

The Role of Chemical Factors in the Inflammation and Infection of Cervico-facial Actinomycosis

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Inflammation is a reflex reaction of the body to the action of some harmful agents, a reaction that manifests itself as a complex of functional and structural modifications of a vasculo-tisular nature, this reaction has occurred in the process of evolution. The intensity of the inflammatory reaction depends on the reactive properties of the body, the location of the inflammatory process, the anatomo-physiological particularities of the damaged tissue, and the conditions in which the inflammation develops. As accurate as dental technique and the practitioner's skill, if the specific conditions of each patient are not taken into account, the benefit medical cannot rise to a higher level, with the final result being compromised by complications with unpredictable risks. Actinomycosis is a specific infection with subacute or chronic evolution, common to humans or animals, caused by microorganisms of the actinomycete family. The location of the affection in the cervico-facial sphere is four times bigger than the rest of the body; the disease is manifested by rough nodules, red in the cheek or sub-maxillary region, fistulas and scars on which new lesions appear. In order to achieve the proposed objectives, we conducted a study on a representative human sample of 158 patients, from the Oral and Maxillofacial Clinic, between 1.01.2013-31.12.2017. Risk factors (gender, age, area, dental anxiety score), our findings are unlikely to define separately the potential for the risk of installing actinomycosis. The level of dental anxiety as well as the general status of the patient are the markers that require the greatest attention from the practitioner in order to prevent a dental problem.

Keywords: damaged tissue, inflammation, infection, actinomycosis, microorganisms.

Human actinomycosis has a ubiquitous (universal) spread and can affect any of the body's structures. Sometimes this disease can become generalized. It is estimated that the incidence of actinomycosis is more than ten times higher in the socio - economically disadvantaged population and with a poor oral hygiene [1-3].

Actinomycetes are microorganisms, usually filamentous, with a length varying between 0.3-1.5 microns, star-shaped (actinic). The lesions are in the form of small blue blooms (similar to pollen fine grains), of variable hardness, which has a network of star-shaped filaments provided at the periphery with more *swollen* areas.

The etiological agent of actinomycosis is *Actinomyces Israelii*, which is part of the genre *Actinomyces*, family *Actinomycetaceae*, *Actinomycetales* order. *Actinomyces Israelii* are radially arranged filaments with branches in T or Y. Other variants of *Actinomyces Israelii* occur in bacillary, cocobacillary and diphtheria forms. At microscopy, *Actinomyces Israelii* are presented as yellow particles of *sulfur granules*. Actinomycetes are anaerobic, microaerophilic, Gram-positive, non-nuclear membrane-coated, but covered with a mucopeptidic wall. These bacteria are opportunistic, pathogenic agents [4,5].

Actinomycetes grow on enriched liquid or solid media. The growth of these bacteria is inhibited by penicillin, tetracycline, erythromycin, cefoxitin, chloramphenicol, cotrimoxazole and other antibiotics; are part of the saprophytic microflora of the oral cavity, found in dental caries, gingival bags and other areas of retention.

The protrusion in the soft cervico-facial parts is done by penetrant cavities, gingival bags or osteomucoselike solutions. In one of those ways, actinomycetes penetrate into the bone, with pyogenic germs commonplace, being

driven towards the soft facial cervico tissue where they produce, in the beginning, suppurations with a non-characteristic aspect [6,7].

Very characteristic bone lesions occur at the bone level.

The lymphatic system is not invaded, but sometimes metastases can be produced by the blood stream by spontaneously opening an abscess into a vein.

Characteristic is the defense of the body by the formation of granulation tissue, which spreads slowly, especially in the surface, but also in the depth of the tissues, which appear as being induced [8-10].

On the surface, at different stages of evolution, abscesses, some in the form of nodules, others already formed, others by fistulization, with surrounding red-purple skin, adhering to the deep layers. The characteristic microscopic lesion is the actinomycotic nodule (Pocet, Berald) consisting of three areas: in the form of grain, whether or not put up as a grinding process; the layer of mononuclear cells depilelioidplasmatic type (Unna). Between the two layers is described a granular degenerascention layer with nuclear, cytoplasmic, fat grains and giant cell debris resulting from phagocytic parasite by epitheloid cells; the peripheral layer, made especially out of mononuclear cells, which in the evolution long processes become fibrous, giving the appearance of sclerosis [11-13].

