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Case Report

Catastrophic wound dehiscence in early onset scoliosis secondary to hyperinflammatory response: a case report

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ABSTRACT

Early onset scoliosis (EOS) poses significant treatment challenges, often exacerbated by postoperative wound complications. A novel case of hyperinflammatory wound complications in a child with a confirmed NFKB1 mutation is presented, successfully managed with immunomodulation.

A 6-year-old boy experienced wound dehiscence and persistent inflammation following rod placement, unresponsive to conventional treatments including surgical debridement and antibiotics. Further evaluation identified an *NFKB1* mutation associated with hyperinflammatory states. Targeted treatment with Anakinra, an interleukin (IL)-1 receptor antagonist, resulted in rapid wound healing and normalization of inflammatory markers. Subsequent serial rod expansions, pretreated with Anakinra, were complication-free, and the patient remained stable for 4 years post treatment.

This case emphasizes the critical role of genetic predispositions, such as *NFKB1* mutations, in postoperative complications. Dysregulated IL-1β activity was effectively managed with targeted immunomodulation, highlighting the importance of recognizing and addressing non-infectious hyperinflammatory processes. Patients presenting with very early wound dehiscence, disproportionate inflammatory responses, and unresponsiveness to infection management may benefit from detailed immunologic evaluation. Rare hyperinflammatory conditions should be considered in the differential diagnosis of challenging postoperative wound healing scenarios.

Introduction

Early onset scoliosis (EOS) remains a challenge to treat, with complications associated with spinal fusion higher than in the idiopathic population.[1,2]

We present an EOS case complicated by postoperative wound dehiscence in a child with an NFKB1 gene mutation. The management of EOS becomes significantly more complex in the presence of genetic conditions. Little data are available on hyperinflammatory response to surgery in the setting of NFKB1 mutation, and there is a paucity of literature in pediatric spine surgery. The NFKB1 gene is a key regulator of immune response.[3,4] Mutations may have variable symptoms of immunodeficiency and autoinflammation, and the hyperinflammatory reaction in response to surgical trauma may involve fever and excessive inflammation in the wound area, which may mimic infection.[5] This case demonstrates the interplay between the immune system and postoperative wound healing and highlights the important role of immunomodulatory interventions.

Case presentation

A 6-year-old boy was referred from an outside hospital for a persistent spine infection. He had undergone magnetically controlled growing rods placement for EOS 3 weeks prior. Postoperatively, he developed fever and wound dehiscence within 3 days, for which he underwent multiple irrigation and debridement (I&D) with wound vacuum-assisted closure (VAC) placement. As the wound did not respond to VAC changes and antibiotic treatment, hardware was removed on postoperative day (POD) 11 at the outside hospital. All wound, blood, and urine cultures remained sterile. The patient was then referred to our institution at the family's request.

At presentation to our institution, he had been afebrile for 2 days and was on vancomycin and cefepime through a peripherally inserted central catheter line. He was ambulating without difficulty. There was a functioning wound VAC in place and no areas of palpable fluctuance along his spine. The neurologic examination was normal. A computed tomography of the abdomen revealed no intra-abdominal collection.

An in-depth evaluation of past medical history revealed some events; however, nothing notable for any specific diagnosis. His birth history was insignificant. He did have a submucosal cleft palate and right cleft lip that were repaired at 3 months of age. He had a history of speech and language delays and behavioral difficulties.

He was diagnosed with EOS at an early age and was managed with serial Mehta casting for EOS starting at age 18 months. Magnetic resonance imaging of the spine was negative for any anomaly. He was noted to have macrocephaly with a triangular face, concerning

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for a connective tissue disorder or familial thoracic aortic aneurysm syndrome. A formal cardiac evaluation at age 3, following his father's sudden presumed cardiac demise, did not reveal anything concerning. His father and paternal aunt reportedly had scoliosis; however, they did not require any active treatment.

At the current presentation, he was admitted for wound VAC changes and continued on vancomycin and cefepime. He was eventually discharged after clinical improvement with abating leukocytosis and down-trending C-reactive protein and erythrocyte sedimentation rate.

