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## Case Report Minimal scarring in a premature neonate\*

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## ABSTRACT

*Background:* Scar formation and management is one of the major issues in plastic surgery. Scars are a chronic burden to patients, their families, and the wider healthcare system and while non-surgical and surgical options have been shown to reduce scarring and its impact, there are currently no therapeutic options to completely heal scars or to avoid scarring. Early gestation animals have been reported to heal skin wounds without scarring.

*Case presentation:* We report on a premature, underweight-forage neonate of 30 weeks' gestation that suffered a combination of deep partial thickness abrasions and full thickness wounds following birth trauma, who eventually healed with minimal skin scarring.

*Conclusion:* This case highlights that more research is needed to understand the mechanism and timelines of foetal skin healing, so the knowledge can be used to develop better therapeutic options to treat skin scars in adults.

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\* Declarations: This case report has been written adhering to the STROBE guidelines.

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## Introduction

Scar formation occurs during wound healing following tissue injury. The key stages of wound healing are haemostasis, inflammation, proliferation, and remodelling,<sup>1</sup> Platelets are attracted to injury sites to propagate haemostasis. Neutrophils phagocytose debris and pathogens during the inflammatory phase. During proliferation, keratinocytes and endothelial cells reconstruct the wound surface and blood vessels, respectively. In addition, fibroblasts begin laying down type 1 collagen to replace type 3 collagen which contributes to scar formation. This process continues into the remodelling phase. During the remodelling phase, scar tissue gains its maximum possible tensile strength within a few weeks however it never reaches the full strength of uninjured tissue, and the skin surrounding scar tissue is prone to contracture. The remodelling phase can last months to years and rearrangement of collagen fibres can lead to regression of the scar, but it will always be present. Patients living with scars may suffer from physical dysfunction such as contractures and ulceration, psychosocial trauma, and psychiatric conditions like anxiety and depression. Moreover, scarring costs healthcare systems time and money. The National Health Service in the United Kingdom spends approximately £8.3 billion annually on the clinical management of scars,<sup>2</sup> Various non-surgical and surgical treatments exist for scars, however, none of them leads to a scarless clinical outcome.<sup>1</sup> The only scenarios that lead to scarless healing in animals have been reported in foetuses.

Foetal wound healing has a different mechanism than adult wound healing, leading to scarless healing. This is only true for the skin. In other tissue systems, like the gastrointestinal tract, scars are produced following tissue injury.<sup>3</sup> The pathophysiology of scarless foetal wound healing is largely unknown however a mix of factors are thought to contribute. This includes reduced inflammatory responses, looser collagen structures, altered levels of extracellular matrix components, and keratinocytes stimulating the proliferation and migration of foetal fibroblasts.<sup>3</sup> Previous research has observed that at approximately 24 weeks of gestation, foetal skin wound healing results in scarring therefore it is thought that at this stage foetal skin transitions to a structure resembling adult skin.<sup>1,3</sup>

We report on a premature female neonate older than 24 weeks of gestation (30 weeks of gestation at birth) who suffered a combination of deep partial thickness abrasions and full thickness wounds secondary to birth trauma during an emergency Caesarean section. Five years after sustaining these wounds, the patient had excellent cosmetic outcomes with minimal scarring.

#### Case

The mother of the patient had a history of multiple sclerosis and subfertility and required Clomid (clomiphene citrate) to stimulate ovulation. She became pregnant with triplets. At 16 weeks' gestation, intrauterine surgery was required due to complications with the multiple pregnancy and, soon after, one foetus died in utero. Oligohydramnios developed over the next few weeks, making managing the pregnancy more difficult and closely monitored. At 30 weeks, an emergency caesarean section was indicated due to foetal distress. As a result, the patient suffered a combination of deep partial thickness abrasions and full thickness wounds on the anterior lower abdomen, both thighs and knees and the right foot (14 % TBSA) (see Figure 1 and Supplementary Figure 1). The patient's birthweight was 425 g, compared to their living twin which was 1328 g. Emergency management of the patient was carried out over the next 12 h. The patient was resuscitated and had surgery inside an incubator. The wounds were cleaned and Biobrane was applied. Biobrane is a composite biosynthetic skin substitute that was introduced in 1979<sup>4</sup>. It is composed of short porcine collagen peptides bonded to a nylon layer surrounded by silicone. Seven days after application, Biobrane was completely separated from the skin of the neonate. At this point, regeneration of the skin was observed over the damaged areas (see Figure 2).

