Perianal actinomycosis: diagnostic and management considerations
A review of six cases

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SUMMARY
Introduction — Primary anal actinomycosis of cryptoglandular origin, mainly due to Actinomyces israelii, a specific and rare cause of anal supplicative disease, needs to be recognized because it can be cured using specific treatments.

Method — Data were reviewed from 6 patients with actinomycotic anal abscesses of obvious cryptoglandular origin observed in a single proctology unit between 1983 and 2000. Therapeutic management included conventional surgical treatment of anal sepsis followed by a specific oral antibiotic therapy maintained until the surgical wound had completely healed.

Results — All but one of the patients were men (median age, 53 years). All abscesses, except one, were indolent. No patient presented macroscopic “sulphur granules” in the pus, but one presented “watery pus”. The diagnosis was established by histological study of the surgically excised tissue or by anaerobic culture of the pus. In the one HIV-positive patient, an uncommon organism was isolated: Actinomyces meyeri. Two cases of recurrence were observed without evidence of Actinomyces infection.

Conclusion — Actinomycosis should be suspected particularly in indolent anal suppuration. The absence of macroscopic “sulphur granules” does not mean this diagnosis can be ruled out. Careful histological examination of the excised tissue and appropriate anaerobic cultures of pus should be carried out to achieve complete eradication of this rare, but easily curable disease.

RÉSUMÉ
Actinomycose périanale : diagnostic et prise en charge. À propos de six cas
Introduction — L’actinomycose anale primitive de localisation cryptoglandulaire, principalement due à Actinomyces israelii, cause spécifique et rare de suppuration anale, nécessite d’être reconnue, car elle relève d’un traitement spécifique.

Malades et méthodes — Les données, concernant 6 malades atteints d’un abcès anal actinomycotique d’origine cryptoglandulaire pris en charge dans un unique centre de proctologie entre 1983 et 2000, ont été analysées. La prise en charge thérapeutique comprenait le traitement chirurgical classique d’une suppuration anale, suivi d’une antibiothérapie per os maintenue jusqu’à la cicatrisation complète de la plaie chirurgicale.

Résultats — Tous les malades, sauf un, étaient des hommes (âge moyen de 53 ans). Tous les abcès, à l’exception d’un, étaient indolores. Aucun malade ne présentait dans le pus de « grains sulfureux » macroscopiques, l’un cependant présentait un « pus aigue ». Le diagnostic était établi par l’analyse histologique de la pièce d’excision chirurgicale ou sur la culture en anaérobie du pus. Chez le seul malade positif pour le VIH, un microorganisme peu commun était isolé : Actinomyces meyeri. Deux cas de récidive étaient observés, sans preuve d’une infection à Actinomyces.

Conclusion — Une actinomycose doit être particulièrement suspectée devant une suppuration anale indolore. L’absence de « grains sulfureux » macroscopiques ne doit pas faire rejeter ce diagnostic. Une étude histologique attentive des tissus excisés et des cultures adaptées en anaérobie du pus doivent être mises en œuvre pour obtenir l’éradication complète de cette maladie rare, mais aisément curable.

Introduction
An actinomycotic anal infection of cryptoglandular origin is a specific and extremely rare cause of anal suppuration [1-5]. Recognizing it is important because surgical treatment and specific antibiotic therapy are mandatory to achieve complete eradication of actinomycotic infection and to avoid multiple inappropriate surgical procedures. We report on 6 cases diagnosed and treated in our unit from 1983 to 2000. The aim of this retrospective study was to evaluate possible changes in clinical and microbiological features of this entity, its current incidence and main diagnostic and therapeutic advances.

Patients and methods
From January 1983 to December 2000, patients presenting anal actinomycosis were diagnosed on the basis of one of the two following criteria: a positive anaerobic culture of Actinomyces species or the presence of spherical clusters of filamentous hematoxyphilic organisms in the excised tissue stained with hematoxylin and eosin and also stained positively with Gram stain, Grocott’s methenamine — silver nitrate stain.

Case notes and follow-up data of the patients diagnosed were reviewed and clinical features, diagnostic aspects, HIV status and treatment details were analyzed.

