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Cutaneous clonal mature plasmacytoid dendritic cell dermatosis in patients with myeloid neoplasms

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Abstract:

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Cutaneous clonal mature plasmacytoid dendritic cell dermatosis in patients with myeloid neoplasms.

Short title: Clonal mature pDC dermatosis

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Abbreviations used:

AML, acute myeloid leukemia; CCUS, clonal cytopenia of undetermined significance; CMML, chronic myelomonocytic leukemia; CPSS-mol, molecular CMML specific prognostic scoring system; CR, Complete response; HSCT, hematopoietic stem-cell transplantation; iDC, indeterminate dendritic cell; IPSS-M, Molecular International Prognostic Scoring System; MC, Myelodysplasia cutis; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasm; NGS, next-generation sequencing; NR, no response; pDC, plasmacytoid dendritic cell; PR, partial response; UV, ultraviolet

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Abstract : Mature pDC dermatosis associated with myeloid neoplasms are characterized by papulo-nodular itchy dermatosis with clonal relationship to underlying myeloid neoplasm using next-generation sequencing (NGS) in skin and blood samples and high association with chronic myelomonocytic leukemia.

Dear editor,

Mature plasmacytoid dendritic cell (pDC) expansions have been described in the blood, lymph-node and bone marrow in various myeloid neoplasms (MN) (chronic myelomonocytic leukemia (CMML), myelodysplastic syndrome (MDS), myeloproliferative neoplasm (MPN), and acute myeloid leukemia (AML)). [1,2,3,4,5] Blood pDC in pDC-AML are clonally related to blast cells [6,7] The cutaneous infiltration by pDC and/or indeterminate dendritic cell (iDC) has been reported in CMML patients, and the term pDC dermatosis has recently been coined to describe this pathological finding.[8,9] It can be differentiated from CMML skin tumors, blastic pDC neoplasm and blastic iDC neoplasm based on morphology and phenotype.[8] While pDC infiltrate in bone marrow seems to be associated with poor prognosis in CMML,[10] the significance and clinical findings of cutaneous pDC expansion in CMML/MDS/AML has not yet been well documented. Here, we report 14 cases of pDC dermatosis manifesting as papulo-nodular itchy dermatosis associated with MN, and study its clonal relationship to underlying MN.

We included all patients followed at Hôpital Saint-Louis, Paris, France, between January 2010 and April 2022 according to the following criteria: (1) non-blastic pDC (with or without iDC) cutaneous infiltrate, (2) skin eruption, (3) diagnosis of MN (AML, MDS, or CMML) according to the 2022 International Consensus Classification (ICC) of MN.[11] Mature pDC were defined as CD123+ TCF4+ CD2AP+ CD1a- S100- CD207- CD163- granzyme B +/- CD56- MPO-, and mature iDC as CD1a+ S100 +/- CD207- CD163- CD123- TCF4- CD2AP- CD56- MPO-. The percentage of pDC, iDC, and CD163+ myeloid cell over total nucleated cells in skin sample was evaluated independently by 3 pathologists. We used next-generation sequencing (NGS) to screen at least 30 genes recurrently mutated in MN on DNA extracted from skin lesion formalin-fixed paraffin-embedded tissue sections, bone marrow aspirate or peripheral blood from patients. MN prognosis was evaluated using the Molecular

International Prognostic Scoring System (IPSS-M) for MDS and the molecular CMML specific prognostic scoring system (CPSS-mol) for CMML.[2,12,13]

Clinico-histological characteristics and NGS analysis of the 14 patients are summarized in Table 1. Patients were mainly male (sex-ratio 3.6; 11M/3F). Median-age at first skin lesion appearance and at MN diagnosis were 78 and 79 years respectively. Diagnosis of pDC dermatosis occurred before diagnosis of MN in 4 cases, at the same time in 7, and during follow-up in 3. Patients had diffuse pruritus (n=12, 86%) with fixed or recurrent flares of papules (n=12, 86%), nodules (n=5), mainly on the trunk (n=6) (figure 1a-d). Two patients had lesions limited to the face. No clinical difference was seen according to the presence of iDC. Associated MN were CMML (n=10), MDS (n=2), AML (n=1) while 1 patient had clonal cytopenia of undetermined significance (CCUS) rapidly evolving to AML. No increase in pDC was reported in flow cytometry of bone marrow aspirate or blood at MN diagnosis.

