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CASE REPORT: ACNE FULMINANS ASSOCIATED WITH ISOTRETINOIN

RELATO DE CASO: ACNE FULMINANTE ASSOCIADA COM ISOTRETINOÍNA

REPORTE DE CASO: ACNÉ FULMINANTE ASOCIADO CON ISOTRETINOÍNA

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Lara Vitória Loução Durães Salgado[1], Marcella Pereira Palma[2], Yasmin Santos Sá[3], Giovana Ortega Praliola[4], Brunamelia de Oliveira Sattin[5], Nathalie Manoel Lopes[6], Thaís Rennó Campos[7], Rúbia Camargo dos Santos[8]

ABSTRACT

Introduction: The pathology of acne fulminans is based on the formation of Propionibacterium acnes as a superantigen that incites a highly inflammatory response in pilosebaceous follicles and musculoskeletal components. Common triggers are the introduction of isotretinoin and the indiscriminate use of exogenous hormones. The clinical presentation begins with comedones, papules, and pustules, progressing to multiple inflammatory lesions, as well as nodules and abscesses that can lead to areas of necrosis. Systemic symptoms such as fever and joint pain are frequently reported.

Objective: This study aims to review guidelines to improve the treatment outcomes of patients with Acne Fulminans.

Method: This study is a case report of isotretinoin-induced acne fulminans, focusing on clinical presentation, course, and management. Conducting literature reviews in PubMed, SciELO, and LILACS databases.

Conclusion: This study highlights the importance of early diagnosis and individualized treatment of acne fulminans, with an emphasis on corticosteroid therapy, isotretinoin discontinuation, and ongoing medical monitoring to prevent complications.

Keywords: Acne Fulminans. Isotretinoin. Corticosteroid Therapy. Acne Fulminans Grade III. Exogenous Hormones.

[1] Medical Student. Universidade Municipal de São Caetano do Sul. E-mail: lara.salgado28@gmail.com
Orcid: https://orcid.org/0009-0008-3316-4008 Lattes: https://lattes.cnpq.br/8966841424956152
[2] Medical Student. Universidade Municipal de São Caetano do Sul. E-mail: marcella.palma@hotmail.com
Orcid: https://orcid.org/0009-0009-3562-866X Lattes: http://lattes.cnpq.br/6635514960807354
[3] Medical Student. Universidade Municipal de São Caetano do Sul. E-mail: yasmimsantossa.ys@gmail.com
Orcid: https://orcid.org/0009-0004-3403-9760 Lattes: http://lattes.cnpq.br/3363399871992413
[4] Medical Student. Universidade Municipal de São Caetano do Sul. E-mail: giovanaortega_@hotmail.com
Orcid: https://orcid.org/0009-0004-8264-552X Lattes: https://lattes.cnpq.br/1190616688715496
[5] PhD in Dentistry. Universidade Municipal de São Caetano do Sul. E-mail: brunameliadeoliveira@gmail.com
Orcid: https://orcid.org/0000-0003-3424-3046
[6] Postgraduate in Leadership and Human Development (lato sensu specialization). Universidade Municipal de São Caetano do Sul E-mail: natha_mlopes@hotmail.com Lattes: http://lattes.cnpq.br/8833649231442867
[7] Medical Student. Universidade Municipal de São Caetano do Sul. E-mail: thais.renno0@gmail.com
Orcid: https://orcid.org/0009-0003-1114-1829 Lattes: http://lattes.cnpq.br/1581805554212827
[8] Medical Degree. Universidade Municipal de São Caetano do Sul. E-mail: rubiacamargo.med@gmail.com
Orcid: https://orcid.org/0009-0009-8092-0600 Lattes: https://lattes.cnpq.br/2691174259270702

RESUMO

Introdução: A patologia da acne fulminans se baseia na conformação do Propionibacterium acnes como um superantígeno que incita uma resposta altamente inflamatória nos folículos pilossebáceos e em componentes musculoesqueléticos. Fatores desencadeantes comuns são a introdução da isotretinoína e o uso indiscriminado de hormônios exógenos. A apresentação clínica começa com comedões, pápulas e pústulas, evoluindo para múltiplas lesões inflamatórias, além de nódulos e abscessos que podem originar áreas de necrose. Frequentemente são relatados sintomas sistêmicos como febre e dores nas articulações.

Objetivo: Este trabalho tem o objetivo de revisar os guidelines para melhorar o desfecho do tratamento de pacientes com Acne Fulminans.

