Neutrophil rich CD30 Positive Primary Cutaneous Anaplastic Large Cell Lymphoma: A Case Report and Review of Literature

Neutrophilenreiches CD30-positives primär kutanes großzellig-anaplastisches T-Zell-Lymphom: Ein Fallbericht mit Literaturbesprechung

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Bibliography
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Abstract

We describe a case of neutrophil rich variant of primary cutaneous anaplastic large cell lymphoma (PCALCL) and the clinicopathological features of cases reported in the literature. In all cases the male to female ratio is 1.4 : 1. The age at presentation ranges between 12 and 82 years with a mean age of 50.73 years. Various clinical lesions including nodules (47.8%), tumormasses (34.8%), plaques (21.7%) and unusual variants (13.4%) are noted. 47.8% of lesions are associated with ulceration. Multifocal lesions are seen in about 18.4% of cases. Lesions are located in extremities (44.7%), trunk (36.8%), head and neck (34.2%). Around 10.5% of patients are immunocompromised. About 5.3% of cases show peripheral neutrophilia. Histopathological examinations show diffuse dermal infiltrate of large anaplastic (53.5%), pleomorphic (27.9%) or small to medium sized atypical lymphocytes (18.6%) in inflammatory background. Subcutaneous tissues are involved in about 43.5% of biopsies. Some biopsies show epidermal changes as epidermotropism (32.6%), hyperplasia (20.9%) or ulceration (7%). 18.6% of specimens show necrosis and angiodestruction. We try to increase awareness of this rare variant.

Introduction

Anaplastic large cell lymphoma (ALCL) was originally described by Stein et al. in 1985 [1]. It is a biological and clinical heterogeneous subtype of T-cell lymphoma. Clinically, ALCL may present as localized (primary) cutaneous disease or widespread systemic disease. These two forms of ALCL are distinct entities with different clinical and biological features, while both types share similar histology [2]. The primary cutaneous anaplastic large cell lymphoma (PCALCL) is defined as a non-Hodgkin T-cell lymphoma of the skin without systemic involvement at the time of the diagnosis [3]. The neutrophil rich variant is one of the morphological variants of ALCL reported by Mann et al. in 1995 [4].

Case report

A 66-year-old woman with a history of primary cutaneous anaplastic large cell lymphoma (treated with surgical excision) presented to our clinic 7 months later with a tumor mass on the left side of the back and also a small nodule on the back. The bigger lesion has been presented for approximately 6 months with progressive course and associated with slight pain. Over a course of 20 years, the patient complained of recurrent large nodular lesions which resolved spontaneously with scarring. The patient did not experience fever, loss of weight, night sweating or easy fatigability.

Physical examination revealed an erythematous indurated tumor mass with ulceration about 7 × 10 cm, there were also scattered papulonodular lesions on the trunk measuring less than 1 cm diameter. Additionally hypopigmented scars presented at sites of the spontaneously healed nodular masses (**Fig. 1**).

Laboratory test results including full blood account and serum were within normal ranges without peripheral neutrophilia. Chest X-ray, lymph node and abdominal ultrasound were normal.

Clinically, recurrence of CD30 positive anaplastic large cell lymphoma was suspected. Histopathological examination of a first biopsy of a smaller nodule revealed pseudoepitheliomatous hyperplasia of the epidermis, and the dermis was interspersed with a dense polymorphous infiltrate with multiple abscesses suggesting a neutrophil rich dermatosis. A second biopsy was performed

