Platelet and leukocyte rich fibrin (L-PRF) applied in necrotizing Fasciitis treatment: case report

Fibrina rica em plaquetas e leucócitos (L-PRF) aplicada ao tratamento de Fasceíte necrotizante: relato de caso

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ABSTRACT

The reconstruction of extensive defects on the face caused by infections is a challenge for the oral and maxillofacial surgeon. Platelet and leukocyte-rich fibrin (L-PRF) is an excellent option for rehabilitative treatment, as it contains molecular and cellular elements that induce repair, being a therapeutic biomaterial with high potential for soft tissue regeneration. This article presents the clinical case of the patient C.T.A.S., female, 21 years old, who reported multiple tooth extractions, with an evolution of 30 days of volume increase and intense algesia in the left bucal space. Diagnosing necrotizing fasciitis, the patient underwent IV antibiotic therapy and surgery to drain and debride the lesion.

Postoperatively, therapy with platelet- and leukocyte-rich fibrin was initiated for tissue regeneration in the area affected by fasciitis. As an adjuvant to L-PRF membranes, low-level laser therapy and hyperbaric oxygenation sessions were performed. When using L-PRF to resolve this case, a satisfactory result was observed regarding the aesthetic-functional repair. In addition to having the advantage of being cost-effective, and having a simple protocol to be performed, L-PRF proved to be effective in promoting tissue regeneration.

Keywords: platelet rich fibrin, tissue regeneration, facial defects.

RESUMO

A reconstrução de extensos defeitos na face causados por infecções é um desafio para o cirurgião oral e maxilofacial. A fibrina rica em plaquetas e leucócitos (L-PRF) é uma excelente opção de tratamento reabilitativo, pois contém elementos moleculares e celulares que induzem a reparação, sendo um biomaterial terapêutico com alto potencial de regeneração de tecidos moles. Este artigo apresenta o caso clínico da paciente C.T.A.S., do sexo feminino, 21 anos de idade, que relatou múltiplas extrações dentárias, com uma evolução de 30 dias de aumento de volume e intensa algesia no espaço vestibular esquerdo. Diagnosticando a fascite necrosante, a paciente foi submetida a antibioticoterapia e cirurgia intravenosa para drenar e enterrar a lesão. No pós-operatório, foi iniciada terapia com fibrina rica em plaquetas e leucócitos para regeneração dos tecidos na área afetada pela fascite. Como um adjuvante das membranas L-PRF, foram realizadas sessões de laser de baixo nível e oxigenação hiperbárica. Ao utilizar a L-PRF para resolver este caso, foi observado um resultado satisfatório em relação ao reparo estético-funcional. Além de ter a vantagem de ser econômico e ter um protocolo simples a ser realizado, a L-PRF provou ser eficaz na promoção da regeneração dos tecidos.

Palavras-chave: fibrina rica em plaquetas, regeneração de tecidos, defeitos faciais.

1 INTRODUCTION

In 1871 the term necrotizing fasciitis was described for the first time but the same term had been mentioned before by Wilson in 1952, denominating the infections on the soft tissues that were undergoing necrosis. The necrotizing fasciitis shows as an infection that occurs on skin, subcutaneous tissue, superficial fascia, and it could also attack deeper layers[1].

This kind of infection presents a fast growing and a great risk of lethality. From all the infections from head and neck, this one represents 2,6% from the cases. Clinically, some aspects related to necrosis that come from bacterial metabolism can be noticed, such as the increasing of the volume soften by palpation with purple-colored spots and also, a palpation crepitus can be felt. Some individuals like alcoholics, drug addicts, immunosuppressed and smokers are more likely to developed these kinds of infections. The most common cause of those infections is tooth infection[2,3].

The pathogenicity of this disease comes from some bacteria, and the most usual in the necrotizing fasciitis are streptococcus e staphylococcus species, especially β-hemolytic group (streptococcus pyogenes)[2,4-6]. Due to the improvement of the culture techniques, anaerobic and negative gram bacteria were found on the lesion[7].