Histologically, the pDC and iDC skin infiltrates were perivascular or diffuse in the dermis (figure 1e-h), with variable density (Table 1), always intermixed with CD3+ T-cells, and rarely with neutrophils (n=3) or eosinophils (n=4). Myeloid CD163+ cells were less abundant than pDC and iDC population, no blast cells were present in the skin and Ki67 was ≤20% in all skin infiltrates.

Paired NGS of skin and bone marrow (or blood) samples were available for 13 patients. The same gene mutations were detected in both tissues in all patients, with small differences in clone sizes and detection of smaller clones in skin, blood, or bone marrow. Pathogenic mutations of *TET2, SRSF2, ASXL1,* and *RUNX1* were the most frequent in skin biopsies (57%, 50%, 42% and 28% respectively). Mutations of RAS pathway genes (*KRAS, NRAS, CBL, NF1*) were detected in 8 cases (57%). Maximum VAF of mutated genes in the skin was positively correlated with pDC+iDC percentage in skin sample (r=0.72, Pearson correlation), but not with CD163+ myeloid cell (r=0.06).

Six patients were treated with high potent topical corticosteroids (3 partial response, (skin lesions disappearance up to 30%) (PR), 3 no response (NR)). Prednisone (0.1-1mg/kg/day) was consistently efficient in 4 patients (4 complete response (CR), median duration of response: 15 months) with relapse after treatment discontinuation. MN-directed therapies didn't show efficacy both on the dermatosis and the MN. Allogenic hematopoietic stem cell transplantation (allo-HSCT) was consistently efficient on skin lesions (CR = 3/3).

Median follow-up was 36 months (range, 3-84) and 4 patients out of 14 died (29%). Three patients with CMML (2) or CCUS (1) died of progression to AML (time from skin symptoms and CMML diagnosis to death: 13 and 6 months), and one CMML patient died of sepsis.

We herein describe the features of pDC dermatosis in MN, and demonstrate for the first time the clonal relationship between skin infiltrate and underlying MN. Among myeloid cells in skin infiltrate, pDC and iDC were the predominant populations and positively correlated to gene mutation VAF. Further work using single-cell or flow-sorted-cell sequencing approaches, mutational signatures, and phylogenomic analyzes on fresh tissue samples will be necessary to precisely assess the mutational landscape of pDC and iDC in this context, as we cannot exclude that other myeloid cells may also carry mutations detected in the skin sample.

All our patients had a chronical, itchy, papular or nodular skin eruption occurring mostly during the course of a MN, and sometimes before its diagnosis. As in previous reports, pDC dermatosis was mostly associated with CMML[8,9]. Differential diagnosis included prurigo nodularis, but lesions mostly involved the trunk and face, and less predominantly the limbs, the dermal infiltrate was usually too dense and/or deep, and phenotyping showed abundant mature pDC and iDC infiltrate. Myelodysplasia cutis (MC) was ruled out by the absence of non-blastic histiocytoid MPO+ cells in the infiltrate, and the absence of plaques and

annularity of skin lesions[14]. Leukemia cutis in AML and blastic pDC neoplasm typically presents as non-itchy erythemato-violaceous nodules, with infiltrate made of blast cells.