His incision healed with a large scar during a course of 6 weeks of intravenous (IV) vancomycin, cefepime, and 2-week oral amoxicillin. However, no definite diagnosis of postoperative implant-related infection was made. Metal patch testing and lymphocyte transformation tests were non-confirmatory for any metal allergy. Brace treatment was started to control the curve progression, and a decision was made to wait on any surgical intervention for about a year to ensure that there were no ongoing infectious findings.

A year after the growing rods removal his curve continued to progress, and he underwent growing rod insertion from T4 to L4 with apical control (single level fusions using allograft at T4-T6 and L3-L4).[6] Surgery and initial post-operative period were uneventful, and he was discharged home on POD3.

He presented to the emergency department (ED) on POD5 with fever, apparent purulent discharge from the surgical site, and skin necrosis (Figure 1). His parents stated that as soon as they arrived home, he had noticeable drainage. He received wound debridement, washout, and wound VAC application. He was admitted, and IV vancomycin and cefepime were initiated. After connecting with his surgeon at the previous institution, it was confirmed that this was the exact presentation that he had after the prior growing rod insertion. His blood and wound cultures remained negative. He was evaluated by infectious disease for an infectious etiology. With the lack of treatment response to wound debridement, VAC application, and antibiotics, as well as the similar presentation to the prior growing rod insertion and the questionable history of a genetic condition, a decision was made to have the allergy and immunology team evaluate him for non-infectious hyperinflammatory etiology. A primary immunodeficiency (PID) panel and immunoglobulin assay were done to rule out any immunodeficiency for this second instance of post-surgical complication. The results revealed very low levels of IgG with normal levels of IgM and IgA. Given the severity of the wound healing, intravenous immunoglobulin was administered.

Gram stain and all cultures (aerobic, anaerobic, fungal, acid-fast bacilli) remained sterile.

HIGHLIGHTS

- This case highlights a rare genetic mutation in NFKB1 leading to a hyperinflammatory response after surgical intervention for early onset scoliosis, complicating postoperative wound healing.
- The patient experienced recurrent wound dehiscence and drainage without evidence of infection, which was managed through immunosuppressive therapy targeting the IL-1B pathway.
- The introduction of Anakinra significantly improved wound healing and minimized inflammatory markers, marking a novel therapeutic approach for managing hyperinflammatory states post surgery.
- Continued use of preoperative Anakinra prevented recurrent wound complications during subsequent surgical interventions.

Figure 1. On postoperative day 5, part of the incision showed signs of dehiscence, and the skin around the incision presented as a large blood-filled blister with superficial necrotic changes.

Serial debridement every 2-3 days was continued to manage the wound. The right-side rod was also exchanged, and the left rod was removed to decrease implant load, with the concern of metal reaction or infection. During the third surgical debridement, new areas of purulence in non-instrumented areas were encountered. Infectious disease recommended IV Daptomycin to cover Gram-positive organisms. Tissues sent for 16s ribosomal amplification failed to demonstrate evidence of any organism.

His PID panel revealed 2 likely pathogenic mutations, 1 in a splice-site in NFKB1 and 1 in a splice-site in DUOX2. In light of this result, as well as continued wound dehiscence despite serial surgical debridement and antibiotic treatment (Figure 2), presuming that poor healing could be attributed to his hyper-inflammatory state, the Allergy and Immunology team recommended Anakinra to manage the hyperinflammatory state. Anakinra targets the IL-1B pathway that has been reported to be upregulated in cases with NFKB1 mutations. Steroid treatment was not favored, given the added risk of poor wound healing.

Anakinra treatment was initiated at 50 mg/day for the first 2 days, then the dose was increased to 50 mg twice a day. Following the initiation of Anakinra, granulation tissue and wound healing response were visible within 3 days (Figure 3). The wound was further managed with dressing changes. Inflammatory markers started to trend downwards. At this point, it was decided that this was not an infectious process, and all antibiotics were discontinued. Following complete wound healing (Figure 4), Anakinra was discontinued.