Results
Out of the 2482 patients operated on for anal fistulas or abscesses during the period under review, 6 presented an actinomycotic abscess (one patient in 1983, 1990, 1995 and 2000, respectively and two cases in 1994). There were 5 males and
patients came from France. In the single case involving a woman [case 3] she had not been fitted with any kind of intrauterine device. Only one male homosexual patient [case 2], was found to be HIV positive, with a normal CD4 count. No patient had previously undergone surgery. In 5 patients the predominant symptom was a slowly growing indolent perianal or ischioanal mass. Only one patient [case 5] complained of anal pain caused by a subacute ischioanal abscess. Anal discharge of pus was observed in the HIV-positive patient (high intermuscular abscess with mucosal ulceration at the primary internal opening located on the dentate line). Mean time interval from the beginning of symptoms to the date of diagnosis was 1 year (range: 3 weeks to 4 years). In 5 patients, a primary internal opening located on the dentate line and a fistulous tract were identified during the first operation and in one case [case 3] during a second operation 14 months later because of controlateral recurrence of abscess but without histological or bacteriological signs of actinomycotic infection. No patient exhibited macroscopic small yellow granules (“sulfur granules”) classically described in the pus. One patient [case 1] exhibited a thin, serosanguinous fluid after incision. The systematic histological examination of the excised tissue and specific bacteriologic analysis (not performed in routine practice, except in abnormal presentation of anal suppuration, particularly if indolent) allowed us to move toward a diagnosis (table I). Fistulous tracts were classified as low trans-sphincteric (N = 1), high trans-sphincteric (N = 2), high inter-sphincteric (N = 1), or horseshoe abscesses with high trans-sphincteric fistulous tract (N = 2). The high inter-sphincteric abscess (N = 1) was laid open. The other abscesses were widely incised and drained (N = 5); the low fistulous tract was excised (N = 1), and a rubber seton placed through the high trans-sphincteric fistulous tract was identified during the first operation and in one case [case 3] during a second operation 14 months later because of controlateral recurrence of abscess but without histological or bacteriological signs of actinomycotic infection. No patient exhibited macroscopic small yellow granules (“sulfur granules”) classically described in the pus. One patient [case 1] exhibited a thin, serosanguinous fluid after incision. The systematic histological examination of the excised tissue and specific bacteriologic analysis (not performed in routine practice, except in abnormal presentation of anal suppuration, particularly if indolent) allowed us to move toward a diagnosis (table I). Fistulous tracts were classified as low trans-sphincteric (N = 1), high trans-sphincteric (N = 2), high inter-sphincteric (N = 1), or horseshoe abscesses with high trans-sphincteric fistulous tract (N = 2). The high inter-sphincteric abscess (N = 1) was laid open. The other abscesses were widely incised and drained (N = 5); the low fistulous tract was excised (N = 1), and a rubber seton placed through the high trans-sphincteric fistulous tract was gradually tightened (N = 4). All patients but one received oral antibiotic therapy until the surgical wound was completely healed (table II). Evolution was favourable with normal continence during the follow-up (average of 3.6 years after complete healing). One patient was lost to follow-up [case 5] before complete healing; he underwent surgery in another hospital, 6 years later, for an anal abscess of an imprecise localisation, without obvious evidence of Actinomyces involvement (reurrence or new abscess?)..

**Discussion**

The genus *Actinomyces* (A.) consists of a heterogeneous group of Gram positive, non spore-forming, non acid-fast, mainly facultative anaerobic or microaerophilic rods with various degrees of branching. It has undergone considerable expansion in recent years, with a plethora of new species defined and disease correlation among genospecies [6, 7]. Although *A. israelii* is the key species responsible for classical actinomycosis, other agents are involved: *A. meyeri*, *A. naeslundii*, etc. [7, 8]. In an anaerobic environment the *Actinomyces* species grow in tissues as clusters of branching bacterial filaments. When purulent drainage is present, these clusters may be observed macroscopically as small, yellow, “sulphur granules”. These sulphur granules in histological specimens are mainly reported with *A. israelii* and *A. meyeri* [8]. Anaerobic actinomycosis is thought to begin in the Hermann and Desfosses anal glands and female genital tract and their pathogenicity is usually low [9]. There are three main loci of infection: cervicofacial, after dental infection or manipulation, thoracic, associated with aspiration, and abdomino-pelvic. The pathogenesis of anal actinomycosis is not thoroughly understood, but the source of the infection comes from the gastrointestinal tract. What occasionally converts this anaerobic saprophyte into a pathogen is not clear. It appears incapable of penetrating normal mucosa; hence the development of an actinomycotic infection is supposed to be preceded by inoculation at a break in this mucosal barrier due to pre-existing infection and tissue injury. Indeed, nearly all cases of actinomycosis yield a variety of other microorganisms on culture [1-5, 9], which may be essential in promoting *Actinomyces* infections by reducing local oxygen tension and inducing anaerobiosis inhibition of phagocytes [10, 11], thus allowing the anaerobic bacteria to proliferate. However the possibility that *Actinomyces* merely colonize pre-existing anal gland suppuration cannot be dismissed; this hypothesis would make *Actinomyces* the predominant pathogen of a polymicrobial infection.