As reported in MC[14,15], pDC dermatosis can predate MN diagnosis. Physicians should be aware about this entity and may perform hematological workup (blood and/or bone marrow) including NGS and blood monocyte subset phenotyping[16] when this type of skin infiltrate is found. Nodal and bone marrow pDC proliferation in CMML have been associated with poor prognosis, with high risk of AML transformation.[4,10] The prognosis of pDC dermatosis in CMML is less clear. A previous report of 16 patients with CMML and mature pDC dermatosis suggested a better prognosis than patients with other CMML-related skin infiltrate.[8] In a more recent study, 4 patients out of 6 with pDC dermatosis died of infection or hematological progression.[9] In our series, 4 patients out of 14 died after 36 months follow-up. Thus more data are needed to clarify the prognosis of pDC dermatosis.

The mechanism of skin pDC expansion in CMML and other MN is unclear. Clonal expansion of skin pDC could derive from a common mutated myeloid progenitor or from differentiation of circulating tumor cells. *TET2* mutation, found in 50% of our skin samples, is known to promote IRF7 expression, a transcription factor responsible for pDC proliferation.[17] Similarly, *RUNX1* mutation found in 28% of our cases is known to upregulate pDC transcriptional programs in pDC-AML.[6] Another interesting hypothesis is the involvement of UV-radiation in the skin in shaping the mutation landscape of cells that may recirculate, as described in blastic plasmacytoid dendritic cell neoplasm. [18]UV-radiation or various other local stimuli may participate to dendritic cell transdifferentiation as described in juvenile CMML.[19]

Overall, clonal mature pDC dermatosis is characterized by 1/ a chronic itchy skin eruption with papules or nodules, 2/ a frequent occurrence at time of underlying MN diagnosis, 3/ a high association with CMML, 4/ shared mutational profile in skin sample and MN, 5/ efficacy of oral corticosteroids and allo-HSCT, 6/ an uncertain risk of AML progression.

This non-interventional study was performed in accordance with the declaration of Helsinki. Patients gave written informed consent for the publication of their clinical pictures and for inclusion of their tissue sample in the Lymphoteq tissue bank

Authorship

TM, AO and MB designed the research and analyzed data and wrote the paper.

None of the authors has a relevant conflict of interest.

Legend of the figures

Figure 1.

a,b,c,d Papulo-nodular skin eruption in patients with pDC dermatosis ; e,f Dense perivascular dermal infiltrate without blast cells (case 12, HES x40 and x330), g CD123 expression in mature pDC (case 12, x330), h TCF4 expression in mature pDC (case 12, x 200), i CD2AP expression in mature pDC (case 12, x 200).

Table 1: Clinico-pathologic, genetic and therapeutic features of 14 patients with MNs and with pDC dermatosis

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Table 1: Clinico-pathologic, genetic and therapeutic features of 14 patients with myeloid neoplasms and with pDC dermatosis

