Case study

Amazon and Brazilian polyherbal preparation for treatment of necrotizing fasciitis

ABSTRACT

Antibiotic resistance is becoming a serious challenge to the public health, particularly in the treatment of infectious diseases. We report one case of a leg with severe necrotizing fasciitis (flesh-eating disease), which was at risk of being amputated due to infection, before and after treatment with medicinal plants which have empirical broad-spectrum antibiotical and anti-inflammatory properties. All the usual medical attempts with conventional antibiotics failed and we had to act rapidly in order to cure the infection and prevent the amputation. Regardless of the presence of risk factors, necrotizing fasciitis is a condition with a high mortality rate.

The prescription of such medicinal plants was initiated as soon as possible and the lesion skin was completely cured. One of these is *Psidium guajava* leaves which has antibiotic, anti-inflammatory, anti-viral (against coronavirus) and anti-fungal properties.

These results show that it is possible to introduce medicinal plants as adjunctive therapy or as the main therapy for the treatment of necrotizing fasciitis.

Key words: coronavirus, phytotherapy, wound, necrotizing fasciitis, infectious disease, antibiotic resistance.

INTRODUCTION

Necrotizing fasciitis (NF) is an uncommon complicated infection (3 cases per 100,000 people-year) of the soft tissues, often associated with life-

threatening conditions due to severe sepsis, if early medical treatment is not performed (1, 2).

Bacterial resistance against antibiotics of natural, semi-synthetic origin or purely synthetic compounds such as the fluoroquinolones or those which do not even enter the cells such as vancomycin has been reported (3).

The treatment of infectious diseases using medicinal plants has been carried out by the mankind since ancient Egypt. Sometimes, these natural medications serve as therapeutic alternatives or, in some cases, as the only effective treatment. A combination of nine plants: *Psidium guajava* (guava tree), *Nicotiana tabacum* (tobacco), *Anacardium occidentale* l. (cashew tree), *Caesalpinia ferrea Martius* (Brazilian Ironwood), *Schinus terebinthifolius Raddi* (aroeira or Brazilian pepper tree), *Hymenaea courbaril L.* (jatobá), *Rubus sellowii.* (black capinuriba or Brazilian Rubus), *Ischnosiphon polyphyllus* (arumã), *Jatropha gossypiifolia* (Pinhão-Roxo or Pião-Roxo) was used to design a protocol in order to regress and cure necrotizing fasciitis. This decoction has shown antibiotic and anti-inflammatory properties with no side effects.

CASE REPORT

A 61-year-old white female non-diabetic patient with necrotizing fasciitis on her lef leg. On November 16th, 2017, she consulted a physician who prescribed her ciprofloxacin 500mg (1 tablet – twice a day or b.i.d. = "bis in die" in Latin), dipyrone or metamizole 1 gram (1 tablet - 4 times a day or q.i.d. = "quater in die" in Latin), and clindamycin 300mg (1 tablet - 4 times a day or q.i.d.).

Figure 1 – Necrotizing fasciitis on left leg before starting the treatment with conventional antibiotics.

The treatment was prolonged during 60 days (until January 15th 2017) without any positive results (after 2 months the wound was worse). The patient complained of pain in her belly. Antibiotic causes changes in intestinal flora, which justifies such pain. Then, the physician suggested her the debridement technique using fly larvae (*Crysomya megacephal*). Neither treatment produced regression of the necrotizing fasciitis. The patient noticed that the lesion was worse (figure 2). As final solution another physician told her that the leg would be amputated.

The patient stopped taking antibiotics. Desperate, she came to our laboratory with her medical report. Immediately, we prescribed her probiotics, during 1 week, in order to restore the intestinal flora. After we examined her leg, we prescribed the following:

Solution 1 (topical use only) 7:00 AM, 10:00 AM, 1PM, 3PM, 5PM, 7PM, 9PM

Jatropha gossypiifolia (popular names: Pião-Roxo or Pinhão-Roxo). Boil 50 grams in water (1000 ml) for 5 to 10 minutes. Percolate this solution. Wash the wound with this solution. Put leaves (clean and sanitized) on the wound. Place gauze over the leaves for 2 hours. After 2 hours remove the gauze.

