

Spontaneous Necrotizing Fasciitis in a Patient with Endogenous Cushing Syndrome: Six-Year Follow-Up: Case Report

Endojen Cushing Sendromu Olan Hastada Spontan Nekrotizan Fasiit Olgusu: Altı Yıllık Takip

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ABSTRACT Opportunistic infections in endogenous Cushing's syndrome are associated with excess cortisol level and carry a high mortality risk due to cortisol associated immunosuppression. Necrotizing fasciitis is an uncommon but life-threatening complication in immunocompromised hosts. We report a rare case of endogenous Cushing's syndrome due to adrenal tumor complicated by necrotizing fasciitis on the lower leg, where the patient improved with antimicrobial therapy, localized debridement and fasciotomy without control of excess cortisol secretion. In conclusion, we strongly believe that endogenous hypercortisolism should be considered in patients with severe life-threatening infections, and treatment of the underlying hypercortisolism with cortisol lowering drug prior to the surgical therapy is essential for reducing mortality and morbidity.

Key Words: Cushing syndrome; fasciitis, necrotizing; adrenocortical adenoma

ÖZET Endojen Cushing sendromunda fırsatçı enfeksiyonlar yüksek kortizol seviyesi ile ilişkili olup kortizole bağlı immunsupresyon nedeniyle yüksek mortaliteye sebep olmaktadır. Nekrotizan fasiit immunkompromize konaklarda sık olmayan ancak hayatı tehdit eden bir komplikasyondur. Bu yazıda, bacaklarında nekrotizan fasiit ile komplike olup kortizol seviyesi baskılanmaksızın antimikrobiyal tedavi, bölgesel debridman ve fasiyotomi ile iyileşme gösteren adrenal tümör kaynaklı nadir bir Cushing sendromu olgusu sunduk. Sonuç olarak, hayatı tehdit eden ağır enfeksiyonlarda endojen hiperkortizolizmden kuşkullanması ve cerrahi girişim öncesi medikal tedavi ile kortizol seviyelerinin düşürülmesinin mortalite ve morbiditeyi azaltmada önemli olduğuna inanıyoruz.

Anahtar Kelimeler: Cushing sendromu; fasiit, nekrotizan; adrenokortikal adenom

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Necrotizing fasciitis (NF) is a severe form of soft tissue infection, which primarily involves the superficial fascia and develops as the infectious organisms proliferate and extend from the subcutaneous tissue along superficial and deep facial planes. It has a high mortality rate of at least 38% and lower limbs are the most frequent site of infection (53%).^{1,2} Majority of the patients (82%) have some form of chronic debilitating disease such as diabetes mellitus, alcohol abuse, or renal insufficiency.^{3,4} However, approximately one-half of the cases are young and previously healthy patients. Other apparent predisposing factors are advanced age, peripheral vascular disease, malignancy, obesity, malnutrition, and possibly other states predisposing patients to immunodeficiency, such as being under corticosteroid treatment.^{5,6} Hypercortisolism can also be endogenous, as in Cush-

ing's syndrome. The infectious complications of Cushing's syndrome (CS) include fungal, bacterial (including reactivation of tuberculosis), and, rarely, opportunistic infections.⁷⁻⁹ Among them, NF is a very rare life-threatening complication.⁵ We report herein a case of spontaneous lower leg NF in a woman with uncontrolled hypercortisolism due to adrenal adenoma.

CASE REPORT

A 40-year-old, female dentist was admitted to the orthopedics department with compression fractures of the spine (L1 and L4) after a fall. The day of surgery, she had a painful erythematous swelling of the lower left foot with overlying hemorrhagic bullae, which then transformed into cellulites. She had no history of trauma to this region. The patient was found to have tachycardia and fever. On the basis of clinical presentation, a diagnosis of necrotizing fasciitis was made. After drawing blood for culture, broad-spectrum antibiotic coverage with Cefazidime, Gentamicin, and Clindamycin was started without control of excess cortisol secretion. The patient's condition raised concern about whether or not she was able to tolerate an extensive emergency operation. Therefore, a localized wide debridement and fasciotomy over the left leg was performed. Although the patient was not on a cortisol-lowering drug such as Metyrapone, the postoperative course was uncomplicated, and the patient's condition progressively improved. The blood taken before the operation was sent for culture, which subsequently grew Cefazolin-susceptible *Escherichia coli*, which is the most likely culprit pathogen known to produce gas. Antibiotics were switched to Cefazolin alone and the therapy was continued for 6 weeks. A skin graft from the left thigh was performed over the surgical site. Titanium rod was attached to the spine before discharge from the hospital. The patient was stable 2 months after admission, and she was referred to our endocrinology clinic for investigation of severe osteoporosis.