Patient, Sex, age	Clinical presentation	Pruritus	Myeloid neoplasm (ICC 2022) and time of diagnosis related to pDC dermatosis	Pronostic scoring (IPSS-M or CPSS-mol)	Skin histology (% of cell type in the sample*) ; total percentage of pDC+iDC in the sample*	Percentage of CD163+ myeloid cells in the skin sample	Targeted sequencing of skin biopsy (gene, VAF %)	Targeted sequencing of bone marrow or blood (gene, VAF%) / cytogenetic	Hematological Treatment and response	Skin-directed treatment and response	Death, follow-up time after cutaneous sign, after diagnosis of myeloid neoplasm and cause of death
#1, F, 46	Papules, face, trunk	No	AML with myelodysplasia-related gene mutations concurrent	-	Dermal infiltrate of pDC (30), iDC (1); 31%	*5*	*RUNX1 x 2 (26,23) BCORL1 (23) FLT3-ITD (duplication)*	*RUNX1 x2 (45,43) BCORL1 (41) FLT3-ITD (duplication) / normal*	Allo-HCT (CR)	Allo-HCT (CR)	No, 3 years and 3 years
#2, M, 74	Papules, legs	yes	MDS, NOS with multilineage dysplasia 4 years later	Low -0,81	Dermal infiltrate of pDC (10), iDC (15); 25%	*10*	*BRCC3 (16) TET2 (10) SRSF2 (9) RUNX1 (9)*	*TET2 (38) SRSF2 (43) RUNX1 (44) BRCC3 (NA) / normal*	NA	NA	No, 4 years and 4.4 years
#3, M, 65	Papules, head, trunk, arms, legs	yes	CMML 1 year before	Intermediate 1	Dermal infiltrate of pDC (20), iDC (10); 30%	*15*	*IDH2 (19) BRCC3 (18) SRSF2 (10) NF1 (8) CBL (6)*	*CBL (73) IDH2 (43) SRSF2 (35) NF1 (4) CBL (73) / normal*	Azacitidine and Allo-HCT (CR)	Azacitidine and Allo-HCT (CR)	No, 6 years and 7 years
#4, M, 63	Papules, trunk	yes	CMML 3 months later	Intermediate 2	Dermal infiltrate of pDC (25),iDC (10); 35%	*10*	*TET2 x2 (23, 19) 20CTCF (1930) NRAS (1019) ASXL101 (17)20*	*TET2 x2 (53, 22) NRAS (53) SRSF2 (40) ASXL1 (35) / normal*	Allo-HCT (CR)	Allo-HCT (CR)	No, 2.25 years 2 years
#5, M, 84	papules, trunk, arms, legs	yes	CMML Concurrent	Intermediate 1	Dermal infiltrate of pDC (35); 35%	*20*	*JAK2 (3106) TET2 5(27) SRSF2 10(22)*	*JAK2 (70) TET2 (44) SRSF2 (43) / normal*	NA	NA	NA
#6, M, 84	Papules, nodules, Head	yes	CMML 1 year later	Intermediate 2	Dermal infiltrate of pDC (45),	*30*	*TET2 x3 (55,20,17) ASXL1 (31)*	*TET2 x3 (88,4,4) SRSF2 (44) ASXL1 (42) NRAS (24)*	No treatment, surveillance	High potent topical corticosteroids	Yes, 4 years, 3 years,