The center of the nodule lapses, abscises, fistulises spontaneously, while new nodules are formed at the periphery, evolving towards the abscess, affection propagating through contiguity, without observing any tissue, affecting predilectionally the connective tissue. It appears that the diffusion would take place along the cleft

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of the head and neck, the infectious process destroying the fascicles.

Actinomycetes are a very common source, because these bacteria are commonly found in the oral cavity, especially if the person suffers from chronic dental, paradental and tonsillar lesions. Actinomycetes determine clinical manifestations in the oro-cervical, pleuro-pulmonary, mediastinal, liver, abdominal, pelvic, central nervous system, muscular and skeletal regions. The incubation period in actinomycosis is variable, from days to weeks, months, and even years. The onset of the disease is not characteristic and can cause diagnostic difficulties. In the state, actinomycosis slowly evolves, with a general insignificant impairment. The patient may have moderate fever, may lose weight, and a leukocytosis with neutrophilia may be present in the hemoleucogram.

Clinically, actinomycosis takes various forms, from a simple, nodule circumscribed, to swelling, which includes large areas of pseudotumoral tissues and forms. The condition starts slowly, with no characteristic signs. It can occur in the form of a painful nodular swelling with a slow evolution, infiltrating the surrounding tissues, clinging to the center, where the fluctuation is perceived [14,15].

At times, the onset is in the form of an acute perimaxillary infiltration which, after surgical or spontaneous opening, removes the causative factor, continues to evolve chronically, the tissues suffer, and the skin gets a red-purple coloration. Usually the general condition is not affected, than in acutely onset cases.

In the state, the clinical picture is characterized by the appearance of a tough, woody swelling, on which small, oval shaped abscesses are formed, at different stages of evolution. The abscess area teeth are red and between the abscesses the skin thickens and adheres to depth.

On palpation, swelling is a little painful, perceiving areas of hardness that alternate with superficial fluctuation zones at the abscess level.

Regional adenopathy is present only in cases where the disease has started in the form of a non-specific banal inflammation. Trismus occurs in localizations in the masseteric region. In a more advanced period, teguments become purple, they relax, thinning themselves, the abscesses spontaneously open, leaving the fistula, the skin taking the appearance of sprinklers.

Through the fistula, a small amount of characteristic purulent solution, serous, unbound, containing pollen-like white to yellowish grunts. Some of the fistulas advance in depth, making real pockets, more or less deep, others may spontaneously close. At this stage, on a loose tissue basis, along with the fistulas and the scars left after the closure of the fistulas, there may be abscesses in formation or fistulization; the skin has a purple, marbled appearance, showing creases between the fistulas due to very fibrous tissue abundant in the dermis. It is also characteristic that at this stage the general condition is not affected. Sometimes the clinical appearance can be changed by the occurrence of an overinfection acute, common infection when the general condition is altered, and local swelling grows and becomes painful. Chronic patients may have abscesses that fistulate and eliminate a yellowish pus, with a tendency for destructive invasion of neighboring areas.

The acute phase of disease onset, to be followed by the chronic phase, slow. The born lesions can be single or multiple. The middle of the lesion will contain pus, and at the probe will have a fluctuant aspect.

Chemical factors

Chemical factors that cause various diseases are generally a subject of study of pharmacology and toxicology. Chemicals can have different actions and often causes illness.

The occurrence of pathological processes due to the action of chemicals depends on their dose, their solubility in biological humors, their way of administration, and the resistance of the body. One and the same chemical exerts, depending on the dose, a curative action, a toxic effect and even deadly intoxication. Toxic substances include toxins of inorganic and organic origin. Among the chemical factors there are special toxic substances causing pathological phenomena in the body. These are substances that come in contact with the surface of the body-skin or mucous-can cause a number of serious injuries [16-25].

Experimental part

Material and method

In order to achieve the proposed objectives, we conducted a study on a representative human sample consisting of 158 patients from the Oral and Maxillofacial Clinic, studied between 1.01.2013 - 31.12.2017.

It was considered that in this context, particular attention should be paid to the detailed knowledge of all clinical manifestations of actinomycosis, the role of the practitioner being crucial in setting up the therapy. In our quest to be as realistic as possible in the interpretation of the findings, we have detailed each study item: risk factors that are specific to the patient (gender, age, pre-existing general conditions), dental anxiety score; risk factors related to the specificity of interference: type of dental or surgical intervention; special conduct required for dental or surgical intervention.