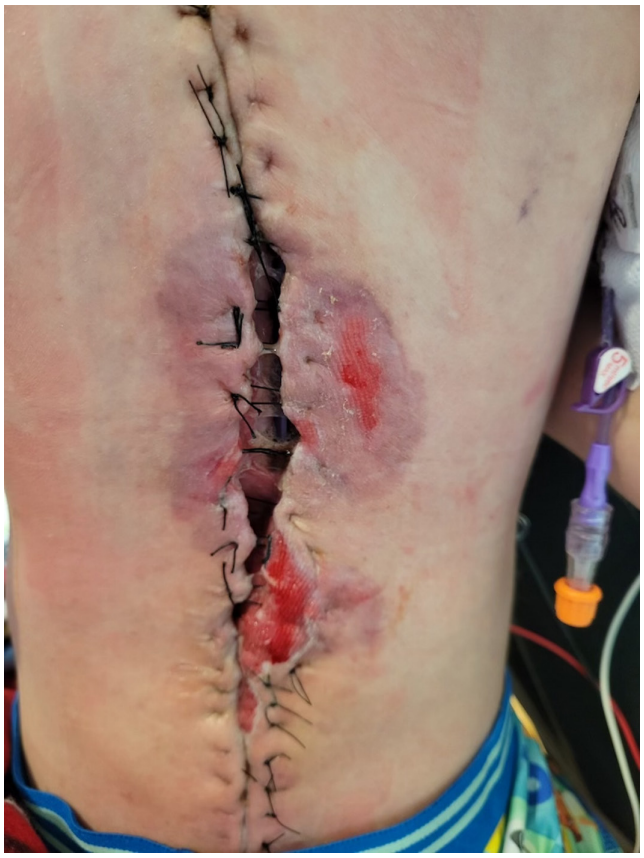

Figure 2. Persistent wound dehiscence despite wound revision and serial debridements, along with negative pressure dressing changes during the second week of treatment. Further serial debridements were done.

Figure 3. Granulation tissue and visible wound healing 3 days after initiating Anakinra (IL-1 receptor antagonist). No further debridements were done, and the wound was managed with dressing changes as the drainage and dehiscence stabilized.

After 9 months from this event, growing rod lengthening and re-insertion of a left-sided rod were done. Per allergy and immunology, as a prophylaxis for the hyperinflammatory response after surgical insult, Anakinra was started a week prior to surgery. He was discharged on Anakinra with a daily subcutaneous 100 mg, eventually tapered and stopped 3 months postoperatively.

Since then, he has undergone 3 serial expansions at intervals of 9-months each and was pre-treated with Anakinra 1 week pre-operatively and for 4-6 weeks post-operatively, without any wound or other postoperative complications.

At his most recent visit, he was 10 years old, 3 years since the growing rod placement, and doing well with no wound issues while maintaining spine deformity correction. The current plan is to continue growing rod expansions every 9 months and then a final fusion at around age 12.

Discussion

Wound drainage after spine fusion or growing rod application in children is not rare.[7] Kabrian et al[8] assessed infection rates in Early Onset Scoliosis (EOS) across different diagnostic categories, identifying infection prevalence rates of 14.7% in neuromuscular cases, 15.9% in congenital cases, 10.2% in syndromic cases, and 2.7% in idiopathic cases. Their analysis revealed that each revision surgery after the initial growing rod procedure, but before the onset of a deep surgical site infection, increased the infection risk by 3.3 times. By the eighth procedure, the likelihood of a deep surgical site infection approached 50%. Furthermore, stainless-steel implants were found to carry a 5.7-fold greater risk of deep wound infection compared to titanium implants.[8]

Majority of wound drainage is minor and self-limited. Wound dehiscence and infection may be problematic and require aggressive treatment. However, wound complication without any evidence of infection is extremely rare, and knowledge on this matter is mostly anecdotal. This report describes a case of early wound dehiscence secondary to a hyperinflammatory reaction in the absence of infection.