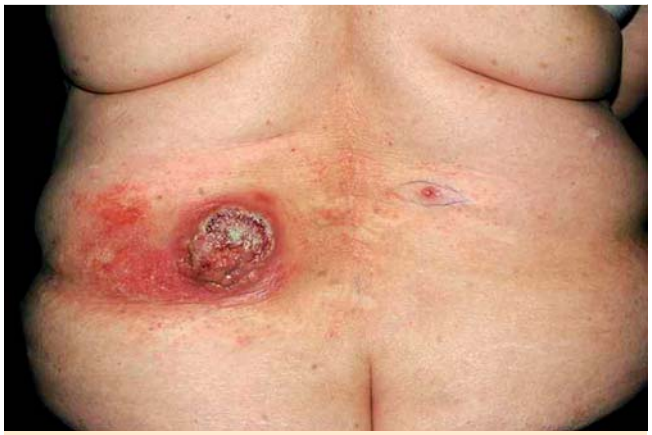

Fig. 1 An erythematous tumor mass with ulceration and another small nodule on the back of the patient.

with reevaluation of both biopsies which revealed diffuse infiltrate extending into the deep dermis. However, this infiltrate was composed of large pleomorphic lymphoid cells dispersed between the dense neutrophilic infiltrate and some histiocytes (**Fig. 2**, **Fig. 3**). On immunohistochemistry, the neoplastic cells showed an expression of CD30 (**Fig. 4**) and also stained with CD3 and CD4 (partially). The neoplastic cells were negative for CD8, granzyme B, CD20, CD56, anaplastic lymphoma kinase (ALK-1) and epithelial membrane antigen (EMA). The neutrophils (not the atypical lymphoid cells) were positive for CD15 and also were positive for myeloperoxidase. Finally, CD68 showed positive staining of histiocytes. Special stains (PAS, Giemsa, Gram and Ziehl-Neelsen) did not reveal any infectious agent. TCR beta gene rearrangement analysis showed a clonal biallelic rearrangement.

Discussion

ALCL belongs to the group of T-cell non-Hodgkin's lymphomas [6]. PCALCL is the second most common form of cutaneous T-cell lymphomas [7]. It represents about ten percent of all cases of cutaneous T-cell lymphomas [8]. It is defined according to the following criteria:

- Predominance (>75%) of large clusters of $CD30^+$ blast cells in the initial skin biopsy [9].
- There is no clinical evidence or history of lymphomatoid papulosis, mycosis fungoides or another type of CTCL [9].
- No extracutaneous localization at the time of diagnosis [3].

The neutrophil rich variant is characterized by presence of $CD30^+$ anaplastic T-cells amongst a neutrophil rich inflammatory background [9].

According to the afore mentioned criteria, we selected cases of neutrophil rich PCALCL from the literature to focus on this rare variant [9–18]. The age of the hitherto published 38 patients at presentation ranged from 12 to 82 years with the median age about 50.37 years. The male : female ratio was 1.4 : 1 (**Tab. 1**). Our study did not show any difference of neutrophil-rich PCALCL according age and sex statistics comparing to the conventional PCALCL. PCALCL affected more frequently males than females with a ratio of 1.5 – 2 : 1 [19, 20]. Regarding the age group, it affected more adults in the sixth decade of life [21].

Clinically the conventional type presented with nodules, papules or plaques over trunk, extremities or head [22]. Multifocal lesions

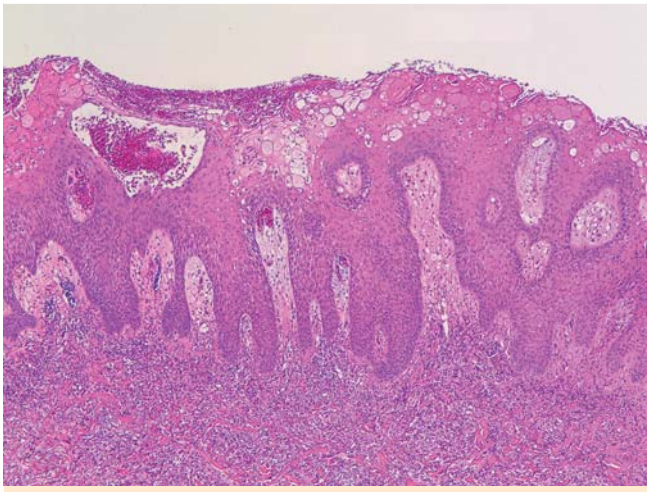

Fig. 2 Irregular acanthosis of the epidermis with a dense dermal polymorphous infilterate (HE 50×).