Método: O presente trabalho é um relato de caso de acne fulminante induzida por isotretinoína, com foco na apresentação clínica, evolução, conduta. Realizando revisões bibliográficas nas bases PubMed, SciELO e LILACS

Conclusão: O presente estudo destaca a importância do diagnóstico precoce e do tratamento individualizado da acne fulminante, com ênfase na corticoterapia, suspensão da isotretinoína e acompanhamento médico contínuo para evitar complicações.

Palavras-chave: Acne Fulminante. Isotretinoína. Corticoterapia. Acne Fulminante Grau III. Hormônios Exógenos.

RESUMEN

Introducción: La patología del acné fulminante se basa en la formación de Propionibacterium acnes como superantígeno que induce una respuesta altamente inflamatoria en los folículos pilosebáceos y los componentes musculoesqueléticos. Los desencadenantes comunes son la administración de isotretinoína y el uso indiscriminado de hormonas exógenas. La presentación clínica comienza con comedones, pápulas y pústulas, progresando a múltiples lesiones inflamatorias, así como nódulos y abscesos que pueden dar lugar a áreas de necrosis. Se reportan con frecuencia síntomas sistémicos como fiebre y artralgia.

Objetivo: Este estudio busca revisar las guías para mejorar los resultados del tratamiento de pacientes con acné fulminante.

Método: Este estudio es un reporte de caso de acné fulminante inducido por isotretinoína, centrándose en la presentación clínica, la evolución y el manejo. Se realizaron revisiones bibliográficas en las bases de datos PubMed, SciELO y LILACS.

Conclusión: Este estudio destaca la importancia del diagnóstico precoz y el tratamiento individualizado del acné fulminante, con énfasis en la terapia con corticosteroides, la suspensión de la isotretinoína y la monitorización médica continua para prevenir complicaciones.

Palabras clave: Acné Fulminante. Isotretinoína. Terapia con Corticosteroides. Acné Fulminante Grado III. Hormonas Exógenas.

1 INTRODUCTION

Acne fulminans represents an uncommon and severe form of acne, characterized by intense inflammation and associated systemic manifestations. Its pathophysiology involves an exacerbated immune response, triggered by the action of Propionibacterium acnes as a superantigen. This pathogenic behavior leads to dysregulated activation of immune system cells, resulting in an intense inflammatory reaction in pilosebaceous follicles, with repercussions also on adjacent musculoskeletal tissues.

Among the factors commonly associated with the onset of this condition, the beginning of the use of isotretinoin for the treatment of acne stands out, as well as the inappropriate or indiscriminate use of exogenous hormones, especially androgenic hormones. These elements seem to alter the local immune response, favoring the appearance of fulminant symptoms.

From a clinical point of view, acne fulminans usually begins with typical acne lesions, such as open and closed comedones, papules, and pustules. However, it evolves to nodular lesions and painful abscesses, with the potential to form areas of ulceration and skin necrosis. The lesions mainly affect the trunk, although they can also involve the face. In addition to cutaneous manifestations, the presence of important systemic symptoms, such as fever, arthralgia, generalized weakness, anorexia, and significant weight loss, is common, which reinforces the systemic and severe nature of the disease.

Due to its aggressive clinical presentation and the high risk of deep and disfiguring scarring sequelae, therapeutic management requires immediate and effective intervention. The treatment of choice usually involves the use of systemic corticosteroids, with the aim of controlling the inflammatory response, and antibiotics. It is of paramount importance to emphasize that early and appropriate treatment under medical supervision is essential to minimize complications.

2 CASE PRESENTATION

The clinical case described refers to a 15-year-old male patient, previously healthy, who sought dermatological care due to severe acne of insidious onset, with important aesthetic, functional and psychological repercussions on his quality of life.

The patient reported a history of previous treatment with oral isotretinoin at a dose of 1 mg/kg/day, initiated three weeks before the consultation, without showing clinical improvement. A progressive worsening of the skin lesions was noted, accompanied by the