The nuclear factor K light-chain enhancer of activated B-cells (NFKB) pathway regulates inflammation, apoptosis, and stress responses among many other cellular processes, and hence plays a key role in host defense and inflammatory responses.[3] The NFKB1 mutation is intriguing because first, it is a splice-site mutation, which makes it very likely that an abnormal protein product will be made. Second, NFKB1 is a key regulator of the innate immune response, and heterozygous mutations have been reported to have a wide array of immunologic phenotypes. Kaustio et al[5] described that within 3 families, 71.4% had antibody defects and recurrent respiratory infections, 35.7% had febrile attacks, and 28.6% had hyper-inflammatory responses to surgery. Other manifestations of this mutation include small vessel vasculitides, gut disease, and aphthous ulcers. In patients with hyper-inflammatory responses to surgery, the authors described a spectrum of "hyper-inflammatory

Figure 4. Completely healed wound with a large scar about a month after the commencement of immunomodulatory treatment.

responses to a dental procedure" vs. "post-operative necrotizing cellulitis." The mutation associated with hyper-inflammatory response to surgery also seemed to be a premature stop codon (e.g., like our patient's, but at a different site). When in vitro studies were performed, this mutation seemed to function in a dominant-negative fashion of the p50/p105, leading to high levels of NLRP3 inflammasome activation and IL-1B release.[5] There are studies looking at larger samples of NFKB1 heterozygous mutations; however, do not comment on surgical complications.[9] Recent literature describes patients with NFKB1 mutations with varying clinical manifestations and therapeutic implications.[10]

Orthopedic surgeons should be aware of rare hyperinflammatory conditions that may complicate wound healing. Patients who present with very early wound dehiscence and an inflammatory reaction out of proportion, with no response to infection management may benefit from detailed immunologic evaluation.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Informed Consent: Informed consent was obtained from the parents of the patient who agreed to take part in the study.

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References

1. Tis JE, Karlin LI, Akbarnia BA, et al. Early onset scoliosis: modern treatment and results. *J Pediatr Orthop*. 2012;32(7):647-657. [CrossRef]
2. Gillingham BL, Fan RA, Akbarnia BA. Early onset idiopathic scoliosis. *J Am Acad Orthop Surg*. 2006;14(2):101-112. [CrossRef]
3. Karin M, Lin A. NF-kappaB at the crossroads of life and death. *Nat Immunol*. 2002;3(3):221-227. [CrossRef]
4. Cogswell PC, Scheinman RI, Baldwin AS Jr. Promoter of the human NF-kappa B p50/p105 gene. Regulation by NF-kappa B subunits and by c-REL. *J Immunol*. 1993;150(7):2794-2804. [CrossRef]
5. Kaustio M, Haapaniemi E, Göös H, et al. Damaging heterozygous mutations in NFKB1 lead to diverse immunologic phenotypes [published correction appears in *J Allergy Clin Immunol*. 2021;148(6):1603. doi:[CrossRef]]. *J Allergy Clin Immunol*. 2017;140(3):782-796. (https://doi.org/10.1016/j.jaci.2016.10.054)
6. Dede O, Demirkiran G, Yazici M. Self-growing instrumentation with gliding connectors for collapsing spine deformities in children: a novel technique. *J Pediatr Orthop*. 2015;35(4):367-373. [CrossRef]
7. Dede O, Bosch P, Bowles AJ, Ward WT, Roach JW. Clinical decision making in early wound drainage following posterior spine surgery in pediatric patients. *Spine Deform*. 2014;2(2):104-109. [CrossRef]
8. Kabirian N, Akbarnia BA, Pawelek JB, et al. Deep surgical site infection following 2344 growing-rod procedures for early-onset scoliosis: risk factors and clinical consequences. *J Bone Joint Surg Am*. 2014;96(15):e128. [CrossRef]
9. Lorenzini T, Fliegauf M, Klammer N, et al. Characterization of the clinical and immunologic phenotype and management of 157 individuals with 56 distinct heterozygous NFKB1 mutations [published correction appears in *J Allergy Clin Immunol*. 2021;148(5):1345. [CrossRef]]. *J Allergy Clin Immunol*. 2020;146(4):901-911. (doi:10.1016/j.jaci.2019.11.051)
10. Eddens T, Lue J, Sojati J, et al. A novel splice-site mutation in NFKB1 presenting as common variable immunodeficiency and postoperative hyperinflammation responsive to anti-IL-1 therapy. *J Allergy Clin Immunol Pract*. 2024;12(10):2873-2876.e1. Published online June 18, 2024. [CrossRef]