

Supplementary Material**Paraneoplastic Syndromes in Patients with Keratinocyte Skin Cancer**

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Table S1. Paraneoplastic syndromes in patients with keratinocyte skin cancer: Compilation of the clinical features stratified according to patients' gender.

Keratinocyte skin cancer		Total (N=41)	Male (N=34)	Female (N=7)
Localization ^a	Head / neck	7	4	3
	Trunk	19	17	2
	Extremities	14	12	2
	N/A	1	1	0
PNS	MAH / HHM	32	27	5
	Anemia	4	3	1
	Bazex syndrome	2	2	0
	Other ⁱ	3	2	1
Timing of PNS ^b	before	3	3	0
	simultaneously	22	16	6
	after	16	15	1
Primary ^c	No	21	15	3
	Yes	17	15	2
	N/A	3	4	1
Recurrence ^d	No	27	21	6
	Yes	11	11	0
	N/A	3	2	1
Metastases	No	20	16	4
	Yes	17	15	2
	N/A	4	3	1
Predilection ^e	No	9	5	4
	Yes	23	21	2
	N/A	9	7	2
	<i>Genodermatosis</i> ^g	4	3	1
	<i>Acquired</i> ^h	19	18	1
	Scar/Ulcus	9	8	1
	(burn) Scar	6	6	0
	Ulcus	3	2	1
	Hidradenitis suppurativa	8	8	0
	Chronic arsenic intoxication	1	1	0
	Lymphedema	1	1	0
Resolution ^f	Yes	25	20	5
	No	13	12	1
	N/A	3	2	1

Abbreviations. N/A: not available, PNS: paraneoplastic syndrome, MAH: malignancy associated hypercalcemia, HHM: humoral hypercalcemia of malignancy.

^aLocalization: localization of the primary neoplasm.

^bTiming of PNS: time point of PNS diagnosis relative to the diagnosis of skin cancer.

^cPrimary: primary tumor only

^dRecurrence: local tumor recurrence after treatment.

^ePredilection: Presence of a condition that predisposes to skin cancer development.

^fResolution: resolution of paraneoplastic syndrome after skin cancer treatment. inflammatory arthralgias, neuropathy, antiphospholipid syndrome

^gGenodermatoses: recessive dystrophic epidermolysis bullosa, porokeratosis Mibelli, xeroderma pigmentosum

^hAcquired: acquired predilection.

Table S2. Paraneoplastic syndromes in patients with keratinocyte skin cancer. Compilation of the clinical features stratified according to the different skin cancer types. No (%): Number of cases and distribution of the cases among the different cancer types (% of cases with available information).

Keratinocyte skin cancer, No (%)		Total 41(100)	BCC ^a 4(10)	SCC 35(85)	Other ^b 2(5)
Sex, No (%)	Male	34	2 (6)	30 (88)	2 (6)
	Female	7	2 (29)	5 (71)	0 (0)
Localization ^c , No (%)	Head / neck	7	2 (29)	3 (42)	2 (29)
	Trunk	19	2 (11)	17 (89)	0 (0)
	Extremities	14	0 (0)	14 (100)	0 (0)
	N/A	1	0	1	0
PNS, No (%)	MAH / HHM	32	0 (0)	30 (94)	2 (6)
	Anemia	4	3 (75)	1 (25)	0 (0)
	Bazex syndrome	2	0 (0)	2 (100)	0 (0)
	Other ⁱ	3	1 (33)	2 (67)	0 (0)
Timing of PNS ^d , No (%)	before	3	0 (0)	3 (100)	0 (0)
	simultaneously	22	1 (5)	19 (85)	2 (10)
	after	16	3 (19)	13 (81)	0 (0)
Primary ^e , No (%)	No	21	1 (5)	20 (95)	0 (0)
	Yes	17	2 (12)	13 (86)	2 (12)
	N/A	3	1	2	0
Recurrence ^f , No (%)	No	27	2 (7)	23 (86)	2 (7)
	Yes	11	1 (9)	10 (91)	0 (0)
	N/A	3	1	2	0
Metastases, No (%)	No	20	3 (15)	15 (75)	2 (10)
	Yes	17	1 (6)	16 (94)	0 (0)
	N/A	4	0	4	0
Predilection ^g , No (%)	No	9	2 (22)	7 (78)	0 (0)
	Yes	23	0 (0)	22 (96)	1 (4)
	N/A	9	2	6	1
	Genodermatosis ^j	4	0 (0)	4 (100)	0 (0)
	Acquired ^k	19	0 (0)	18 (95)	1 (5)
	Scar/Ulcus	9	0 (0)	8 (89)	1 (11)
	Hidradenitis suppurativa	8	0 (0)	8 (100)	0 (0)
Resolution ^h , No (%)	Other ^l	2	0 (0)	2 (100)	0 (0)
	Yes	25	2 (8)	21 (84)	2 (8)
	No	13	1 (8)	12 (92)	0 (0)
	N/A	3	1	2	0

^aAbbreviations. BCC: basal cell carcinoma, SCC: cutaneous squamous cell carcinoma, N/A: not available, PNS: paraneoplastic syndrome, MAH: malignancy associated hypercalcemia, HHM: humoral hypercalcemia of malignancy.