					iDC (2); 47%		*NRAS (23)* *SRSF2 (21)*	/46,XY,add(11)(p11)/46, XY		and tacrolimus (PR) Prednisone 1 mg/kg/d (CR)	sepsis from lung infection
#7, F, 86	Papules	no	CMML, 8 months before	Intermediate 2	Dermal infiltrate of pDC (30), iDC (1); 31%	*10*	*KRAS(22),* *SF3B1 (21)* *SMC3 (17)* *RUNX1 (17)* *FLT3-ITD*	*KRAS (43)* *SF3B1 (42)* *SMC3 (42)* *RUNX1 (13)* *FLT3-ITD* */ normal*	Sorafenib 200 mg twice a day and decitabine (NR)	High potent topical corticosteroids (NR) Prednisone 1m/kg/day (CR)	Yes, 1.1 years, 6 months, AML
#8, M, 89	Papules	Yes	CMML, concurrent	Intermediate 1	Dermal infiltrate of pDC (10), iDC (30); 40%	*10*	*ASXL1 (17)* *ETV6 (19)* *BRAF(17)* *CUX1 (15)* *SRSF2 (11)* *TET2 (11)*	*ASXL1 (41),* *ETV6 (38),* *BRAF (37)* *CUX1 (35)* *SRSF2 (32)* *TET2 (16)* */ normal* *(BLOOD)*	Hydroxycarbamide (NR)	high potent topical corticosteroids (NR)	Yes, 3 years, 3 years AML
#9, M, 80	Papules	yes	MDS, NOS with multilineage dysplasia, concurrent	Low -1,41	Dermal infiltrate of pDC (10), iDC (10); 20%	*20*	*ASXL2 (11)* *CBL (9)* *CHEK2 (9)* *TET2 (15)* *BRCC3 (15)* *TP53 (2)*	*TET2 (40)* *BRCC3 (40)* *ASXL2 (25)* *CBL (16)* *CHEK2 (15)* */ normal*	No treatment	High potent topical corticosteroids (PR) Prednisone 0.1mg/kg/d (CR)	No, 7 years, 7 years
#10, M, 64	Papules	yes	CMML concurrent	Intermediate 2	Dermal infiltrate of pDC (20), iDC (5); 25%	*10*	*ZRSR2 (56)* *TET2 (9)* *ASLX1 (4)*	*TET2x2 (35, 42)* *ASXL1 (32)* *ZRSR2 (3)* *PTPN11 (2)* */ normal*	NA	High potent topical corticosteroids (PR)	No, 2.5 years 2.5 years
#11, M, 87	Papules, face	yes	CMML concurrent	NA	Dermal infiltrate of pDC (5), iDC (80); 85%	*5*	*TET2 (73)* *ZRSR2 (19)* *KRAS (17)* *ASXL1 (7)*	*TET2 (86) ZRSR2 (19)* *ASXL1 (9)* */ normal* *(BLOOD)*	Transfusion, no treatment	No treatment	No, 3 months, 3 months
#12, F, 80	Papules,and nodules Trunk	yes	CCUS 6 month later	NA	Dermal infiltrate of pDC (40); 40%	*10*	*RUNX1 (25)* *SF3B1(22)* *WT1 (16)* *KRAS (9)*	NA	no	Anti-H1 (NR)	Yes, 1.1 year, 6 months AML
#13, M, 76	Papules, Nodules, Trunk, legs, arms	yes	CMML concurrent	Intermediate 2	Dermal infiltrate of pDC (15), iDC (10); 25%	*10*	*ARID2 (24)* *RIT1 (24)* *ASXL1 (24)* *SRSF2(19)* *SMC3 (8)*	*ARID2 (NA)* *RIT1 (NA)* *ASXL1 (NA)* */ normal*	EPO for anemia (no progression)	Anti H1 (NR) High potent topical corticosteroids (NR)	No, 2 years, 2 years

# 14, M, 60	Papules, head and neck	no	CMML 3 years before	Intermediate 2	Dermal infiltrate of pDC (20), iDC (15); 35%	*15*	*SH2B3 (22) NF1 (21) SRSF2 (16) IDH2 (11)*	*SH2B3 (36) NF1x3 (50, 33 & 2), SRSF2 (42) IDH2(46) KRAS (7) MPL (5) / normal*	Hydroxycarbamide (NR)	Prednisone 0.5mg/kg/d (CR) -	No, 4 years, 3 years

AML: acute myeloid leukemia, CCUS : clonal cytopenia of undetermined significance, CMML: chronic myelomonocytic leukemia, iDC: indeterminate dendritic cell, MDN: myelodysplastic neoplasm, NA: non available, NR: no response, pDC: plasmacytoid dendritic cell, PR: partial response, CR: complete response

*Percentages of cells in the skin sample correspond to: the number of CD123+ TCF4+ CD2AP+ cells on immunohistochemistry out of total nucleated cells of the sample for pDC; the number of CD1a+ S100+/- CD207- cells on immunohistochemistry out of total nucleated cells of the sample for iDC; the sum of pDC percentage and iDC percentage for total percentage of pDC+iDC in the sample.