Anorectal actinomycotic suppurations were probably more frequent in the pre-antibiotic era [12, 13]. Actinomycosis, although rare, should be considered in the spectrum of disorders involving the anorectal region (acute abscess, chronic abscess, fistula, rectal stenosis mimicking carcinomatosis) of immunocompetent populations and HIV infected patients, even if the prevalence of actinomycosis in the HIV infected population remains low [1-5, 10, 14-27].

At present, since the use of penicillin, primary anoperineal actinomycosis is a rarity with, to our knowledge, only 32 documented cases in the literature [1-5, 10, 14-25, 28], including only 7 cases of obvious cryptoglandular origin [1-5]. The sex ratio (only men), median age (58 years) and duration of anal supp-

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NP: not performed; * controlateral recurrence.
Perianal actinomycosis

acts before diagnosis (2 weeks to 40 years) in the literature are in accordance with our reports. As in our series, one patient was also HIV positive [4]. In the cases previously reported, 6 patients had a history of anal surgery prior to diagnosis [1, 2, 4, 5]; two of these patients had undergone three [5] and four [2] incisions and drainage of anal abscesses, respectively; three of these patients had multiple secondary perianal orifices [1-5]. In contrast, none of our 6 patients had been previously operated on. As in our series, all patients except one [3], presented indolent anal suppuration. Macroscopic “sulphur granules” in the pus were observed before or during the surgical operation in 4 previously reported cases [1, 2, 4], while in contrast none of our cases exhibited these yellow granules. The thin, serosanguinous fluid observed in one of our patients has been previously reported by others [2, 4]. For Fry et al. [4] when “watery pus” is observed in an anal abscess this should be an indication of an unusual infection.

Ideally, the diagnosis of actinomycosis should require both sulphur granules to be demonstrated in purulent materiel or infected tissue and a positive anaerobic culture. Indeed, on the one hand isolation of Actinomyces filamentosus alone is theoretically insufficient to make a diagnosis because they may represent a mere colonization without active infection [9]; on the other hand, although sulphur granules are highly suggestive of actinomycosis, they are neither a consistent finding nor a pathognomonic sign, as they can also be observed in other infections, notably nocardiosis [9, 17, 29]. In actinomycotic tissue sections stained with hematoxylin and eosin, sulphur granules are round or oval basophilic masses with a radiating arrangement of eosinophilic terminal “clubs”. Tissue Gram staining revealed dense clusters of branching Gram positive organisms extending radially from the periphery of the granules. These organisms also stained positively with Grocott’s methenamine – silver nitrate stain. Nocardia stained negatively with Ziehl staining.

Bacterial isolation of Actinomyces is often difficult for several reasons: culture in anaerobic conditions, slow growth (7 to 10 days) optimal at 37°C, the need for an enriched media, bacterial overgrowth, and the frequency of previous antibiotic treatment on this organism which is sensitive to the latter. These microorganisms were isolated in only 23 and 25% of cases, respectively, in Brown and Fiorino’s series [30, 31], in only 1/3 of cases of putative actinomycosis reported in HIV infected patients [9], in 4 of the 6 cultured cases of primary actinomycosis anal suppuration of cryptoglandular origin [1-5], and in 2 of the 5 cultured cases in our series. When both histological study and anaerobic cultures were performed, diagnosis of primary actinomycotic anal sepsis in the literature was based on pathological analysis in 3 cases and on anaerobic cultures in the 4 other cases [1-5], and in 4 and 2 cases respectively in our series.

The above information highlights the diagnostic dilemmas that actinomycosis creates for the clinician: only some patients fulfill both criteria [7].

In clinical practice, we agree with all authors that, in the absence of bacteriological evidence, the histopathological characteristics of the materials obtained should be accepted as a key element for diagnosis when the clinical presentation suggests this and after other specific anal suppurations of cryptoglandular origin, especially Crohn’s disease and tuberculosis, have been excluded [32].

