Evaluation of post-inflammatory hyperpigmentation in a porcine VCA model

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Purpose of Study

Post-inflammatory hyperpigmentation (PIH) arises following skin inflammation or injury. The severity and persistence of PIH often increase with darker skin tones, particularly in individuals with Fitzpatrick skin types III to VI[1]. Swine skin is structurally, cellularly, and antigenically similar to humans, making them an appropriate animal for use in preclinical PIH studies[2,3]. This study aimed to assess the utility of a porcine vascularized composite allotransplantation (VCA) model in examining histologically observed edema and initial skin pigmentation with the development of PIH as potential predictive markers.

Methods Used

Two autologous vertical rectus abdominus myocutaneous (VRAM) flap transplants were performed using Yucatan pigs. The VRAM flaps were isolated from the left lower abdominal quadrant of each pig and transplanted to the right anterolateral neck of the same pig, as previously described[3]. Dermal edema was assessed through histological examination of biopsies taken daily from graft sites. The degree of edema was categorized as none, mild, moderate, or severe based on the extent of interstitial fluid accumulation observed in the tissue sections. Epidermal edema was quantified histologically by measuring the distance between the deepest and most superficial points of the stratum basale to the stratum corneum. Gross hyperpigmentation was evaluated via photo documentation each day.

Summary of Results

In the autologous grafts, a direct correlation was observed between the severity of histologically assessed edema and a darker baseline skin tone with the development of PIH. In one pig, PIH was visible by POD5 following moderate to severe edema. In the other pig, dermal edema remained mild, the baseline skin tone was lighter, and PIH was absent. Hematoxylin and eosin staining also revealed an increased prominence of melanocytes in the epidermis as edema progressed. For the pig that experienced hyperpigmentation, there was a 110.73 μm total change in epidermal thickness by POD5. In contrast, the pig that exhibited normal pigmentation had only a 71.37 μm change in epidermal thickness by POD5.

Conclusions

The findings of this study reveal a correlation between post-surgical edema levels, baseline skin tone, and the development of PIH following autologous VRAM flap transplants. Notably, moderate to severe edema preceded the onset of hyperpigmentation, suggesting that increased skin graft edema could serve as a risk factor for PIH. Although there is no direct equivalent of the Fitzpatrick skin grading scale for swine, these findings underscore the importance of managing edema early after transplantation to potentially reduce the risk of PIH. Additionally, in this study, swine with darker baseline skin tones exhibited hyperpigmentation, whereas those with lighter skin tones did not, reflecting the pattern of PIH commonly observed in humans. This finding supports the use of porcine VCA models in future research investigating the etiology of PIH and potential therapies.