The analysis of the 158 patients revealed the following distribution on the sex index: 61 women, 38.60%, and 97 males - 61.40%. We can therefore conclude that both men and women have the potential to trigger an actinomycosis, but men are more exposed to trigger an unforeseen medical event.

The most common areas of development of actinomycetes are lesions of the oral cavity, cervical and facial area. These are often confused with neoplasms. The migration of actinomycetes in these areas can cause otitis, sinusitis, which can spread to the central nervous system and to the chest cavity.

Results and discussions

Oral-cervical-facial actinomycosis is the most frequent form of manifestation of the disease; occurs as a result of a dental work or a trauma in the mouth. However, this form of illness may also occur spontaneously in patients with poor oral hygiene.

The main complaints of the patients in study are: fever, pain, and general blood analysis - leukocytosis. The bones become infected with actinomycetes after trauma or haematogenic causes. There were also 6 cases of periostitis (3.79%) and acute osteomyelitis (3 cases - 1.89%). Actinomycetes, through the bloodstream, may cause localized infections in various organs. These infections may be asymptomatic and create difficulties in diagnosis.

In this form of actinomycosis, 14 ill persons (8.86%) complained of chest pain, fever, and a weight lost. The radiological findings differentiate the diagnosis of other diseases (another kinds of pneumonia and cancers). Bronchopulmonary and pleural actinomycosis may present a risk of mediastinal enlargement to the chest wall.

In the central nervous system, actinomycosis is present in the form of a single or multiple abscess. Infection at this level usually occurs by haematogenic dissemination or by direct extension from an oro-cervico-facial actinomycosis. There were 6 cases (3.79%) of meningitis.

The positive diagnosis in actinomycosis was based on clinical diagram (symptoms) and on paraclinical data. The diagnosis was supported both on clinical and laboratory data. Any fistula was suspected in actinomycosis, which cannot be attributed to any specific cause (periapical dental process-11 cases (6.96%) , included teeth-17 cases (10.75%) , suppressed cysts - 28 cases (17.72%) , superinfected fracture - 5 cases (3.16%), osteomyelitis - 3 cases (1.89%) , or any perimaxilar absces or flegmon which, after incision, drainage and suppression of the causal factor continue to evolve subacutely.

The negative microbiological examination does not avoid the diagnosis of actinomyose (139 cases (87.97%) and 19 cases have not been examined.

Histopathological aspects showed the presence of filamentous microorganisms, Gram-positive organisms and sulfurous-like granules.

Differential diagnosis is made with acute perimaxial inflammatory diseases, with fistulised osteitis and osteomyelitis with cervico-facial dermatoses, with specific infections, with suprainfected tumors of the skin, and of the cervico-facial soft parts.

The results of the blood tests were unspecific; 5 cases (37.34%) with signs of anemia, mild leukocytosis - 18 cases (11.39%) , low VHH - 27 cases (17.08%) , higher values than normal C reactive protein - 31 cases (19.62%) . The concentration of alkaline phosphatase was increased in the liver actinomycosis 13 cases.

The imaging aspects are unspecific in the early stages of the disease and have no diagnostic value, as these aspects can also be found in other local inflammatory or neoplastic processes (especially in the case of pulmonary tumors). The results of computerized tomography or nuclear magnetic resonance provide nonspecific information about an abscess or phlegmon, but indicate exact anatomical localization that facilitates the production of tissue samples. In the advanced stages of actinomycosis, the imaging aspects show infiltrations of neighboring tissues along the tissue planes, with the formation of sinuous traits, characteristic but non-specific, for this infectious disease.

Diagnostic certainty required the direct isolation of actinomycetes in a biological sample or from the sulfur granules. The most suitable biological samples are pus, tissue or sulphurous granules. Actinomycetes can be grown on selective agar media under anaerobic conditions at 37 ° C for up to three weeks.

New methods of molecular genetics are applied in research laboratories. The therapy is complex, long-lasting, requiring both clinical and laboratory data to be followed. It has taken into account the location of the infection, as well as other pathogens that may be present, even if their role in the pathogenesis of actinomycosis is unclear. The actinomycosis patient requires a long-term therapy with high doses of antibiotics. In order to destroy actinomycosis, daily doses of antibiotic are administered intravenously for 2-6 weeks; then, for 6-12 months the antibiotic is administered per oral.