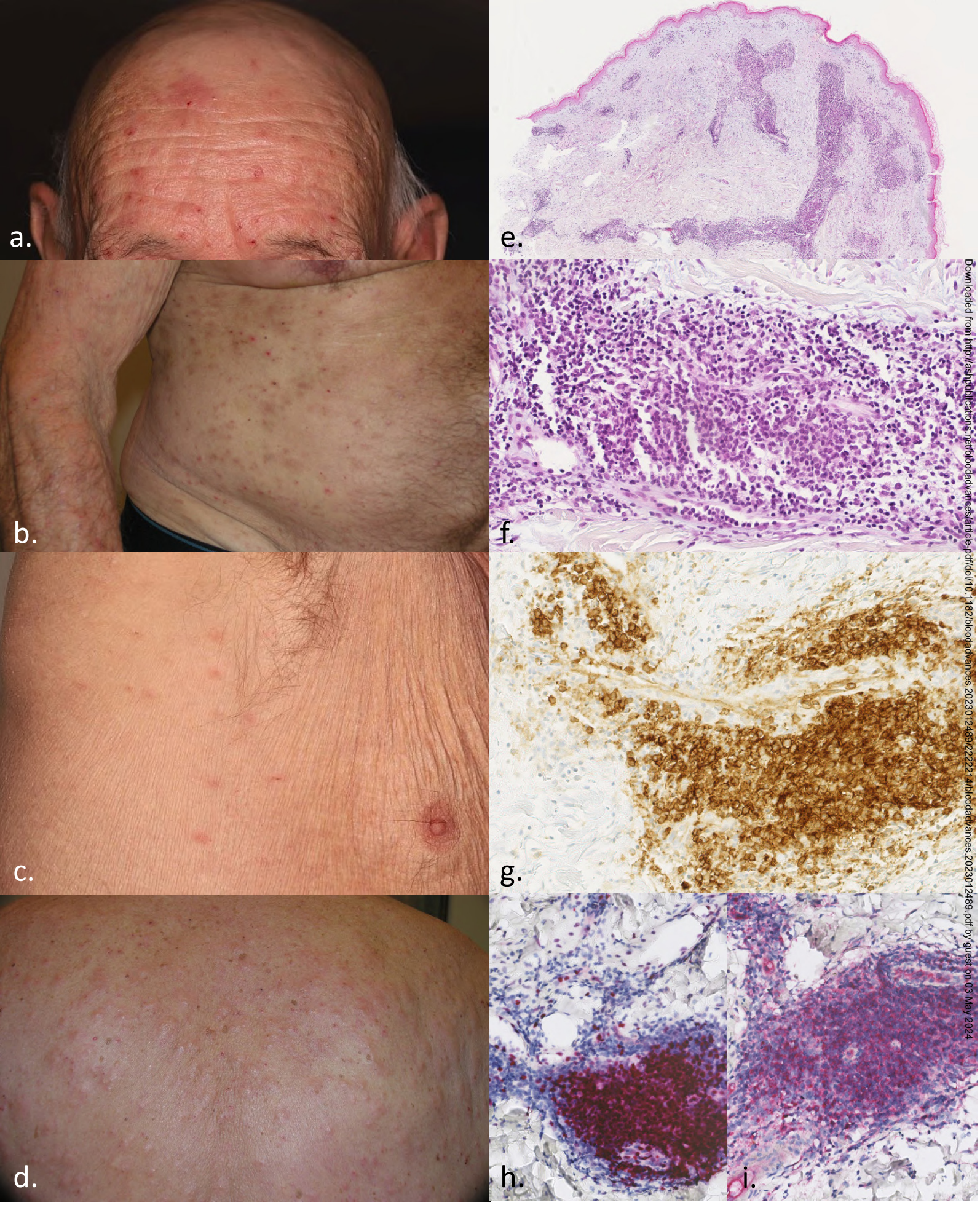

Figure 1. a,b,c,d Papulo-nodular skin eruption in patients with pDC dermatosis ; e,f Dense perivascular dermal infiltrate without blast cells (HES, x40 and x330), g CD123 expression in mature pDC (x330), h TCF4 (x200), i CD2AP (x200)

Table 1

Table 1: Clinico-pathologic, genetic and therapeutic features of 14 patients with myeloid neoplasms and with pDC dermatosis