References

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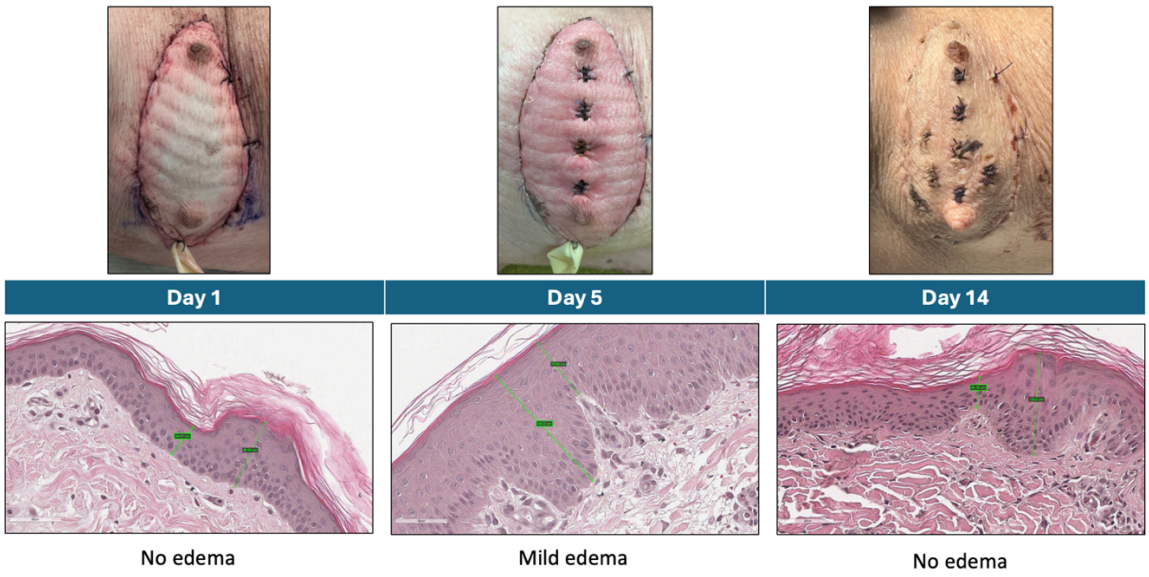
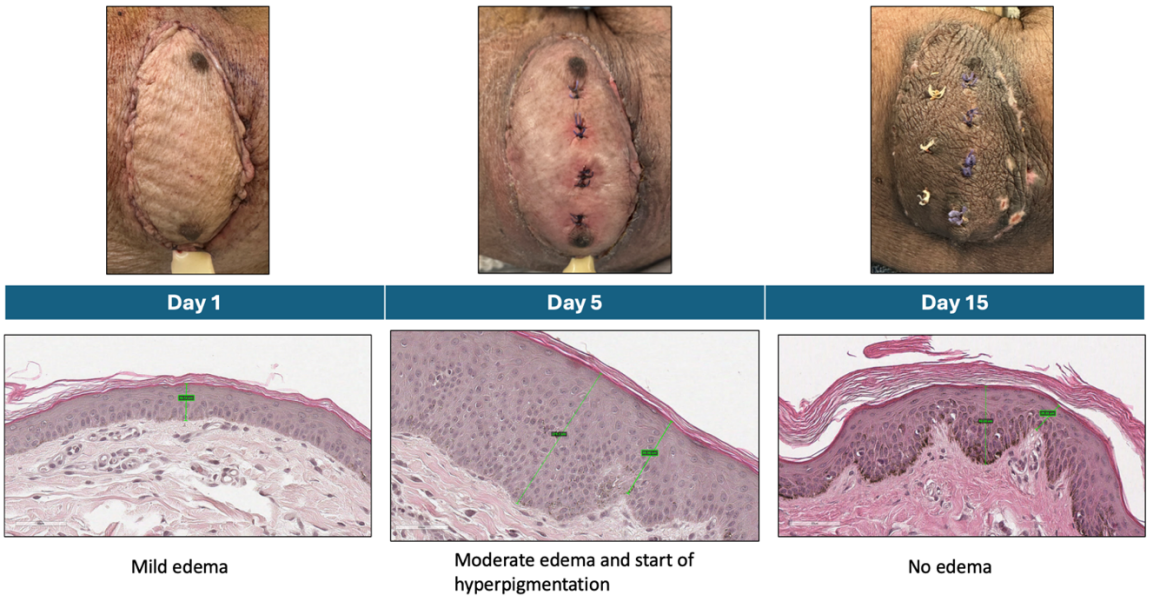
2. Blades CM, Greyson MA, Dumanian ZP, et al. Development of a Porcine VCA Model Using an External Iliac Vessel-Based Vertical Rectus Abdominus Myocutaneous Flap. J Reconstr Microsurg. Published online August 6, 2024. doi:10.1055/s-0044-1788812
3. Wang Y, Herringshaw E, Anderson RR, Tam J. The Yucatan miniature swine as a model for post-inflammatory hyperpigmentation. Pigment Cell Melanoma Res. 2024;37(3):403-410. doi:10.1111/pcmr.13162

Figures and tables for the poster, not for the abstract:

Figure 1: Gross images and histology of the autologous swine with normal pigmentation and post-inflammatory hyperpigmentation.



Autologous normal pigmentation



Autologous hyperpigmented

Table 1: Post-operative change in epidermal thickness over time in the proposed swine model

Pig and days post-operation	Average measured thickness (μm)	ΔThickness from day 0 (μm)
Normal pigmented swine:		
D0	61.28	
D1	60.75	-0.53
D2	69.17	7.89
D3	72.39	11.11
D4	84.73	23.45
D5	132.65	71.37
D6	93.92	32.64
D7	103.51	42.23
D14	75.99	14.71
Hyperpigmented swine:		
D0	42.9	
D1	43.72	0.82
D2	63.56	20.66
D3	120.68	77.78
D4	107.74	64.84
D5	153.63	110.73
D6	106.5	63.6
D7	132.39	89.49
D15	65.79	22.89