Solution 2 (topical use only) 9:00 AM:

A combination of *Nicotiana tabacum* (tobacco) leaves (50 grams), naphthalene (mothballs) (100 grams), *Libidibia ferrea*, formerly *Caesalpinia ferrea* (popular name: Brazilian Ironwood) leaves (50 grams) in water (1,000 ml). This mixture was boiled during 10 minutes and then percolated. After cooled, this decoction was used to wash the wound in the morning.

Note: Tobacco leaves cause burning sensation and naphthalene have the function of softening this sensation.

Solution 3 (topical use only) 1:00 PM:

Anacardium occidentale (cashew tree bark) (50 grams) + *Psidium guajava L.* (guava tree bark) (50 grams) in water (1,000 ml). Boil the water and percolate the solution (decoction). Use this "tea" to wash the wound.

Solution 4 (topical use only) 5:00 PM:

Schinus terebinthifolius (common names: Brazilian peppertree, aroeira, rose pepper) (50 grams) and *Hymenaea courbaril* (common names: jatobá, courbaril, Stinkingtoe, and West Indian locust) (50 grams) in water (1,000 ml). Boil the water and percolate the solution (decoction). Use this "tea" to wash the wound.

Solution 5 (topical use only) 9:00 PM:

Rubus sellowii (black capinuriba) (50 grams) and arumã bark (50 grams) in water (1,000 ml). Boil the water and percolate the solution (decoction). Use this "tea" to wash the wound.

Repeat this procedure between washes with solutions from other plants.

Solution 6 (oral use only) 1:00 PM:

Ten guava tree leaves (well washed) in 250 ml of water. After boiling ten minutes, wait for it to cool down and it is ready to be drunk.

The intense pain, disproportionate to the phlogistic signs present, and the rapid recovery of bullous lesions, with an area of necrosis of deeper tissues and fascia, reinforce the hypothesis of necrotizing fasciitis (4).

After three days of treatment the intense pain subsided. After 15 days of treatment, an improvement was noticed (figure 3A) and 23 days of treatment (lesion was completely cured).

Figure 2: after 60 days of antibiotic treatment (clindamycin and ciprofloxiacin) and debridement the lesion got worse.

A **B**

Figure 3:

A) Skin lesion after 15 days of phytotherapy treatment (left photo) on February 1st 2018;

B) 28 days of treatment (February 13th 2018 - lesion completely cured) (right photo).

DISCUSSION

The decreasing reduction of antibiotics efficacy and the increase of multidrug-resistant microoganisms are causing a major scourge to the global public health. Natural products from Brazilian and Amazon plants have been the resource of new compounds with antimicrobial effects.

As most cases of necrotising fasciitis are polymicrobial, empirical broad spectrum antibiotic coverage should be administered (5).

As the medical report of the patient was not describing the type of necrotizing fasciitis, we had to prescribe plants that produce compounds with antibiotic effect against the microorganisms which cause the main types (I, II and III): *Clostridium perfringens*, *Staphylococcus aureus*, *Escherichia coli*, haemolytic group A streptococcus, staphylococci including methicillin resistant strains/MRSA.

Due to the urgency of the case, our strategy was to combine 9 plants that have a broad bactericidal, fungicidal and anti-inflammatory effect. Two of them (Guava and cashew) in addition to the antibiotic effect against various bacteria, have effect against *Clostridium ssp*. Since two broad-spectrum antibiotics (clindamycin and ciprofloxacin) were tested for 60 days and no success has been achieved, we assume that we could be facing a necrotizing faceitis type III (which is caused by Clostridium ssp).