Patient, Sex, age	Clinical presentation	Pruritus	Myeloid neoplasm (ICC 2022) and time of diagnosis related to pDC dermatosis	Pronostic scoring (IPSS-M or CPSS-mol)	Skin histology (% of cell type in the sample*) ; total percentage of pDC+iDC in the sample*	Percentage of CD163+ myeloid cells in the skin sample	Targeted sequencing of skin biopsy (gene, VAF %)	Targeted sequencing of bone marrow or blood (gene, VAF%) / cytogenetic	Hematological Treatment and response	Skin-directed treatment and response	Death, follow-up time after cutaneous sign, after diagnosis of myeloid neoplasm and cause of death
#1, F, 46	Papules, face, trunk	No	AML with myelodysplasia-related gene mutations concurrent	-	Dermal infiltrate of pDC (30), iDC (1); 31%	*5*	*RUNX1 x 2 (26,23) BCORL1 (23) FLT3-ITD (duplication)*	*RUNX1 x2 (45,43) BCORL1 (41) FLT3-ITD (duplication) / normal*	Allo-HCT (CR)	Allo-HCT (CR)	No, 3 years and 3 years
#2, M, 74	Papules, legs	yes	MDS, NOS with multilineage dysplasia 4 years later	Low -0,81	Dermal infiltrate of pDC (10), iDC (15); 25%	*10*	*BRCC3 (16) TET2 (10) SRSF2 (9) RUNX1 (9)*	*TET2 (38) SRSF2 (43) RUNX1 (44) BRCC3 (NA) / normal*	NA	NA	No, 4 years and 4.4 years
#3, M, 65	Papules, head, trunk, arms, legs	yes	CMML 1 year before	Intermediate 1	Dermal infiltrate of pDC (20), iDC (10); 30%	*15*	*IDH2 (19) BRCC3 (18) SRSF2 (10) NF1 (8) CBL (6)*	*CBL (73) IDH2 (43) SRSF2 (35) NF1 (4) CBL (73) / normal*	Azacitidine and Allo-HCT (CR)	Azacitidine and Allo-HCT (CR)	No, 6 years and 7 years
#4, M, 63	Papules, trunk	yes	CMML 3 months later	Intermediate 2	Dermal infiltrate of pDC (25),iDC (10); 35%	*10*	*TET2 x2 (23, 19) 20CTCF (1930) NRAS (1019) ASXL101 (17)20*	*TET2 x2 (53, 22) NRAS (53) SRSF2 (40) ASXL1 (35) / normal*	Allo-HCT (CR)	Allo-HCT (CR)	No, 2.25 years 2 years
#5, M, 84	papules, trunk, arms, legs	yes	CMML Concurrent	Intermediate 1	Dermal infiltrate of pDC (35); 35%	*20*	*JAK2 (3106) TET2 5(27) SRSF2 10(22)*	*JAK2 (70) TET2 (44) SRSF2 (43) / normal*	NA	NA	NA