In order to the treatment succeed, it is necessary a fast and precise diagnosis, follow by surgical intervention and a systemic antibiotic therapy. In case of failure of surgical intervention, the case may evolve to septicemia, leading to multiple organ failure and consequently death. The PRF (platelet rich fibrine leukocyte) it is an important stimulating for wound healing. Its capacity of releasing growth elements in one to four weeks endorse that[8].

The hyperbaric oxygen therapy consists in managing the pure or a 100% oxygen through a hyperbaric chamber. This treatment causes beneficial effects for the wound healing and it could be applied in other adjunctive methods[9].

The low-level laser therapy (LLLT) which has anti-inflammatory and repairing properties can also be used to enhance the results[10].

Often times, oral and maxillo-facial surgeons face this kind of issue, when the infection is so severe and there is a large tissue loss caused by necrosis it becomes a challenge on the systematic management, tissue regeneration and the aesthetic-functional rehabilitation.

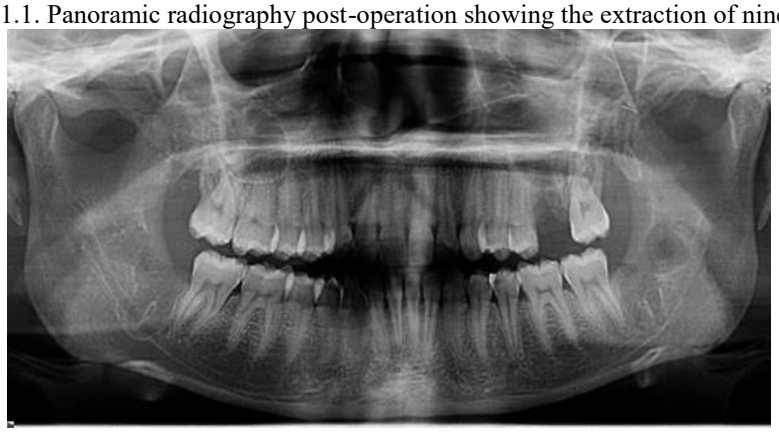
This article aims to demonstrate, through a clinical case, the necrotizing fasciitis treatment and its consequences, along surgical drainage, systematic antibiotic therapy and L – PRF application, associated to a hyperbaric oxygenation and laser therapy to tissue repair.

2 CASE REPORT

Female patient, 21 years old, came to Samaritano Hospital from Santa Bárbara D'oeste-SP, complaining about a swollen on the left part of her face and halitosis. She reported that 30 days ago she had gone under multiple dental extractions, evaluating to the increasing of the volume and left analgesia hemiface (Figure 1 and Figure 1.1). She also reported tachycardia and toxic facies.

Figure 1. Pre-operatory panoramic radiography showing the third molars and multiple supernumerary teeth.

Figure 1.1. Panoramic radiography post-operation showing the extraction of nine teeth.



After the physical examination, it was noticed an increasing of the volume soften by palpation on the left side of the mouth, with some purplish spots that suggested tissue necrosis. It showed crepitation to palpation, trismus and halitosis.

Laboratory tests:

- C-REACTIVE PROTEIN 365 mg/dL

HEMOGRAM was compatible with anemia conditions:

- ERYTHROCYTES 1,97 million/mm^3
- HEMOGLOBIN 5,9 g/DL

LEUKOGRAM

- LEUKOPENIA 3.800 mil/mm^3
- TYPICAL LYMPHOCYTES 608 mil/mm^3

PLACHETOPENIA 112.000mm^3

After all the exams and tests, it was determinate the need of hospitalization and immediate surgical intervention, respiratory monitoring and antibiotic therapy. The chosen intravenous antibiotic therapy was Amoxillin 500mg, associated with Clavulanate Potassium 120mg, and Metronidazole 500mg every eight hours. It was also prescribed

Dipyrone 1g ever six hours, Tramadol 50mg if necessary for the pain control and Dexamethasone 8mg every eight hours.

