: (1) the etiological agents of the disease belong to various representatives of diverse genera (i.e. Actinomyces, Propionibacterium, and Bifidobacterium), and (2) usual actinomycotic lesions basically contain concomitant bacteria (of up to ten diverse bacterial species) [3,4]. These synergistic pathogens empower the moderate growth rate and virulence of the Actinomyces and are primary accountable for the early symptoms of the disease. In this light renaming the term “Actinomycosis” (in the singular) into “Actinomyces” (in the plural) seems to be highly appropriate and would accentuate the polyetiological character of the disease instead of attributing to a single pathogen (but yet has to be determined by the microbiological community). Most commonly the diagnosis is made by histopathological examination of excised tissue, as it is more sensitive than culture alone, which remains sterile in more than 50% of cases [4,10,12]. Pathognomonic (but not exclusively proving) for Actinomycosis infection are sulfur granules, which are yellowish (or reddish to brownish) particles of up to 1 mm in diameter representing actinomycete microcolonies, concomitant bacteria tissue reaction material enclosed by clubbed filaments and polymorphonuclear neutrophils [4,8,11]. The reason for frequent failure of culture is previous antibiotic therapy, inhibition of
Causative agents

Actinomycosis genus (family Actinomycetaceae, order Actinomycetales), including Arcanobacterium, Actinobaculum, Mobiluncus, Treponella and Varibaculum with a dynamic genomic evolution of members of the family Actinomycetaceae. Infection can be associated with bacteria of different genera (Actinomyces, Propionibacterium, Corynebacterium, Mycobacterium, Nocardia and Rickettsia) in ≥98% of cases the causative agents are Actinomyces spp. >30 species of Actinomyces (A. israelii [median, ~73.3% of cases], A. naeslundii [median, ~7.0%], A. viscous [median, ~4.8%], A. gerencseriae [median, ~2.0%], A. odontolyticus [median, ~1.4%], A. meyeri [median, ~1.0%]). The causative agent has to be isolated from a sterile body site (i.e. surgical biopsies: deep needle aspirates, pus, sulfur granules) from draining sinuses, tissue biopsy specimens. Avoid swabs, urine, sputum or bronchial washing specimens.

Virulence factors

Actinomycosis has in general both a low growth rate and a low virulence capacity. Most relevant virulence factors: (1) filmbriae (property to bind collagen) and (2) porous biofilm production (impeding the antibiotic therapy of associated infections). Microbes belong in general to the indigenous microflora of human mucous membranes (e.g. bronchial system, gastrointestinal and urogenital tract). Local tissue ischemia (circulatory or vascular diseases, crush injuries, foreign bodies, or necrotizing capacity of simultaneously present additional microbes) is leading to infection spreading. Disease has endogenous origin, therefore neither liable to cause outbreaks nor to be transmitted among humans (except punch actinomyces – human bites or fist-fight injuries).

Clinical specimen

The causative agent has to be isolated from a sterile body site (i.e. surgical biopsies: deep needle aspirates, pus, sulfur granules) from draining sinuses, tissue biopsy specimens. Avoid swabs, urine, sputum or bronchial washing specimens.

Laboratory

Mild leukocytosis, increased C-reactive protein levels and "granules" (blood agar) inhibits overgrowth of concomitant microbes) is leading to infection spreading. Disease has endogenous origin, therefore neither liable to cause outbreaks nor to be transmitted among humans (except punch actinomyces – human bites or fist-fight injuries).

Molecular genotypic techniques:

(1) 16S rDNA sequencing (standard method)
(2) 16S rDNA DNA restriction analysis
(3) Real time Polymerase chain reaction (PCR) with specific primers
(4) Fluorescence in situ hybridization (FISH)
(5) Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry

Culture

test accuracy: (1) appropriate specimens (see above); (2) prompt notification of the laboratory; (3) rapid transport to the laboratory (process time: <15 minutes); (4) prolonged culture on appropriate media.

Culture mediums: chocolate blood agar, brain heart infusion broth, Brucella Blood Agar with hemin and vitamin K1. Use of semi-selective media (i.e. phenylethyl alcohol or mupirocin-metronidazole blood agar) inhibits overgrowth of concomitant organisms and hence increases isolation rates. Classical phenotypic tests (i.e. urease, catalase, fermentation of sugars) may lead to misidentification of species and genus.

Histopathology

Staining: Hematoxylin & Eosin (H&E), Gram stain, Periodic Acid-Schiff (PAS) reaction and Grocott-Gomori Methenamine Silver Stain (GMS). Complex of threads and club-shaped patterns, granulomatous border tissue containing fibroblasts, plasma cells, giant cells and polymorphonucleates. “Sulfur granules”: basophilic central part and radiating border of eosinophilic clubs (H&E staining).

Treatment

(1) 2–6 weeks intravenous Penicillin G therapy (12–24 million U daily) followed by (2) 6–12 months oral penicillin V (or amoxicillin) therapy

Alternative regimen: intravenous amoxicillin/ampicillin followed by oral amoxicillin. Alternative agents: amoxicillin/clavulanic acid, imipenem, ceftriaxone, chloramphenicol, erythromycin, doxycycline and clindamycin (in case of allergy or nonresistance to penicillin).

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Ethical approval

Approval was not required.

Declaration of competing interest

None.

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