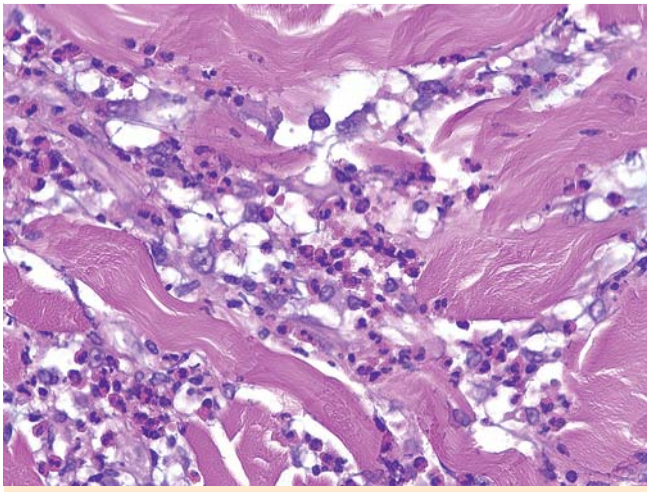

Fig. 3 Large pleomorphic lymphoid cells dispersed between a dense neutrophilic infiltrate and some histiocytes (HE 200×).

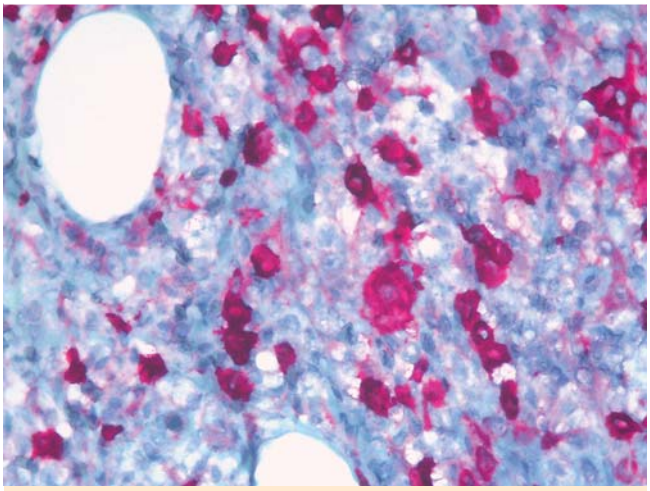

Fig. 4 Immunochemistry showing CD30-positivity of the neoplastic cells.

Table 1 Summary of the clinical features of cases of neutrophil rich variant reported in literature (M: Male, F: Female, KA: Keratoacanthoma, H&N: Head and neck).