It was performed a surgical drainage and installed a hard drain for extraoral access on the left side of the mouth. The patient went under general anesthesia and nasal intubation with no complications.

During the surgery it collected contented for culture and antibiogram that resulted in *staphylococcus aureus* while anatomopathological examination showed a gangrenous inflammatory process, with no signs of malignance in the sample.

After the surgery the patient remained intubated and was referred to the intensive care unit because of the risk of bleeding during the extubating, due to the post operation hemoglobin. The patient was extubated 24 hours after the surgery, after blood transfusion and the hemoglobin stabilization.

The hard drain was removed on the second day post operation since there was no active drainage. The patient was discharged from ICU, no fever and no complaining of pain. It was performed the wound debridement, the PRF membrane adaptation and the bandage using tegaderm + laser low frequency laser therapy

The patient remained hospitalized for seven more days, keeping the PRF change and also laser therapy every two days, totalizing a number of 4 sessions during the period of hospitalization.

After the patient was discharged, she went through 10 sessions of hyperbaric oxygenation therapy once a week and low frequency laser therapy was performed only while she was hospitalized as well as the PRF applications. On the first month after the discharge, the patient conducted the change of PRF only once a week and on the following months once every 15 days at an ambulatory care facility, which totalized 10 PRF exchanges (Figure 2-10).

By the end of the proposed therapy the outcomes were satisfying regarding to the aesthetics functional repair. In three-month, post operation the aesthetic result was considered good, with a slight scar on the left side of the mouth area.

2.1 OBTAINING L-PRF METHOD

The patient's blood is collected using a 10ml sterile vacutainer (two to 12 tubes). The tubes with the samples are taken right away (around two minutes after the blood collection) and they are put in a centrifuge and processed in only one centrifugation step[11].

The tubes should be balanced and put two tubes opposite to the others two in order to stabilize the centrifigation and avoid vibrations during this process. Dohan Ehrenfest Group (Platelet and leukocyte-rich fibrin [L-PRF]): 2.700 rpm/ 12 minutes.

By the end of the centrifugation, the L-PRF cover are (not i-PRF) are removed and the tubes are put in a sterile stand. The blood sample with the clots are left rest and maturation for approximately four to eight minutes before removing clot from the tube[12].

The PRF clot is removed from the tube with a sterile clamp. The fibrin clot is separated from the blood smear, about 2 mm under the dividing line, using a scissor. The clot session attached to the fribin clot contain the stem cells. The PRF clots are set in a gradebox (France, Process) or in a Kit Xpression™ (Intra-Lock, Boca Raton, Flórida) and covered.

The PRF membranes are ready for being used in 2 minutes. It offers a three-dimensional array of platelets, leukocytes and growth factors. Since the PRF is correctly prepared and conserved in physiological conditions it remains useful for many hours after the preparation[13].

Figure 2. Pre operation aspect, it can be noticed a purplish floating point, determinizing a tissue necrosis point.

Figure 3. Post operation aspect – it was done an infection drainage, hard drain in position, showing low drainage, the patient was still in the ICU under nasotracheal intubation. Colostomy bad to observe the drainage volume and the evolution of the infection.

Figure 4. (A, B and C) – 48 hours post operation and the patient was already extubated, conscious, well oriented and able to make contact with other people. A – the colostomy bag in position, with no drain. B – the surgical wound in a necrotic aspect of the top layer of the skin. C – shows how it looked after the debridement; it also shows the exposure of the oral fat – it was performed the first L-PRF + laser therapy session.

Figure 5. (A, B and C) – four days post operation – the PRF aspect under the tegaderm bandage, previously adapted. B – the wound after the PRF, already showing improvement around the wound and the oral fat exposure. C – (2 sessions of PRF + laser therapy).