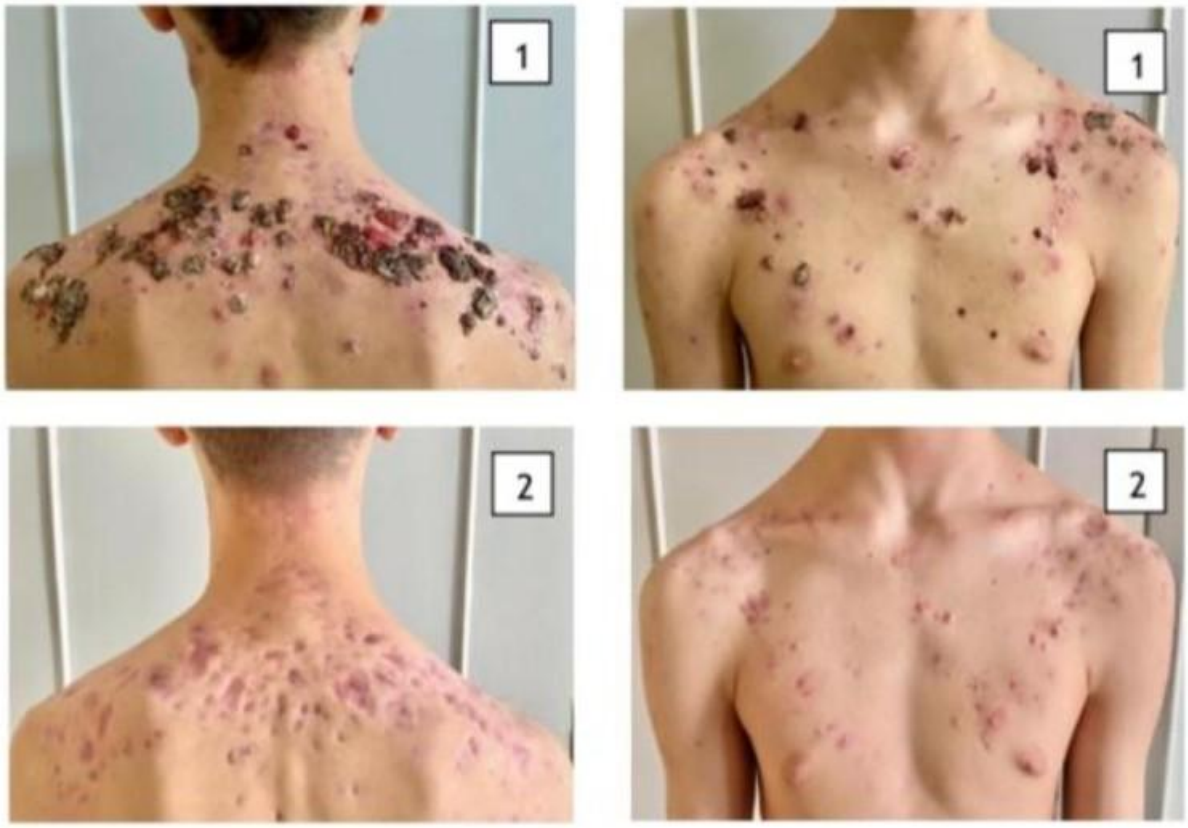
appearance of systemic symptoms, such as intermittent fever, general malaise, myalgia, and arthralgia in large joints. On physical examination, multiple nodular, inflammatory, painful, ulcerated, and crusted lesions were observed, predominantly in the upper thoracic region and on the face. The lesions consisted of papules, pustules, coalescent nodules, plaques with areas of necrosis and hemorrhagic crusts, in some regions, seroppurulent exudate was observed.

The main diagnostic hypothesis was isotretinoin-induced grade III acne fulminans, especially considering the sudden pattern of worsening after drug initiation, the presence of ulcerated lesions with necrosis, and systemic symptoms.

Laboratory tests were requested to investigate infectious and autoimmune causes, which were discarded. The blood count did not show leukocytosis, but the C-reactive protein (CRP) was elevated, compatible with an acute inflammatory process.

Figure 1

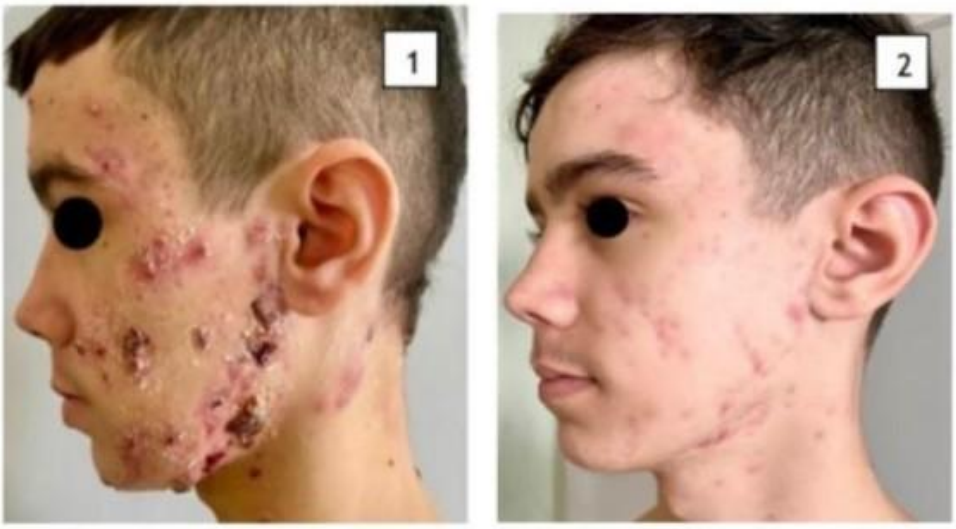
Back and chest of the patient with acne fulminans before (1) and after treatment (2)