Study	Number of cases	Immunosuppression	Age	Sex	Lesion			Peripheral neutrophilia
				M/F	Site	Isolated/ Multifocal	Shape & Ulceration	
Monte-marano	1	–	68	1/–	– Trunk: 1	1/–	– Nodule: 1 – Ulcer: 1	–
Jhala	2	2 (HIV)	– Youngest: 41 – Oldest: 44 – Mean: 42.5	2/–	– H&N: 2	2/–	– Tumor mass: 2	1
Burg	4	–	– Youngest: 35 – Oldest: 60 – Mean: 43.75	3/1	– H&N: 4 – Trunk: 1 – Extremities: 1	3/1	– Tumor mass: 3 – Nodule: 2 – Ulcer: 2	1
Kato	1	–	47	–/1	– Extremities: 1	1/–	– Nodule: 1	–
Lin	1	–	55	–/1	– H&N: 1	1/–	– KA like: 1	–
Salama	1	1 (Post transplantation chemotherapy)	59	1/–	– Extremities: 1	1/–	– Panniculitis like (painful erythematous nodules): 1	–
Boudova	1	–	57	–/1	– H&N: 1	1/–	– Plaque: 1 – Ulcer: 1	–
Massone	15	–	– Youngest: 14 – Oldest: 82 – Mean: 55.73	9/6	– H&N: 2 – Trunk: 5 – Extremities: 8	15/–	Not described	–
Kong	9	1 (Post Hodgkin chemotherapy)	– Youngest: 25 – Oldest: 67 – Mean: 39	5/4	– H&N: 3 – Trunk: 5 – Extremities: 4	5/4	– Tumor mass: 2 – Nodule: 5 – Plaque: 3 – Ulcer: 4	–
Paplas	2	–	– Youngest: 12 – Oldest: 38 – Mean: 25	1/1	– Trunk: 1 – Extremities: 2	1/1	– Tumor mass: 1 – Nodule: 1 – Cellulitis like: 1 – Ulcer: 2	–
Our case	1	–	66	–/1	– Trunk: 1	–/1	– Tumor mass: 1 – Nodule: 1 – Ulcer: 1	–
Total	38	4 (10.5%)	– Youngest: 12 – Oldest: 82 – Mean: 50.73	22/16 (1.4:1)	– H&N: 13 (34.2%) – Trunk: 14 (36.8%) – Extremities: 17 (44.7%)	31/7, multifocal: 18.4%	– Tumor mass: 34.8% – Nodule: 47.8% – Plaque: 21.7% – Unusual variants: 13.4% – Ulcer: 47.8%	2 (5.3%)

were seen in 20% of the cases [8]. It was often characterized by ulcerations [8].

However, analysing the published data (**Tab. 1**) skin lesions of the neutrophil-rich PCALCL presented as nodules (47.8%), tumor masses (34.8%), plaques (21.7%) or unusual variants as cellulitis-like, panniculitis-like and keratoacanthoma-like documented in about 13.4% of cases. Multifocal lesions were reported in 18.4% of cases. Lesions on extremities showed slight predominance by 44.7% of cases while lesions on trunk and head and neck were reported in 36.8%, 34.2% of cases respectively. Ulcerations were associated in 47.8% of cases. Interestingly, 10.5% of patients were immunocompromised. 5.3% of cases had also peripheral neutrophilia.

Microscopically the *conventional* type showed a diffuse infiltrate with cohesive sheets of large $CD30^+$ tumor cells. In most cases the tumor cells had the characteristic morphology of anaplastic cells, showing round, oval, or irregularly shaped nuclei, prominent eosinophilic nucleoli, and abundant cytoplasm. Less commonly (20%–25%), they had a non-anaplastic (pleomorphic or immunoblastic) appearance [8]. Massone et al. reported that large anaplastic cells are as frequent as large pleomorphic cells (33% vs. 36% respectively), whereas immunoblasts were never the predominant cell type. Small to medium-sized atypical lymphoid cells were the predominant cell population in 26% of cases [16]. Reed-Sternberg like cells were observed in 14% of cases [16]. The epidermis may show ulceration (63%), pseudoepitheliomatous hyperplasia (55%) and epidermotropism (40%) [23,24]. Krishnan et al. reported in their study tumor necrosis and angioinvasion in 55% and 44% of cases, respectively [23]. The infiltrate commonly extended into subcutaneous tissue [24].

In the literature (**Tab. 2**), cases diagnosed as *neutrophil rich variant* showed microscopically a diffuse dense polymorphous infiltrate. The infiltrate was composed predominantly of large anaplastic lymphocytes (53.5%), less commonly of large pleomorphic lymphocytes (27.9%) and small to medium sized atypical lymphoid cells (18.6%). Immunoblasts were never presented. Reed-Sternberg-like cells were presented in 37.2% of cases. The atypical lymphoid cells were presented in either cohesive sheets, dissolute growth pattern or both within inflammatory background. The inflammatory background formed mainly of neu-

Table 2 Summary of the pathological features of neutrophil rich PCALCL cases.