Approximately three months post birth, the patient developed a volvulus which required a laparotomy. At five years of age, there were minimal signs of conventional clinical scarring including hypopigmentation of the lower abdomen, and both thighs and knees with barely visible shallow and contracted areas (see Figure 3). On the anterior abdomen, the hyperpigmented and raised transverse scar from the previous laparotomy appeared more prominent than the minimal scarring from the initial birth trauma (see Figure 4).



Figure 1. The premature neonate with a combination of deep partial thickness abrasions and full thickness wounds on the lower abdomen (A), both thighs and knees (B) and the right foot secondary to birth trauma during an emergency Caesarean section.



Figure 2. Regeneration of deep partial thickness abrasions in the premature neonate.



Figure 3. Anterior view of the lower extremities of the patient at 5 years of age displaying minimal signs of scarring including hypopigmentation and barely visible shallow and contracted areas of the thighs and knees.

## Discussion

In this case, minimal scarring was observed in the premature female neonate despite being 6 weeks older than the approximate start of mature scarring in foetal skin. We hypothesise that this may be due to the delayed development of the foetus in-utero. Maternal stresses may have hindered the patient's foetal development. The patient was born weighing 425 g, which is significantly less than the average weight of premature neonates.<sup>5</sup> The patient's mother suffered from oligohydramnios from the early second trimester.



**Figure 4.** Anterior view of the abdomen of the patient at 5 years of age displaying the hyperpigmented and raised transverse scar from the previous laparotomy and anterolateral hypopigmented shallow scarring from the initial birth trauma.

Preterm birth is a well-recognised association of oligohydramnios which may explain why the patient was born prematurely at 30 weeks' gestation. Foetal growth restriction (FGR) is also associated with oligohydramnios.<sup>6</sup> Foetal growth restriction is a condition characterised by the patient being too small (often measured by fundal height) for their gestational age. The mechanism involves a lack of blood supply being supplied to the growing foetus, and therefore inadequate nutrients and oxygen are supplied to the foetus. We speculate that FGR may have also been exacerbated due to a multiple pregnancy, where the blood supply needs to be shared between the foetuses. FGR is associated with chronic maternal diseases, such as hypertension and diabetes, as well as maternal autoimmune diseases, like Systemic Lupus Erythematosus. MS, which the patient's mother suffered from is also an autoimmune disease. The signs of FGR include low birth weight, hypoglycaemia, and low body temperature. In addition to affecting the overall size of the foetus, FGR can impact the foetal development of organs, tissues, and cells.

We hypothesise that the patient had FGR, associated with oligohydramnios, which led to a lack of growth in-utero and therefore the patient did not reach foetal developmental milestones at the expected times. As mentioned, research has shown that scarring starts to occur around 24 weeks gestation in neonates, likely because the wound-healing mechanisms of neonates begin to resemble adult wound healing. As our patient's development was delayed, this may explain why at 30 weeks' gestation, when they were prematurely born, they still managed to heal complex wounds without conventional scarring.

## Conclusion

In summary, this case reports on how developmental delay in utero may have contributed to better foetal skin healing in a premature neonate with a combination of deep partial thickness abrasions and full thickness wounds post delivery trauma. It is also the first known reported case of this nature which was successfully managed using a commercial skin substitute. However, more research is needed to understand the mechanism and timelines of foetal healing, so the knowledge can be used to develop better therapeutic options to treat skin scars in adults going forward.

#### Ethics approval and consent to participate

No ethical approval or consent to participate was required for this article because it is a retrospective descriptive case report.

## **Consent for publication**

The patient's parents provided written consent to the usage of all included images for presentation and publication.

## Availability of data and materials

Please contact the corresponding author for data requests.

## Authors contribution

All authors have contributed, read, and approved this manuscript.

## **Declaration of Competing Interest**

The authors declare they have no competing interests or conflicts or interest.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10. 1016/j.jpra.2023.10.003.

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