Source: The authors.

Figure 2

Face of the patient with acne fulminans before (1) and after treatment (2)



Source: The authors.

3 METHOD

This is a case report, and aims to report a case of PA triggered by the use of oral isotretinoin, highlighting its clinical presentation, evolution and adopted conduct. For its construction, literature reviews were used through the PubMed, SciELO and LILACS databases, using the descriptors "Acne fulminans", "Isotretinoin", "systemic corticosteroids" and "dermatological complications". In addition, the most recent acne consensus guidelines and updates were consulted. Clinical data and complementary tests were obtained from the anamnesis performed with the patient.

The research also aimed to identify the most current therapeutic protocols and recommended approaches to acne fulminans, with special emphasis on cases associated with the previous use of isotretinoin.

4 DISCUSSION

Acne fulminans (FA), a dermatological manifestation of extreme severity, was first outlined in the medical literature by Burns and Colville in 1959. This pathology, of rare incidence, with an estimate of less than 1% of acne cases, predominantly affects male adolescents and young adults, usually between 13 and 22 years of age, and almost invariably associated with a preexisting history of acne vulgaris (HARTMANN, 2021, VOL 58 3-10 / JANSEN, 2005, VOL 56 1018-26). This is in accordance with the current clinical case and is in line with the epidemiological data presented in the literature.

The characteristic clinical picture of SCA is manifested by inflammatory nodules, intensely painful, which are distributed in the regions typically affected by acne. Such lesions rapidly progress to ulcerations, culminating in the formation of hemorrhagic crusts, giving the condition a dramatic and high-impact cutaneous presentation (NEVES, 2011, VOL 66 15-17).

According to Fakih et al. (2020) (FAKIH, 2020M VOL 26 NO 12), acne fulminans (FA), although rare, can be induced by isotretinoin, this drug acts fundamentally to reduce the size and activity of the sebaceous glands, minimizing skin oiliness, in addition to helping to regulate the keratinization process and attenuate local inflammation. The doses administered and the time between the start of medication and the appearance of acute manifestations may vary. However, it is common for lesions to appear between the fourth and eighth week after the start of treatment (SOUSA, 2001, VOL 76: 291-295 / AZULAY, 2015, vol 60: 179-182). The authors' observations are based on the authors' observations, since a previous treatment with isotretinoin, without significant results, raises the hypothesis that its use may have contributed to the exacerbation of the condition.

As it is a dermatosis of rare incidence, the etiology of acne fulminans (FA) remains largely unknown, additionally, the literature suggests that the high concentration of testosterone may be a contributing factor to the pathogenesis of the condition (PROENÇA, 2027, VOL 92.5: 8-10 / MASSA, 2017, VOL 233: 2-3). What can be

Related to, for example, the peak of puberty hormones, where men have a large amount of natural endogenous steroid hormones.

Recent studies reinforce the hypothesis that immunological alterations play a central role in triggering the condition. The most widely accepted theory proposes that Cutibacterium acnes, when penetrating deeper layers of the skin, undergoes a phenotypic change, starting to act as a superantigen capable of inducing an exacerbated inflammatory response in pilosebaceous follicles and adjacent tissues, including musculoskeletal structures (PROENÇA, 2027, VOL 92.5: 8-10). Such a response would be mediated by an inappropriate activation of the innate and adaptive immune system, resulting in intense release of pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-8 (GUTIÉRREZ-MERÉ, 2023, VOL 144: 763-771). This disproportionate reaction may be exacerbated by hormonal factors, especially in adolescent males, who have elevated levels of endogenous androgens during puberty (PEREZ, 2026, VOL 91:706 / ZAENGLEIN, 2024). Thus, the immune imbalance in the face of a relatively common antigenic stimulus could explain why only a small portion of

patients develop the fulminant form of acne, even when using isotretinoin (PROENÇA, 2027, VOL 92.5: 8-10 / GUTIÉRREZ-MERÉ, 2023, VOL 144: 763-771).

