SKIN AGE DEPOSITS DECREASED ONE YEAR AFTER PANCREAS-KIDNEY TRANSPLANTATION

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INTRODUCTION

AGE accumulation in diabetic patients has been proposed as one of the most important mechanisms leading to microvascular and macrovascular complications. Pancreas-kidney transplantation (PKT), reverting uremia and hyperglycemia, may result in AGE reduction or removal. However, this dynamic process is still unknown.

OBJECTIVES

We conducted a prospective study in 15 patients undergoing PKT to analyze skin AGE deposits evolution after the PKT procedure, comparing with their basal status on the transplantation day (T0).

METHODS

The first skin biopsy was obtained at T0, during the kidney transplantation surgery; the second one was obtained through a 5mm skin punch 12 months after (T12), from the left abdominal wall, 2-3 cm below the scar of the surgical incision used to perform the kidney transplantation (a part of the body with low chronic UV-exposure; and the local of the two biopsies was very close to each other).

Healthy skin from 6 non-diabetic subjects – from the trunk - aging between 30 and 45 years-old were used as control samples, to assess AGE deposition in the absence of diabetes.

Immunochemistry assay utilizing a polyclonal anti-AGE antibody (ab23722, Abcam, Cambridge, UK) was used to evaluate skin AGE deposition, comparing T0 and T12 samples from each patient.

A semi-quantitative AGE assessment was made based on its immunoreaction intensity, and graded on a scale from 0 (absent), to 1+ (weakly), 2+ (moderately) or 3+ (strongly positive). All the samples were analyzed by the same pathologist; in two different occasions; and it was a blind analysis: he did not know the characteristics of patients and the timing of biopsy before observation.

RESULTS

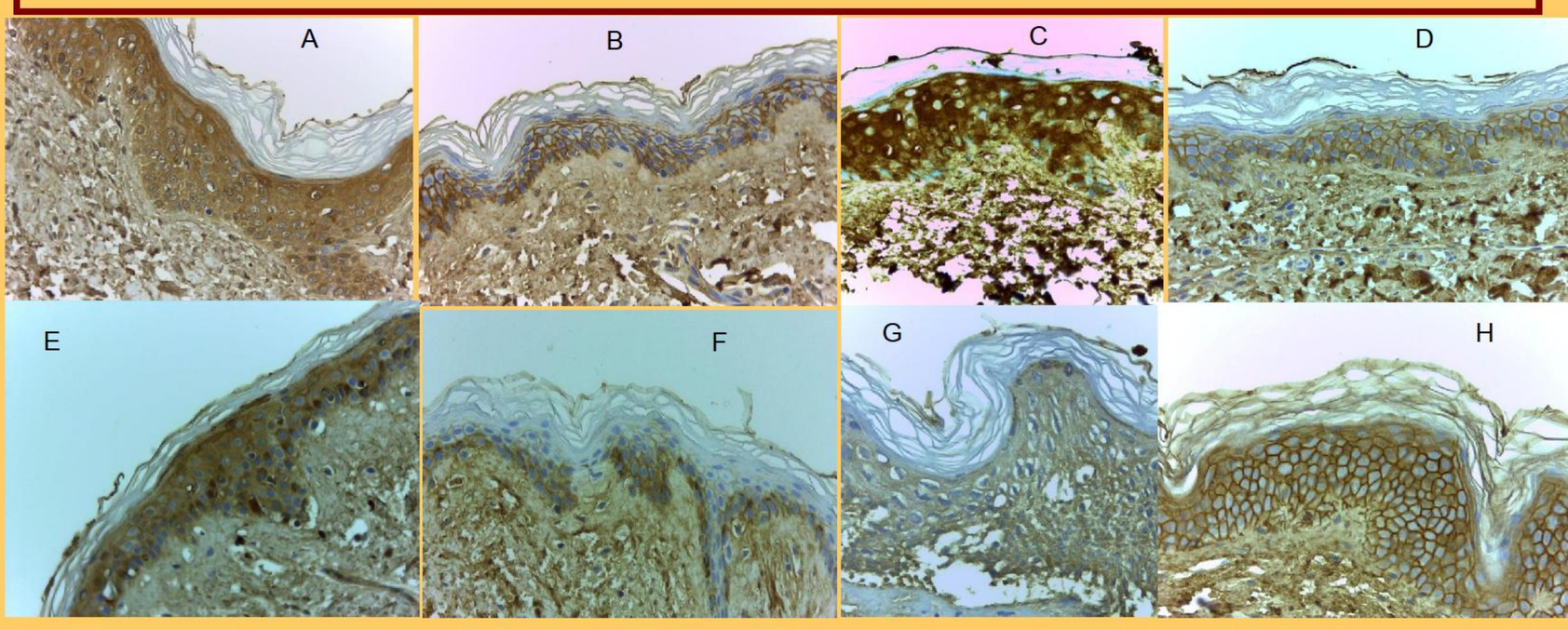
Case (n)	SPKT	Epidermis	Epidermis	Epidermis
		AGE immunoreaction	Immunoreaction pattern	Intensity
(pts)		(layers with + immunostain)		(From 0 to 3+)
1	before	basal, spinous, granular	Diffuse cytoplasmic	2+ (basal layer 1+)
	after	basal, spinous, granular	Peripheral/interkeratinocytic	2+
2	before	basal, spinous	Peripheral/interkeratinocytic	1+
	after	basal	Peripheral/interkeratinocytic	1+
3	before	basal, spinous, granular	Diffuse cytoplasmic	2+
	after	basal, spinous, granular	Diffuse cytoplasmic	1+
4	before	basal, spinous, granular	Diffuse cytoplasmic	3+
	after	basal, spinous, granular	Peripheral/interkeratinocytic	2+
5	before	basal, spinous, granular	Diffuse cytoplasmic	2+
	after	basal, spinous, granular	Peripheral/interkeratinocytic	1+/2+ (spinous 2+)
6	before	basal, spinous, granular	Diffuse cytoplasmic	2+
	after	basal, spinous, granular	Mixt	1+/2+
7	before	basal, spinous, granular	Diffuse cytoplasmic	2+
	after	basal, spinous, granular	Mixt	1+/2+
8	before	basal, spinous, granular	Diffuse cytoplasmic	3+
	after	basal, spinous, granular	Peripheral/interkeratinocytic	1+
9	before	basal, spinous, granular	Mixt	1+
	after	basal	Peripheral/interkeratinocytic	0/1+ (basal 1+)
10	before	basal, spinous, granular	Diffuse cytoplasmic	2+
	after	basal	Peripheral/interkeratinocytic	1+
11	before	basal, spinous, granular	Diffuse cytoplasmic	2+
	after	basal, spinous, granular	Peripheral/interkeratinocytic	2+
12	before	none		0
	after	none		0
13	before	basal, spinous, granular	Diffuse cytoplasmic	2+
	after	basal, spinous, granular	Peripheral/interkeratinocytic	1+
14	before	basal, spinous, granular	Diffuse cytoplasmic	1+
	after	basal, spinous, granular	Peripheral/interkeratinocytic	1+
15	before	basal, spinous, granular	Diffuse cytoplasmic	1+
	after	basal, spinous, granular	Peripheral/interkeratinocytic	1+