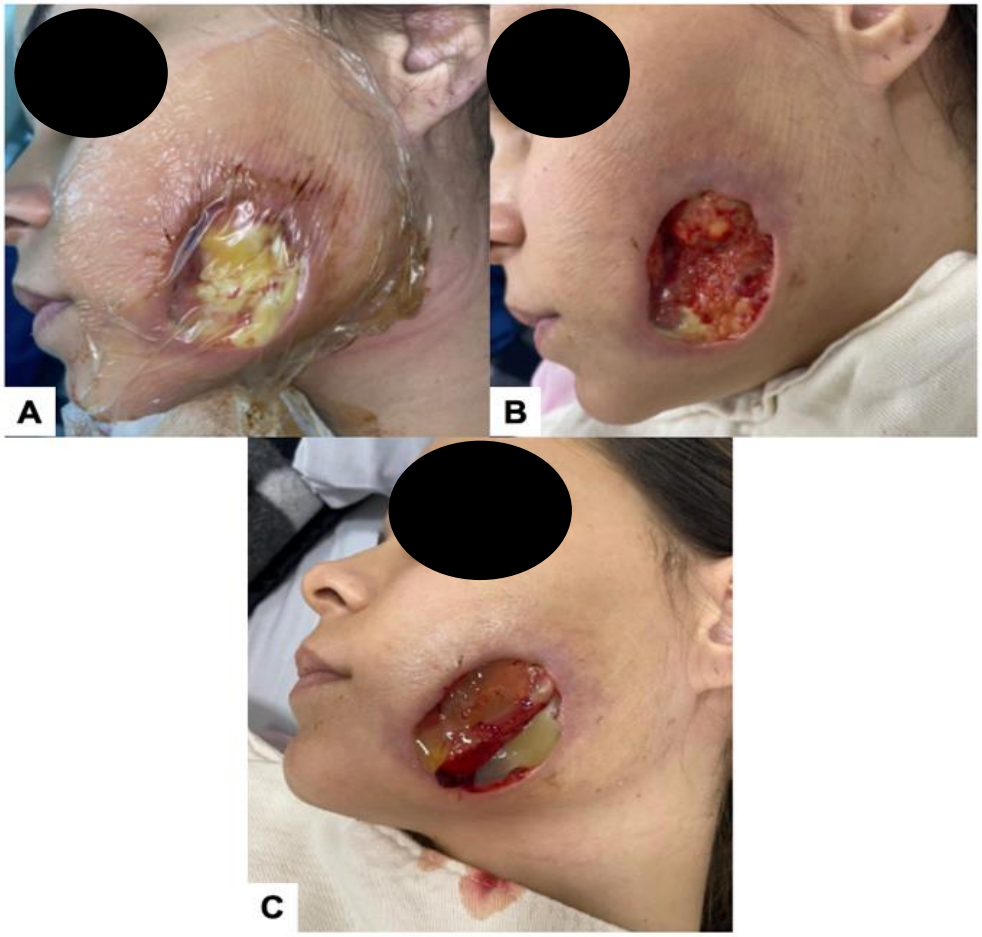


Figure 6. (A e B) – 12 days post operation, A – it can be observed a significant epithelialization of the wound, the exposure of the oral fat can no longer be noticed and the extension of the wound has diminished. B – new adaptations of PRF membranes.