Table 1

#6, M, 84	Papules, nodules, Head	yes	CMML 1 year later	Intermediate 2	Dermal infiltrate of pDC (45), iDC (2); 47%	*30*	*TET2 x3 (55,20,17) ASXL1 (31) NRAS (23) SRSF2 (21)*	*TET2 x3 (88,4,4) SRSF2 (44) ASXL1 (42) NRAS (24)* /46,XY,add(11)(p11)/46,XY	No treatment, surveillance	High potent topical corticosteroids and tacrolimus (PR) Prednisone 1 mg/kg/d (CR)	Yes, 4 years, 3 years, sepsis from lung infection
#7, F, 86	Papules	no	CMML, 8 months before	Intermediate 2	Dermal infiltrate of pDC (30), iDC (1); 31%	*10*	*KRAS(22), SF3B1 (21) SMC3 (17) RUNX1 (17) FLT3-ITD*	*KRAS (43) SF3B1 (42) SMC3 (42) RUNX1 (13) FLT3-ITD / normal*	Sorafenib 200 mg twice a day and decitabine (NR)	High potent topical corticosteroids (NR) Prednisone 1m/kg/day (CR)	Yes, 1.1 years, 6 months, AML
#8, M, 89	Papules	Yes	CMML, concurrent	Intermediate 1	Dermal infiltrate of pDC (10), iDC (30); 40%	*10*	*ASXL1 (17) ETV6 (19) BRAF(17) CUX1 (15) SRSF2 (11) TET2 (11)*	*ASXL1 (41), ETV6 (38), BRAF (37) CUX1 (35) SRSF2 (32) TET2 (16) / normal (BLOOD)*	Hydroxycarbamide (NR)	high potent topical corticosteroids (NR)	Yes, 3 years, 3 years AML
#9, M, 80	Papules	yes	MDS, NOS with multilineage dysplasia, concurrent	Low -1,41	Dermal infiltrate of pDC (10), iDC (10); 20%	*20*	*ASXL2 (11) CBL (9) CHEK2 (9) TET2 (15) BRCC3 (15) TP53 (2)*	*TET2 (40) BRCC3 (40) ASXL2 (25) CBL (16) CHEK2 (15) / normal*	No treatment	High potent topical corticosteroids (PR) Prednisone 0.1mg/kg/d (CR)	No, 7 years, 7 years
#10, M, 64	Papules	yes	CMML concurrent	Intermediate 2	Dermal infiltrate of pDC (20), iDC (5); 25%	*10*	*ZRSR2 (56) TET2 (9) ASLX1 (4)*	*TET2x2 (35, 42) ASXL1 (32) ZRSR2 (3) PTPN11 (2) / normal*	NA	High potent topical corticosteroids (PR)	No, 2.5 years 2.5 years
#11, M, 87	Papules, face	yes	CMML concurrent	NA	Dermal infiltrate of pDC (5), iDC (80); 85%	*5*	*TET2 (73) ZRSR2 (19) KRAS (17) ASXL1 (7)*	*TET2 (86) ZRSR2 (19) ASXL1 (9) / normal (BLOOD)*	Transfusion, no treatment	No treatment	No, 3 months, 3 months
#12, F, 80	Papules,and nodules Trunk	yes	CCUS 6 month later	NA	Dermal infiltrate of pDC (40); 40%	*10*	*RUNX1 (25) SF3B1(22) WT1 (16) KRAS (9)*	NA	no	Anti-H1 (NR)	Yes, 1.1 year, 6 months AML

Table 1

#13, M, 76	Papules, Nodules, Trunk, legs, arms	yes	CMML concurrent	Intermediate 2	Dermal infiltrate of pDC (15), iDC (10); 25%	*10*	*ARID2 (24) RIT1 (24) ASXL1 (24) SRSF2(19) SMC3 (8)*	*ARID2 (NA) RIT1 (NA) ASXL1 (NA) / normal*	EPO for anemia (no progression)	Anti H1 (NR) High potent topical corticosteroids (NR) Prednisone 0.5mg/kg/d (CR)	No, 2 years, 2 years
# 14, M, 60	Papules, head and neck	no	CMML 3 years before	Intermediate 2	Dermal infiltrate of pDC (20), iDC (15); 35%	*15*	*SH2B3 (22) NF1 (21) SRSF2 (16) IDH2 (11)*	*SH2B3 (36) NF1x3 (50, 33 & 2), SRSF2 (42) IDH2(46) KRAS (7) MPL (5) / normal*	Hydroxycarbamide (NR)	-	No, 4 years, 3 years

AML: acute myeloid leukemia, CCUS : clonal cytopenia of undetermined significance, CMML: chronic myelomonocytic leukemia, iDC: indeterminate dendritic cell, MDN: myelodysplastic neoplasm, NA: non available, NR: no response, pDC: plasmacytoid dendritic cell, PR: partial response, CR: complete response

*Percentages of cells in the skin sample correspond to: the number of CD123+ TCF4+ CD2AP+ cells on immunohistochemistry out of total nucleated cells of the sample for pDC; the number of CD1a+ S100+/- CD207- cells on immunohistochemistry out of total nucleated cells of the sample for iDC; the sum of pDC percentage and iDC percentage for total percentage of pDC+iDC in the sample.