In view of this pathophysiology based on an exacerbated immunoinflammatory component, the use of systemic corticosteroids becomes a logical and recommended approach. They act on multiple stages of the inflammatory cascade:

1. Suppression of cytokine production: Corticosteroids directly inhibit the expression of pro-inflammatory genes, such as those encoding TNF-α, IL-1β, IL-6, and IL-8.
2. Stabilization of cell membranes: They reduce vascular permeability and the extravasation of leukocytes into inflamed tissues.
3. Inhibition of T lymphocyte and macrophage activation: Prevents amplification of the adaptive immune response.
4. Inhibition of phospholipase A2: Interrupts the formation of prostaglandins and leukotrienes, important mediators in pain and inflammation.

As pointed out by the Ibero-Latin American consensus and recent narrative reviews, early corticosteroid therapy exerts potent anti-inflammatory and immunosuppressive action, allowing rapid control of systemic and cutaneous symptoms, in addition to preventing irreversible sequelae such as extensive ulcerations and unsightly scars (BAGATIN, 2017, VOL 92: 691-695 / GUTIÉRREZ-MERÉ, 2023, VOL 144: 763-771). Isotretinoin, although effective in severe acne, can initially aggravate the inflammatory condition by sharply reducing sebum activity and altering the local flora, contributing to the development of SCA (ZAENGLEIN, 2024). Therefore, its immediate suspension, associated with the initiation of corticosteroid therapy, is essential for the control of acute inflammatory outbreaks. Such conduct is especially valid in cases where PA appears in the first weeks of isotretinoin use, as described in our case, and as reported by Fakih et al. (2020), who demonstrated PA induced even by low doses of retinoid (FAKIH, 2020M VOL 26 NO 12).

After a thorough anamnesis, a condition compatible with the use of isotretinoin-induced PA was identified. In view of the severity of the clinical exacerbation and in order to avoid complications such as permanent scarring and secondary infections, we decided to temporarily suspend isotretinoin.

As an immediate approach, systemic corticosteroid therapy was instituted in a short-term regimen (2 weeks) with prednisone 20 mg/day, followed by progressive weaning, with the objective of controlling acute inflammation, reducing edema, and modulating the

exacerbated immune response. This type of approach is especially indicated when there is a risk of aggravation of lesions with disfiguring potential.

In parallel, a strict topical care regimen was adopted, including:

1. Proper hygiene with non-comedogenic and gentle products;
2. Intensive hydration to restore the compromised skin barrier;
3. Broad-spectrum photoprotection, essential due to the photosensitivity induced by both isotretinoin and some antibiotics;
4. Topical antibiotic therapy, aimed at controlling bacterial colonization;
5. Topical corticosteroids, with punctual indication for reducing residual inflammation in localized inflamed lesions.

Complementing the management, 1 month of oral antibiotic with Limecycline was performed, which has, in addition to antimicrobial action, a relevant anti-inflammatory effect, helping to stabilize persistent inflammatory lesions and prevent new outbreaks.

The patient had a favorable clinical evolution, with significant regression of acne lesions, absence of signs of systemic infection or laboratory abnormalities, and general improvement of the dermatological condition. After stabilization, outpatient follow-up was maintained with a focus on scar control (such as atrophic or hypertrophic scars), which may include therapeutic modalities such as fractional laser, microneedling, chemical peels, or fillers, depending on the type and severity of skin sequelae.

This case highlights the importance of an individualized and dynamic approach in the management of severe acne, with constant attention to the clinical response and adverse effects of therapies, ensuring safety and better adherence to treatment in the long term.

5 FINAL CONSIDERATIONS

The case illustrates the importance of early recognition of the fulminant condition and the need to individualize treatment in the face of refractoriness to isotretinoin. The central role of systemic corticosteroid therapy in the effective modulation of the acute inflammatory response is confirmed, while the association with oral antibiotic therapy and complementary dermatological care contributes to clinical improvement and prevention of complications. The suspension of potentially inducing agents and the judicious use of anti-inflammatory and antibiotic therapies are highlighted, being essential for the effective control of the disease and the prevention of relevant scarring sequelae. Thus, it is reinforced that an individualized therapeutic approach, accompanied by continued supervision by the medical professional, is

essential to optimize clinical management and ensure favorable outcomes in complex cases of acne fulminans.

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