HISTORY AND ADMISSION FINDINGS

She presented 2 years ago with complaints of facial rounding and menstrual irregularity. When fatigue, weakness, reduction of work performance, psycho-

logical distress, and amenorrhea were added to her initial complaints with time, she was seen by many physicians but none of them considered hypercortisolemia. Then the patient went on vacation, and she fell over the back while skiing. She had an uneventful past medical history, was taking no medications, and had no previous operations. Physical examination revealed a Cushingoid habitus (moon face, plethora, buffalo hump, supraclavicular fullness, hirsutism, paper-thin skin), a very mild truncal obesity, surgical scar and extensive tissue loss on the left leg, and dark purple-colored scar tissue (such as the co-existence of many striae) on the left femoral region for the use of skin graft and flap (Figure 1A, B, and C).

Her blood pressure was 130/80 mmHg, and blood sugar was normal (70 mg/dl). Failure of cortisol suppressions after 1 mg, 2 mg, and 8 mg dexamethasone (22.6 mg/dl, 20.8 µg/dl, and 24.3 µg/dl, respectively) with a suppressible ACTH level (<10 pg/ml) were diagnostic of hypercortisolism. DHEAS level was normal (85.57 mg/dl). On the other hand, LH (1.3 mIU/L), FSH (7.4 mIU/L) and E₂ (28.9 ng/ml) levels pointed to hypogonadotrophic hypogonadism. Bone density revealed osteoporosis with a T-score of -2.9 on the lateral L4-spine. Thereafter, treatment of osteoporosis with bisphosphonate and calcium plus vitamin-D was initiated. Abdominal MRI showed a 3 cm tumor on the left adrenal gland, and it was excised and histologically proved to be an adenoma. During the follow-up at the outpatient clinic, she began to menstruate at the first month of surgery, and Cushing's symptoms gradually disappeared in 5 months (Figure 2A, B, and C).

The pituitary-adrenal axis returned to normal at 11 months, and the steroid replacement therapy was stopped. In addition, bone density returned to normal in a year and bisphosphonate was discontinued. After the elimination of hypercortisolemia, loss of tissue in the leg improved spontaneously at the end of the sixth year (Figure 3).

DISCUSSION

Necrotizing fasciitis is a rare but well recognized clinical entity which most often occurs on the trunk, perineum or legs following surgery or trauma.⁶



FIGURE 1: (A) Cushingoid appearance; (B) and (C) Paper-thin skin, surgical scar and flap on the leg.



FIGURE 2: (A) Cushingoid appearance almost disappeared; (B) and (C) The color of scar tissues turned pale (white arrow) at 5 months.



FIGURE 3: The latest appearance of the leg.

However, it may lack any obvious traumatic etiology.^{5,10} Prompt diagnosis and adequate support to maintain vital functions, as well as thorough and frequent surgical debridement, are the mainstay for achieving a successful outcome of NF.^{2,11,12} It may require different treatments for different causes, but timely debridement of necrotic tissue is essential for reducing mortality.^{2,12} On the other hand, it is well known that patients with uncontrolled hypercortisolism have high mortality because of opportunistic infections.^{7,13} This case had no history of any trauma on her leg skin, she had sudden onset of a life-threatening infection after spinal fracture in the setting of hypercortisolism. She did not have diabetes mellitus, which is a known complication of CS and causes susceptibility to infections itself, possibly due to granulocyte dysfunction from hyperglycemia and poor tissue perfusion as a consequence of peripheral vascular disease.¹⁴ We believe that NF was caused by the fragile connective tissue associated with endogenous CS.

Previous reports of infectious complications in ectopic ACTH-related CS, most frequently caused by small cell carcinoma of the lung (SCCL), suggest

that the frequency and severity of infectious complications are directly proportional to the degree of hypercortisolemia. Among these reports, several case studies have suggested an association between ectopic ACTH-related CS and the risk of life-threatening infection.^{7,15-18} But there are only a few of cases of NF with CS, the etiology of which were; an ACTH-secreting thymic carcinoid tumor,⁵ an ectopic production of adrenocorticotropin caused by SCCL,⁸ and an adrenal carcinoma.¹⁹ Most reported patients with complicated by NF were on corticosteroid treatment.^{9,20} Indeed, patients with all forms of CS are susceptible to infection with opportunistic pathogens. Although opportunistic infections have been described previously in such patients, we believe that this is the first description of spontaneous necrotizing fasciitis which was able to tolerate localized wide debridement and fasciotomy under endogenous hypercortisolism. She is rare in that her skin graft functioned and a spinal rod was able to be attached in spite of high blood cortisol levels. She was diagnosed to have hypercortisolism while searching for the etiology of her osteoporosis, after which the adrenal adenoma was immediately operated on. The scar spontaneously healed with granulation tissue and the antiresorptive therapy was stopped in a year with full clinical recovery. She was also the patient with the longest follow up time, whose skin repaired itself without the help of reconstructive surgery.

CONCLUSION

This case demonstrates the unusual complication of endogenous hypercortisolemia in a severely immunocompromised patient. Although early recognition and treatment remain the most important factors influencing survival of the patients with NF, we strongly believe that endogenous hypercortisolism should be considered in patients with severe life-threatening infections and that treatment of the underlying hypercortisolism with cortisol lowering drugs prior to the surgical therapy is essential.

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