Study	Number of biopsies	Epidermis	Dermis				S.C. tissue
			Pattern of infiltrate	Composition of infiltrate	Necrosis	Angio-destruction	
Montemarano	1	– Hyperplasia: 1	Diffuse: 1	– Large anaplastic lymphocytes: 1 – Reed -Sternberg like cells: 1 – Neutrophils	–	–	–
Jhala	2	–	Diffuse: 2	– Large pleomorphic lymphocytes: 2 – Neutrophils	–	–	2
Burg	4	– Epidermotropism: 1 – Ulcer: 1	Diffuse: 4	– Large anaplastic lymphocytes: 1 – Large pleomorphic lymphocytes: 3 – Neutrophils – Small lymphocytes: 3 – Eosinophils: 2 – Plasma cells: 2 – Histiocytes: 3	–	–	1
Kato	1	– Ulcer: 1	Diffuse: 1	– Large anaplastic lymphocytes: 1 – Reed-Sternberg like cells: 1 – Neutrophils – Small lymphocytes: 1 – Histiocytes: 1	–	–	1
Lin	1	– Hyperplasia: 1	Diffuse: 1	– Large anaplastic lymphocytes: 1 – Neutrophils – Small lymphocytes: 1 – Eosinophils: 1	–	–	–
Salama	1	–	Diffuse: 1	– Large anaplastic lymphocytes: 1 – Reed-Sternberg like cells: 1 – Neutrophils	–	–	–
Boudova	1	– Epidermotropism: 1	Diffuse: 1	– Large anaplastic lymphocytes: 1 – Neutrophils – Histiocytes: 1	1	1	–
Massone	20	– Epidermotropism: 10 – Hyperplasia: 2	Not described	– Large anaplastic lymphocytes: 7 – Large pleomorphic lymphocytes: 6 – Small to medium sized atypical lymphocytes: 7 – Reed -Sternberg like cells: 4 – Neutrophils – Eosinophils: 14	7	7	Not described
Kong	9	– Hyperperplasia: 3 – Epidermotropism: 2	Diffuse: 9	– Large anaplastic lymphocytes: 8 – Small to medium sized atypical lymphocytes: 1 – Reed -Sternberg like cells: 9 – Neutrophils – Small lymphocytes: 2 – Eosinophils: 9 – Histiocytes: 9	–	–	5
Papalas	2	– Hyperplasia: 1 – Ulcer: 1	Diffuse: 2	– Large anaplastic lymphocytes: 2 – Neutrophils – Small lymphocytes: 1	–	–	1
Our case	1	– Hyperplasia: 1	Diffuse: 1	– Large pleomorphic lymphocytes: 1 – Neutrophils – Histiocytes: 1	–	–	–
Total	43	– Hyperplasia: 9/43 (20.9%) – Ulcer: 3/43 (7%) – Epidermotropism: 14/43 (32.6%)	Diffuse: 23/23 (100%)	– Large anaplastic lymphocytes: 23/43 (53.5%) – Large pleomorphic lymphocytes: 12/43 (27.9%) – Small to medium sized atypical lymphocytes: 8/43 (18.6%) – Reed sternberg like cells: 16/43 (37.2%) – Neutrophils: (100%) – Small lymphocytes: 8/43 (18.6%) – Eosinophils: 26/43 (60.5%) – Plasma cells: 2/43 (4.7%) – Histiocytes: 15/43 (34.9%)	8/43 (18.6%)	8/43 (18.6%)	10/23 (43.5%)

Table 3 Immunohistochemistry of neutrophil rich PCALCL cases reported in literature [(+): positive, (–): negative, N. A.: not available].