AGE immunostaining was **invariably negative** in some specific cells/areas: the outer epidermal layer (stratum corneum), the erector pili muscle and the eccrine sweat glands.

It was **invariably positive** in others: fat cells, vascular endothelial cells, dermal collagen fibers (on superficial dermis 2+/3+, on deeper dermis 3+), and perivascular collagen. (It is known that dermal layers have a lower turnover than epidermis).

→In 11 among the 15 cases: a change from a cytoplasmic diffuse immunoreaction pattern on T0, to an interkeratinocytic pattern on T12, only peripherally staining the cells, with an aspect usually described as "chicken wire" pattern.

→At least **in 7 cases**, we have also observed **a decrease on the intensity of AGE immunoreaction** one year after SPKT



Epidermal Immunostaining for AGE: patient 4 before (**A**) and after SKPT (**B**); patient 8 before (**C**) and after SKPT (**D**); patient 10 before (**E**) and after SKPT (**F**); patient 11 before (**G**) and after SKPT (**H**). (400x amplified, hematoxylin counterstained). Images showing the main immunostaining changes, from a diffuse cytoplasmic to an interkeratinocytic or peripheral pattern, often less intense, at time 12.

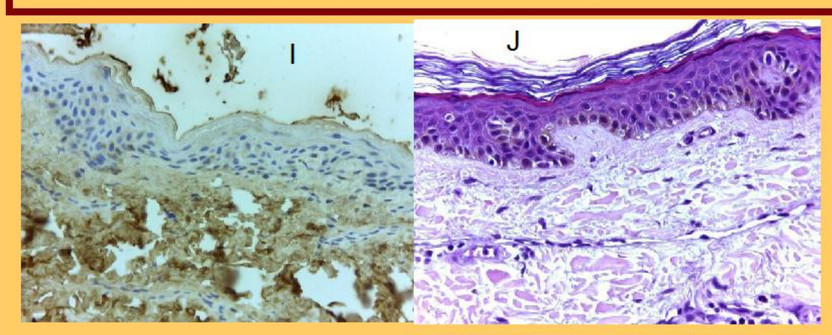


Image I represents a **negative control** for AGE immunostaining, from a young healthy individual. Irrelevant changes were found on hematoxylin-eosin staining in our patient population (exemplified on image **J**)

CONCLUSIONS

→From T0 to T12, there was a decreased AGE immunostaining in the majority of our patients, in epidermal layers.

→We also observed a change from a diffuse to a peripheral pattern (saving the central cytoplasmic area) of the AGE immunostaining. The explanation for the two different patterns is not known, but it seems concordant with a lower intensity of the staining.

→Based on our results, we concluded that skin AGE deposits - glycoxidation markers - in DM1 patients, may start to decrease during the first year after SPKT. Further studies in a larger sample and with extended follow-up are needed to confirm these results.

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M2) Renal transplantation. Clinical.

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DOI: 10.3252/pso.eu.52era.2015

ePosters supported by F. Hoffmann- La Roche Ltd.

52 ERA EDTA CONGRESS London 2015

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