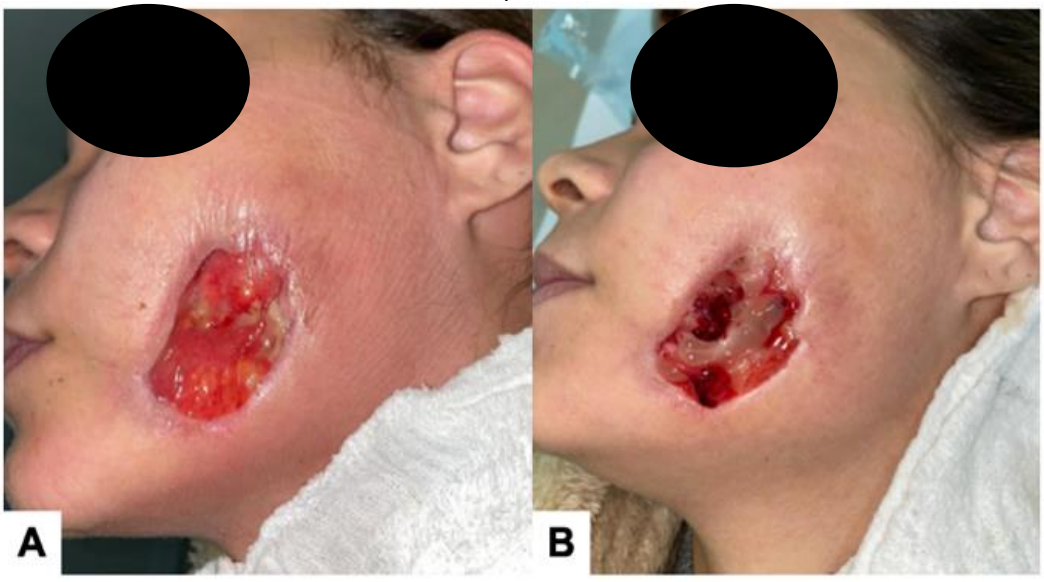


Figure 7. 18 days post operation: it can be seen a significant decrease of the wound extension, showing a good repairer aspect and good epithelialization of the wound.

Figure 8. 25 days post operation - last session.

Figure 9. 32 days post operation.

Figure 10. Three months post operation.

Figure 11. One year post operation showing a good healing aspect.

4 DISCUSSION

In necrotizing fasciitis cases, the male gender is the most affected in a proportion of 3 out 1. In general, the disease affects ages between 12 to 82 years old, which results in an average of 45.2 years old. Its predominance is higher on the lower jaw area than when compared to the upper jaw area. It can also affect perfectly healthy people, differently from the case reported, which the patient presented a case of anemia[2,5,6,14].

This kind of infection spreads around the superficial face areas, initially the muscles are spared, however, with the progression of the lesion it can lead to the necrosis of fascia and also the muscular tissue. Even with the appropriate treatment the evolution of the disease can result in septic shock, especially in immunosuppressed patients[5,15].

Less invasive surgeries such as teeth extractions can lead immunocompromised individuals to necrotizing fasciitis, as described in the reported case[16-18].

The necrosis on the underlying platysma area, skin tissue and skin occur due to the thrombosis and obstruction of arterioles that pass through the platysma to irrigate the skin tissue. At first, the infection causes skin vesicle and then, a purplish color of the overlying skin due to an ischemia, as it can be observed on the reported case. Lastly, the apparent necrosis and the skin divulsion suggests surgical debridement in large areas of the wound[19].

There are three classifying stages of necrotizing fasciitis, such as: stage I: hardness, erythema and edema of the skin, characterizing the early stage.

Stage II: forming a bubble aspect, point to the intermediate stage. Stage III: involving crackling, skin necrosis, may have paraesthesia, indicating an advanced stage, as the case described on the present work[20].

In order to the treatment succeed, it is crucial to choose the right antibiotic therapy[16,18,21], it was used beta-lactams. The authors Hohlweg-Majert et al. (2005)[21] also used nitroimidazole as well as Sahoo and Tomar (2012)[22], on the both cases, which the treatment was completed using aminoglycosides.

On study by Ricalde et al. (2004)[18] was added lincosamides. Still, about aminoglycosides, Kim et al. (2016)[23] also used this sort of antibiotics associated to beta-lactams. And, finally, Muhammad et al. (2014)[24] in his research, used only lincosamides on his therapy treatment.

The authors Farrier et al. (2007)[25] applied on their treatment beta-lactams and nitroimidazole. On the present case, the chosen therapy was 500mg Amoxillin + 125mg Potassium Clavulanate, associated with 400mg Metronizadole.