Study	CD3	CD4	CD8	CD15	CD20	CD56	Granzyme B	ALK	EMA
Montemarano	1 (+)	N. A.	N. A.	1 (–)	1 (–)	N. A.	N. A.	N. A.	1 (+)
Jhala	2 (+)	N. A.	N. A.	2 (–)	2 (–)	N. A.	N. A.	2 (–)	2 (+)
Burg	3 (+)	2 (+)	2 (–)	N. A.	1 (–)	1 (–)	N. A.	N. A.	N. A.
Kato	N. A.	1 (+)	1 (–)	1 (–)	1 (–)	1 (–)	1 (+)	1 (+)	1 (+)
Lin	N. A.	N. A.	N. A.	1 (–)	1 (–)	N. A.	N. A.	1 (–)	1 (–)
Salama	1 (+)	1 (+)	1 (–)	1 (–)	1 (–)	1 (–)	N. A.	1 (–)	1 (+)
Boudova	1 (–)	N. A.	1 (+)	1 (–)	1 (–)	1 (+)	1 (+)	1 (–)	1 (–)
Massone	N. A.	N. A.	N. A.	N. A.	N. A.	N. A.	N. A.	N. A.	N. A.
Kong	4 (+) 5 (–)	4 (+) 5 (–)	2 (+) 7 (–)	9 (–)	9 (–)	9 (–)	6 (+) 3 (–)	9 (–)	2 (+) 7 (–)
Papalas	1 (+) 1 (–)	2 (+)	2 (–)	1 (–)	2 (–)	N. A.	2 (+)	2 (–)	1 (–)
Our case	1 (+)	1 (+)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)
Total	(+): 13/20 (65%) (–): 7/20 (35%)	(+): 11/16 (68.75%) (–): 5/16 (31.25%)	(+): 3/17 (17.6%) (–): 14/17 (82.4%)	(+): 0/18 (0%) (–): 18/18 (100%)	(+): 0/20 (0%) (–): 20/20 (100%)	(+): 1/14 (7.1%) (–): 13/14 (92.9%)	(+): 10/14 (71.4%) (–): 4/14 (28.6%)	(+): 1/18 (5.6%) (–): 17/18 (94.4%)	(+): 7/18 (38.9%) (–): 11/18 (61.1%)

Table 4 Prognosis of neutrophil rich PCALCL cases reported in the literature (LN: lymph node involvement, HIV: Human Immunodeficiency Virus, M.I.: myocardial infarction). Note: Table excludes Lin et al. and Massone et al. as data about prognosis is not available.

Study	Number of cases	Spontaneous regression	Remission & Mean duration of follow-up	Recurrence	Extra cutaneous progression	Death	
						By disease	By other cause
Montemarano	1	–	1 Mean duration of follow-up: 24 months	–	–	–	–
Jhala	2			–	–	–	2 (HIV)
Burg	4	1	4 Mean duration of follow-up: 21 months	–	–	–	–
Kato	1	–		1	1 (LN)	–	–
Salama	1	–		1	–	–	1 (M.I.)
Boudova	1	–	1 Mean duration of follow-up: 72 months	–	–	–	–
Kong	9	1	6 Mean duration of follow-up: 28.1 months	1	1 (LN)	2	–
Papalas	2	1	1 Mean duration of follow-up: 3months	1	–	–	–
Our case	1	–	–	1	–	–	–
Total	22	3/22 (13.6%)	13/22 (59.1%) Mean duration of follow-up: 29.6 months	5/22 (22.8%)	2/22 (9.1%)	2/22 (9.1%)	3/22 (13.6%)

trophils and associated with eosinophils (60.5%), histiocytes (34.9%), small lymphocytes (18.6%) and plasma cells (4.7%). The infiltrate extended into subcutaneous tissue in 43.5% of cases. Epidermal changes varied between epidermotropism (32.6%), hyperplasia (20.9%) and ulceration (7%).

Immunohistochemically, the neoplastic cells in the conventional type showed activated CD4 T-cell phenotype with variable loss of CD3, and frequent expression of cytotoxic proteins (granzyme B, TIA-1, perforin). Some cases (less than 5%) had a CD8 T-cell phenotype. CD30 must be expressed by the majority (more than 75%) of the neoplastic T-cells. They did not express epithelial membrane antigen (EMA), anaplastic lymphoma kinase (ALK) and CD15; while rare cases showed coexpression of CD56 [8].