The preparations used for the therapy of actinomycosis are Penicillin, Tetracycline, Clindamycin, Erythromycin, Minocycline, Generation I Cephalosporins, Imipenem, Ceftriaxone, etc. It is necessary to perform the antibiotic before initiating the therapy.

The therapy scheme included a β -lactamide and $\hat{\alpha}$ inhibitor -lactamase as clavulanic acid or tazobactam, with added protection against possible $\hat{\alpha}$ -lactamase -producing microorganisms e.g. *S. aureus*, Gram negative anaerobes. May many studies have used short antibiotic therapies. Actinomycosis oro - facial can be healed by short therapy of antibiotics in addition with a surgical drainage.

Although antibiotics are the basis of actinomycosis therapy, in some cases where an extensive necrotic tissue is present, or sinuous or fistula tracts, it was necessary the surgical resection of the infected tissues - 64 cases (40.50%) .For these cases the drain has failed through the tissue suction of large abscesses.

Surgical approach is a necessity that needs to be evaluated individualized for each patient; it depends on the load of the initial disease, the success of surgical resection, and the patient's response to therapy.

It is considered the healed condition when the teguments become afflicted, and the local inflammation processes have completely resolved. The evolution and severity of actinomycosis is dependent on the location of the infection.

Most patients are anxious and frightened; they make efforts to self-conceive that the disease does not exist or, unconsciously, develop elaborate defenses to divert attention from the real problem, which they do not perceive as serious or at vital risk. Whatever the patient's attitude, the physician should investigate, specify and consider the area on which a pathological condition occurs.

The superficiality of approaching a healthy patient can lead to the escape of important aspects, with a predictive role in triggering an actinomycosis. An informational history has to be more than an orderly list of symptoms. There is always something to be gained by listening to patients and observing the way they talk about their symptoms. Voice inflections, facial expressions and attitudes can contain important clues about the significance of symptoms for the patient. By listening to the history, the physician discovers not only the details of the disease but details about the patient, too.

Conclusions

The most common areas of development of actinomycetes are lesions of the oral cavity, cervical and facial area. These are often confused with neoplasms.

The oro-cervico-facial actinomycosis occurs as a result of a dental work or a trauma in the mouth. However, this form of illness may also occur spontaneously in patients with poor oral hygiene.

The more predictions in the history of the patient are found in the actinomycosis, the more urgent it is to approach a particular course of action in the sense of triggering the disease. Antibiotic treatment will be sufficient if the patient stays stable, and clinical symptom diminishes progressively in intensity.

In some cases, surgical treatment supported by aggressive drug therapy may be instituted.

Chronic patients may have abscesses that fistulate and eliminate a yellowish pus, with a tendency for destructive invasion of neighboring areas.

A diagnosis of certainty requires the direct isolation of actinomycetes from a biological sample or from the sulphurous granules. The most suitable biological samples are pus, tissue or sulphurous granules.

References

1.ARDEHALI H., BUETENS O., GARCIA DA - Thoracic actinomycoses and liver abscesses. The Osler Medical Journal, 2000, 6: 1-4