^bOne case of trichilemal carcinoma and one case of pilomatrixoma.

^cLocalization: localization of the primary neoplasm.

^dTiming of PNS: time point of PNS diagnosis relative to the diagnosis of skin cancer.

^ePrimary: primary tumor only

^fRecurrence: local tumor recurrence after treatment.

§Predilection: Presence of a condition that predisposes to skin cancer development.

hResolution: resolution of paraneoplastic syndrome after skin cancer treatment.

iInflammatory arthralgias, neuropathy, antiphospholipid syndrome

jGenodermatoses: recessive dystrophic epidermolysis bullosa, porokeratosis Mibelli, xeroderma pigmentosum

kAcquired: acquired predilection.

lChronic arsenic intoxication, lymphedema.

Table S3. Malignancy associated hypercalcemia (MAH) in KSC patients: Per patient laboratory findings of the N=32 cases with MAH.

Ref ^a	Tumor	Age/Sex ^b	Hypercalcemia ^c	Phosphorus	PTH ^{d,e}	PTHrP ^e	D ₃ ^e
12	SCC	67/M	severe	increased	decreased	increased	decreased
13 ^f	SCC	58/M	severe	N/A	decreased	N/A	N/A
14	SCC	82/M	moderate	norm	norm	increased	N/A
16	SCC	38/M	moderate	norm	norm	N/A	norm
17 ^f	SCC	50/M	mild	N/A	norm	increased	N/A
17 ^g	SCC	60/M	mild	N/A	N/A	N/A	N/A
18 ^f	SCC	20/M	severe	norm	norm	increased	decreased
19	SCC	74/M	severe	norm	norm	N/A	decreased
20 ^g	SCC	65/M	moderate	N/A	norm	norm	norm
21	SCC	72/M	moderate	N/A	norm	increased	norm
22	SCC	45/M	severe	N/A	decreased	increased	decreased
23	SCC	59/M	moderate	decreased	decreased	increased	N/A
24	SCC	65/F	severe	N/A	decreased	increased	N/A
25	SCC	80/F	severe	decreased	decreased	increased	norm
26	SCC	17/M	severe	norm	decreased	increased	increased
27	SCC	38/M	moderate	decreased	norm	N/A	norm
28	SCC	68/F	severe	norm	decreased	increased	N/A
31	TRC ^d	42/M	severe	N/A	N/A	increased	N/A
32	PLM ^d	32/M	severe	N/A	decreased	increased	norm
34 ^f	SCC	5/F	severe	norm	decreased	N/A	N/A
35	SCC	83/M	moderate	decreased	decreased	increased	N/A
36 ^g	SCC	35/M	severe	norm	norm	N/A	N/A
37	SCC	81/M	severe	norm	norm	N/A	N/A
38 ^g	SCC	50/M	severe	norm	decreased	increased	norm
39 ^f	SCC	45/M	severe	N/A	norm	N/A	N/A
40	SCC	62/M	severe	norm	N/A	N/A	N/A
43	SCC	53/M	moderate	decreased	decreased	increased	N/A
44 ^g	SCC	68/M	moderate	N/A	N/A	N/A	N/A
45 ^g	SCC	63/M	mild	norm	decreased	increased	norm
46 ^g	SCC	51/M	mild	norm	norm	increased	norm
48	SCC	28/F	severe	N/A	norm	increased	norm
49	SCC	58/M	severe	norm	decreased	increased	decreased

^aRef: Reference number (References list in main text). ^bM: male, F: female. ^cMild: 10.7 – 11.9 mg/dL; moderate: 12.0-13.9 mg/dL; severe: ≥14 mg/dL. ^dAbbreviations. D₃: 1,25 (OH)₂ D₃; KSC: Keratinocyte Skin Cancer; PLM: pilomatrixoma; PTH: parathormone; PTHrP: parathormone related protein; SCC: cutaneous Squamous Cell Carcinoma; TRC: trichilemmal carcinoma. ^eExplanations. norm: within normal range; increased: above norm range; decreased: below norm range; N/A: value not available. ^fHypercalcemia-Leukocytosis cases. ^gAssociated with hidradenitis suppurativa.