In the literature (**Tab. 3**) the neutrophil-rich variant showed positive expression of CD30 in all cases. CD3 and CD4 were positive in 65%, 66.75% of cases respectively, while CD8 was only positive in 17.6% of cases. The cytotoxic protein (granzyme B) was expressed in most of the cases (71.4%). EMA was frequently expressed (61.1%), while ALK (5.6%) and CD56 (7.1%) were rarely positive. The neoplastic cells did not express CD15 and CD20.

It is reported in literature that skin lesions of the conventional type may show spontaneous partial or complete regression in 42% of cases [24]. Also they may show recurrence in 25–40% of cases [3,25]. Extracutaneous dissemination occurred in approximately 10% of the patients, and mainly involved the regional lymph nodes [8]. In general, PCALCL exhibits a favorable prognosis (10-year survival rate >90%) [6,8,25]. It has been shown

quite early, that simple surgery may be suitable in the cases with solitary lesions without extracutaneous involvement [26].

In the literature (**Tab. 4**) neutrophil rich variant with mean duration of follow up 29.6 months did not show major differences in clinical behavior and prognosis in comparison to the ordinary type. Partial or complete spontaneous regression was noticed in about 13.6% of cases. The statistics showed lesser percentage of spontaneous regression than that in ordinary type. Also recurrence was found in 22.5% of cases and extracutaneous dissemination in 9.1% of cases. These results were close to the published data of the ordinary type. About 59.1% of cases showed complete remission without any recurrence, extracutaneous spread or death. Death was reported in 22.7% of cases, but only 9.1% of cases died of lymphoma.

Finally, we focused on a rare histologic variant of PCALCL. It showed similar clinical picture or behavior. The main difference was microscopically. Histologically, diagnosis of the neutrophil rich variant of PCALCL is challenging especially when tumor cells were masked by extensive inflammatory infiltrate. The main difficulty is that it may be misdiagnosed as an inflammatory dermatosis.

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Conflict of Interest

The authors declare no conflict of interest.

Zusammenfassung

Neutrophilenreiches CD 30-positives primär kutanes großzellig-anaplastisches T-Zell-Lymphom: Ein Fallbericht mit Literaturbesprechung

Wir berichten, unter Berücksichtigung der bislang publizierten klinischen und histologischen Besonderheiten, von einer 66-jährigen Patientin mit einer seltenen neutrophilenreichen Variante eines primär kutanen großzellig-anaplastischen T-Zell-Lymphoms. Bisher wurden Ersterkrankungen an dieser seltenen Entität im Alter von 12 bis 82 Jahren beschrieben mit einem mittleren Erkrankungsalter von 50,73 Jahren. Klinisch-morphologisch sind verschiedene Varitanten beschrieben, am häufigsten Knoten (47,8%), Tumore (34,8%), Plaques (21,7%) und selten andere Varianten (13,4%). In 47,8% der Fälle zeigen die Hautveränderungen zusätzlich Ulzerationen. Eine Disseminierung wurde bei 18,4% der Fälle beobachtet. Hierbei traten die Hauterscheinungen zu 44% an den Extremitäten, zu 36% am Stamm und zu 34,2% im Kopf-Hals-Bereich auf. Etwa ein Fünftel aller betroffenen Personen wies eine Immunkompromittierung sowie 5,3% eine Blutneutrophilie auf.

Die histologischen Untersuchungen zeigten überwiegend ein diffuses dermales Infiltrat großer anaplastischer (53,5%), pleomorpher (27,9%) oder klein- bis mittelgroßer atypischer (18,6) Lymphozyten, eingebettet in einem dichten entzündlichen, neutrophilenreichen Begleitinfiltrat. Das subkutane Fettgewebe war in 43,5% der Fälle mit einbezogen. Auch epidermale Veränderungen zeigten sich mit Epidermotropismus (32,6%), Hyperplasie (20,9%) oder Ulzeration (7,0%) variabel. In 18,6% der Präparate waren Nekrosen und Angiodestruktion nachzuweisen. Aufgrund der ausgeprägten Neutrophilie in der Histologie können die histologischen Veränderungen leicht als primär entzündlich respektive phlegmonös-abszedierende Erkrankung verkannt werden. Mit der vorliegenden Arbeit möchten wir das Bewusstsein für diese seltene Lymphomentität schärfen.