Due to high risk of amputation, the "war strategy" was to prescribe as many plants as possible in order to obtain the widest antimicrobial effect; so the wound could be healed in a short period of time. The explanation for prescribing such plants is the following:

Jatropha gossypiifolia (Family: Euphorbiaceae) - Although is a native plant from Brazil, it has also been cultivated in many parts of Singapore, Burma, and India, and used in many countries as a popular medicine for various diseases. **Jatrophenone** (macrocyclic bioactive diterpene) is an isolated compound from this plant with significant antimicrobial activity against *Staphylococcus aureus* and its activity was comparable to that of the standard compound, penicillin G. (6)

Nicotiana tabacum – the plant, now raised for commercial tobacco production, is from South America. Researchers have been reported that antibacterial property could be due to pyridine, 3- (1-methyl-2-pyrrolidinyl) - (S) with a broad spectrum of activity against several microorganisms including *Staphylococcus aureus* (7, 8) *Candida albicans* and *Streptococcus pyogenes* (9).

Libidibia ferrea **(formerly *Caesalpinia ferrea*)** - In the Amazon region of Brazil; the fruit of this plant is widely used as an antimicrobial and healing medicine for infections (10). Some compounds are known to be responsible for biological activity, such as saponins and phenolic (11), catechins which are active against Gram-positive bacteria (12).

Anacardium occidentale - Cashew is a multipurpose tree of the Amazon which produces many resources and products. The bark and leaves of the tree are used medicinally and it has antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa* (13) and *Clostridium perfringens* (14).

Psidium guajava – The guava tree is a small tree native to Central and South America (15). This plant contains catechin and it is active against Gram-positive bacteria (12). Garcia and collaborators (16) describe that the methanol extract and the aqueous extract of guava leaves are effective inhibitors of the production of spores and enterotoxins of *Clostridium perfringens* type A. Beyond this, this plant has antimicrobial effect against *Staphylococcus* sp., *Shigella sp.*, *Salmonella sp.*, *Escherichia coli*, *Pseudomonas* sp., different types of fungi, yeast (Candida), amoebas and *Plasmodium* (17). Guava tree leaves tea prepared by the infusion method were successfully tested against clinical influenza A (H1N1) (18). In addition, there is a Chinese patent on the potential of guava tree leaves to be effective against coronavirus (19, 20) and anticoagulant effect (21, 22).

Schinus terebinthifolius Raddi - popularly known as “Brazilian pepper”, is an evergreen, pioneer and indigenous plant from Brazil (23). A lectin was isolated from leaves and it has shown to be active against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa* and *Salmonella enteritidis* (24). Essential oil of ripened fruits has toxicity against the growth of *Acinetobacter baumannii*, *Bacillus subtilis*, *Escherichia coli*, *Micrococcus flavus*, *Pseudomonas aeruginosa*, *Sarcina lutea*, *Staphylococcus aureus* (25), *Klebsiella oxytoca*, *Corynebacterium* sp., *Enterobacter* sp., *Enterobacter agglomerans*, *Nocardia* sp. and *Streptococcus* group D (26).

Hymenaea courbaril L. is a tree common in South America Caribbean and Central America that is used for furniture, flooring, and decoration. It was extract by Da-Costa and colleagues (2014) a compound called fisetin which has therapeutic potential against fungal infections with low toxicity for animal cells (27).

Rubus sellowii (black capinuriba), is small fruit that grows in a temperate climate, presents an attractive color that varies from red to blue, due to the high anthocyanin and carotenoid content which are the major natural pigments found in such fruits. The major carotenoids found in blackberry were all-trans-β-carotene and all-trans-lutein, making up 39.6% and 28.2% of the total, respectively (11, 28).

Figure 1 shows necrotizing fasciitis before starting the treatment with conventional antibiotics. Figure 2 shows that the lesion got worse after 60 days using clindamycin and ciprofloxacin.

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