We have found only 43 well-documented infections due to A. meyeri in the literature; the gastrointestinal tract (except liver) was never involved [11, 23, 29, 33-43]. Accordingly our HIV positive patient seems to be the first report of an anal abscess caused by A. meyeri. A similar anal sepsis of cryptoglandular origin due to the uncommon A. naeslundii was also reported in a homosexual man infected with the HIV [4]. Out of 2482 patients who were operated on for anal fistulas or abscesses over an 18-year period, only one, hospitalized in 1990, was co-infected with HIV and A. meyeri. He was immunocompetent, and the local suppuration did not display specific clinical signs or symptoms. On the other hand the number of surgical interventions carried out in our unit in patients infected with HIV gradually increased up to 1995 then decreased and fell from 10.8% to 3% of patients who underwent surgical treatments for fistulas or abscesses. Review of the literature revealed only 26 well-documented cases of actinomycosis in HIV positive and AIDS patients [4, 9, 44-49], including 2 cases of anal sepsis [4, 38]. The prevalence of actinomycosis in the HIV infected population seems low and HIV infection does not appear to predispose to actinomycotic infection [9].

As with all other forms of infection, anal actinomycosis necessitates specific antibiotic therapy. The first line antibiotic is penicillin or a penicillin-related antibiotic. Classically, intravenous penicillin G (20 MU/day) is recommended for 4 to 6 weeks, followed by oral amoxicillin for up to one year [50, 51]. In reality, the exact duration of therapy depends on the site and severity of the disease, and probably also on the immune status of the patient [9, 11, 29, 51]. For patients allergic to penicillin, tetracycline and erythromycin are suitable alternatives [50]. Imipenem, clindamycin and ceftriaxone have also been recommended [5, 50, 51]. Surgical removal of actinomycotic fistulas is also recommended as standard procedure (no case of a fistula healing after antibiotic therapy alone has been published).

Our 6 patients were treated with oral ampicillin, amoxicillin, an amoxicillin-clavulanic acid combination or tetracycline for 4 weeks to 19 months until, except for one patient, the surgical wound had completely healed (table II). After correct surgical treatment, no recurrence was observed in the 5 patients with followed-up data (average of 3.6 years). One patient was lost to follow-up before complete healing of the surgical wound, and before the end of the antibiotic therapy: an anal abscess (no information on its localization around the anal margin) occurred 6 years later, was treated in another hospital, but without reappearance of Actinomycosis (reurrence or new abscess)? In the seven cases previously reported oral antibiotics (penicillin, ampicillin, tetracycline, or erythromycin) were also maintained until the patients were clinically cured; the median duration of antibiotic treatment was 10 weeks (range: 3-15). Three patients had no evidence of relapse after a follow-up period of 20 months to 7 years [3-5], but 4 patients were lost to follow-up immediately after healing [1, 2, 4]. Antibiotic therapy combined with surgery is necessary to achieve complete cure of abscesses and fistulae-in-ano of cryptoglandular origin due to Actinomyces [1-5]. Firstly, in one of our cases (case 3), as in the one of Gumbs et al. [3], eradication of Actinomyces was first obtained by oral ampicillin therapy, but a relapse occurred in the form of a horseshoe fistula, because surgical treatment of the cryptoglandular origin of the suppuration had not been performed in the first instance. Secondly, in one of the two cases of Fry et al. [4] the exclusive, appropriate surgical approach achieved healing but recurrence in two months later led to diagnosis of infection by Actinomyces. This was effectively treated with a suitable antibiotic alone (oral penicillin). No further recurrence was observed during the 7-year follow-up.

In conclusion, physicians should be aware of the possibility of actinomycosis as the cause of generally indolent anal abscesses. The absence of previous surgery and/or of macroscopic “sulphur granules” in the pus and/or of multiple perianal secondary external orifices does not exclude the diagnosis which is made on post-operative histology or bacterial isolation. So histological analysis of all excised tissue from fistulas and abscesses should be carried out routinely; a specific request by the clinician to the microbiology and pathology laboratories to isolate Actinomyces is necessary. The outcome for actinomycotic anal sepsis is excellent when appropriate surgical procedures and oral antibiotic therapy are combined. Antibiotic treatment should be continued until the surgical wound is completely healed.
REFERENCES