2. AUREL IVAN, Epidemiology of communicable diseases treaty, Iasi, Polirom Publishing House, 2002;
3. BONACHO I, PITAS, GOMEZ-BESTEIRO MI. The importance of the removal of the intrauterine device in genital colonization by actinomyces. *Gynecol Obstet Invest* 2001 ; 52: 119-2 .
4. BOWDEN GH, GOODFELLOW M. - Actinomyces in Topley & Wilson's Principles of Bacteriology , Virology and Immunity, under editorial to Parker MT and Duerden BI, Ed. Hodder & Stoughton - London, Melbourne, Auckland, 1990, Vol. II, pp. 32-40
5. GARNER, JP, MACDONALD, M., KUMAR, PK., Abdominal actinomycosis . *Int. J. Surg.*, 2007, 5: 441.
6. GILBERT, DN, MOELLERING, RC, ELIOPOULOS, GM, SANDE, MA., The Sanford guide to antimicrobial therapy. 38th ed , 2008.
7. HALL, V., Actinomyces, Collecting evidence of human colonization and infection. Mini-review. *Anaerobe*, 2008, 14: 1.
8. HALL, V., Anaerobic actinomycetes and related organisms. In Principles and Practice of Clinical Bacteriology, 2nd ed., Under the editorial Gillespie's SH Hawkey PM, Chichester (UK, Wiley), 2006, p. 575-586.
9. ISRAEL, J., Neue Beobachtungen auf dem Gebiete der mykosen des Menschen. *Virch Arch. Path. Anat.*, 1878, 74:15.
10. RUSSO TA. Agents of actinomycosis . In: Mandell GL, Bennett JE, Dolin R, eds. Principles and Practice of Infectious Diseases. 7th Ed. Elsevier Churchill Livingstone, 2010: 3209-19.
11. SMEGO RA JR, FOGLIA G. Actinomycosis. *Clin Infect Dis* 1998 ; 26: 1255-661; quiz 62-3.
12. TEDESCHI, A., DIMEZZA, G., D'AMICO, O., ERMANN, A., MONTONE, L., SICILIANO, M., COBELLIS, G. - A case of pelvic actinomycosis presenting as a cutaneous fistula. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 2003, 108: 103.
13. WESTHOFF, C. - IUDs and colonization or infection with Actinomyces . Review article. *Contraception* 2007, 75: S48.
14. WOO, PCY, FUNG, AMY, LAU, SKP, TENG, JLL, WONG, BHL, WONG, MKM, HON, E., TANG, GWK, YUEN, KA . - Novel Actinomyces species isolated from a patient with pelvic actinomycosis . *System. Appl. Microbiol.* , 2003, 26: 518.
15. ANTOHE M., ANDRONACHE M, FEIER R, STAMATIN O, FORNA NC, Statistical studies regarding therapeutic approaches for edentulous social clinical cases in student, practical stages, *Romanian Journal of Oral rehabilitation*, 9(2), 2017, 94-99
16. POPESCU, E., AGOP FORNA, D., EARAR, K., FORNA, N.C., Bone substitutes used in guided bone regeneration technique review, *Mat. Plast.*, 54, no.2, 2017, p. 390-392
17. ANTOHE, M.E., AGOP FORNA, D., DASCALU, C.G., FORNA, N.C., Implications of digital image processing in the paraclinical assessment of the partially edentated patient, *Rev. Chim. (Bucharest)*, 69, no.2, 2018, p.521-524
18. CHECHERITA, L., BELDIMAN, M.A., STAMATIN, O., et al. Aspects on structure of materials used for different types of occlusal splints. *Rev. Chim. (Bucharest)*, 64, no.8, 2013, p.864-867
19. ANTOHE, M.E., AGOP FORNA, D., DASCALU, C.G., FORNA, N.C., The importance of observing the aesthetic requirements in partial edentulous rehabilitation - implications in medical-dental training, *International Journal of education and information technologies* Volume: 10, p. 199-203, 2016
20. GRADINARU, I., IGNAT, L., DASCALU, C.G., SOROAGA, L.V., ANTOHE, M.E., Studies regarding the architectural design of various composites and nanofibres used in dental medicine, *Rev. Chim. (Bucharest)*, 69, no.2, 2018, p.328-331
21. ASAFTEI, I.V., SANDU, I.G., MIHAIL, L., ET AL, Conversion of industrial feedstock mainly with butanes and butenes over B-HZSM-5 and Zn-HZSM-5 modified catalysts, *Rev. Chim. (Bucharest)*, 66, no.3, 2015, p.336-341
22. MATEI, M.N., EARAR, K., TRINCA, L.C., Degradation characteristics of poly-tetrafluoroethylene coatings on stainless steel orthodontic wires immersed in tuna fish derived products, *Rev. Chim. (Bucharest)*, 67, no.4, 2016, p.800-807
23. MATEI, M.N., CHISCOP, I., EARAR, K., et al., Evaluation of corrosion resistance of NiTi Nb orthodontic wires in tomato juice, *Rev. Chim. (Bucharest)*, 66, no.12, 2015, p.2009-2012
24. ROMANEC, C., DRAGOMIR, B., BICA, C., The prophylactic orthodontic treatment with removable appliances in children, *Rev. Chim. (Bucharest)*, 69, no.3, 2018, p.693-696
25. MARECI, D., EARAR, K., ZETU, I., Comparative electrochemical behaviour, of uncoated and coated Ni Ti, for dental orthodontic wires, *Rev. Chim. (Bucharest)*, 52, no.2, 2015, p., 150-153

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