Several studies chose to use beta-lactams and nitroimidazole as the antibiotic therapy applied on the presented case[17,23,26,27]. This was because beta-lactams have a broad spectrum of action and nitroimidazole due to its antibiotic action against the Gram-negative anaerobic bacillus (which cause opportunistic infections in immunocompromised patients), against Gram-positive sporulated bacillus *Staphylococcus aureus*, very common in necrotizing fasciitis), and all anaerobic cocos (*Streptococcus pyogenes*, also usual in necrotizing fasciitis).

Due to the polymicrobial nature of necrosis fasciitis, the combination of two or more antibiotics is extremely necessary. That is the reason of the use of Amoxillin and Potassium Clavulanate, associated with Metronidazole on this present article.

Besides the systemic management to eradicate the infection and the risk of septicemia, there is also the tissue reconstitution challenge. There are several methods, as it was previously mentioned by the authors[27], that refer to the wound reconstitution and through skin grafting, which takes longer to start the defect reconstitution and presents higher surgical morbidity.

On the reported case of this article, it was established as a main method an innovative and promisor technique on the reconstitution of the tissue defects through L-PRF.

The PRF it is the fibrin autogenic matrix composed by leukocytes, and platelets, presenting a triangular structure with cytonics, platelets and stem cells. It acts as a biodegradable structure, favoring the microvascularization development, making the epithelial cells migrate to the surface[8].

Growing factors recruited stem cells to the wound, facilitating the cell mitosis and causing angiogenesis. Platelets cytokines that control the activation and proliferation of leukocytes are released, developing an important role on the inflammatory immunological process[28].

The fibrin matrix makes that the PRF membrane has great density, elasticity, flexibility and resistance, facilitating its manipulation[29].

It can be very effective if applied in wound of immunocompromised patients, such as those who are going through anticoagulant therapy and diabetics patients [30].

The hyperbaric oxygenation emerged in 1622 along with doctor Henshaw. On the Nineteenth Century, Junod (1834) and Pravaz (1837) used this same treatment for tuberculosis, cholera, anemias and hemorrhage. The first application on skin wounds occurred in 1965[31].

The hyperbaric oxygenation it is characterized by the use of pure or 100% oxygen inhalation in a chamber with a higher pressure, two or three times higher than the atmospheric pressure on the sea level. Resulting in an increasing of the blood pressure (2000 mmHg), skin tissue (400 mmHg), which leads to the therapeutics effects of this treatment.

Promoting positive effects in terms of healing this method has been used as adjuvant in many clinical situations as in the case described on the present work, which was applied in combination with PRF and low frequency laser therapy[9].

According to Undersea and Hyperbaric Medical Society, there are 14 indications for the hyperbaric oxygenation, such as: diabetic foot ulcer, tissue injure caused by radiation, cystitis, chronic osteomyelitis, ischemia, carbon monoxide poisoning, gas embolism, sudden sensorineural hearing loss, Central retinal vein occlusion, severe anemia, refractory zygomycotic and skin burns and serious infections of the soften tissue, as showed on the present work, being very effective on the necrotizing fasciitis treatment[32].

Along with PRF method to treat necrotizing fasciitis it is also used the Low Frequency Laser Therapy. Due to its ability to accelerate the healing process through light radiation amplification on the leisure, this method has its precise indication for these cases. Some characteristics result on the improvement of algesia and on inflammatory case, as being: cellular and vascular changes, epithelium and fibroblasts proliferation, collagen synthesis deposition that increase the wound's elastin, proteoglycans and revascularization produce[10].

5 CONCLUSION

The PRF application in necrotizing fasciitis, along with adjuvants factors as hyperbaric oxygenation and low frequency laser therapy has shown an innovative way for the proposed treatment, being very effective and safe for having antibacterial, anti-inflammatory properties and its own repairing characteristics.

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