References

1 *Stein H*, *Mason DY*, *Gerdes J*. The expression of the Hodgkin's disease associated antigen Ki-1 in reactive and neoplastic lymphoid tissue: evidence that Reed-Sternberg cells and histiocytic malignancies are derived from activated lymphoid cells. Blood 1985; 66: 848 – 858
2 *Querfeld C*, *Khan I*, *Mahon B* et al. Primary cutaneous and systemic anaplastic large cell lymphoma: Clinicopathologic aspects and therapeutic options. Oncology (Williston Park) 2010; 24: 574 – 587
3 *Booken N*, *Goerdt S*, *Klemke CD*. Clinical spectrum of primary cutaneous CD30 anaplastic large cell lymphoma: an analysis of the Mannheim Cutaneous Lymphoma Registry. JDDG 2012; 10: 331 – 339
4 *Mann KP*, *Hall B*, *Kamino H* et al. Neutrophil-rich, Ki-1-positive anaplastic large-cell malignant lymphoma. Am J Surg Pathol 1995; 19: 407 – 416
5 *Harris NL*, *Jaffe ES*, *Stein H* et al. A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. Blood 1994; 84: 1361 – 1362
6 *Bekkenk MW*, *Geelen FA*, *van Voorst Vader PC* et al. Primary and secondary cutaneous CD30$^+$ lymphoproliferative disorders: a report from the Dutch Cutaneous Lymphoma Group on the long-term follow-up data of 219 patients and guidelines for diagnosis and treatment. Blood 2000; 95: 3653 – 3661
7 *Fung MA*, *Murphy MJ*, *Hoss DM* et al. Practical evaluation and management of cutaneous lymphoma. Journal of the American Academy of Dermatology 2002; 46: 325 – 335
8 *Willemze R*, *Jaffe ES*, *Burg G* et al. WHO-EORTC classification for cutaneous lymphomas. Blood 2005; 105: 3768 – 3785
9 *Burg G*, *Kempf W*, *Kazakov DV* et al. Pyogenic lymphoma of the skin: a peculiar variant of primary cutaneous neutrophil-rich CD30$^+$ anaplastic large-cell lymphoma. Clinicopathological study of four cases and review of the literature. British Journal of Dermatology 2003; 148: 580 – 586
10 *Montemarano AD*, *Rowe JE*, *Benson PM* et al. KI-1 (CD30) positive anaplastic large cell lymphoma mimicking an infectious granuloma. International Journal of Dermatology 1995; 34: 790 – 793
11 *Jhala DN*, *Medeiros LJ*, *Lopez-Terrada D* et al. Neutrophil rich anaplastic large cell lymphoma of T-cell lineage. A report of two cases arising in HIV-positive patients. American Journal of Clinical Pathology 2000; 114: 478 – 482
12 *Kato N*, *Mizuno O*, *Ito K* et al. Neutrophil rich anaplastic large cell lymphoma in the skin. American Journal of Dermatopathology 2003; 25: 142 – 147
13 *Lin J-H*, *Lee JY*. Primary cutaneous CD30$^+$ anaplastic large cell lymphoma with keratoacanthoma like, pseudocarcinomatous hyperplasia, marked eosinophilia and neutrophilia. The Journal of Cutaneous Pathology 2004; 31: 458 – 461
14 *Salama S*. Primary "cutaneous" T-cell anaplastic large cell lymphoma, CD30$^+$, neutrophil rich variant with subcutaneous panniculitic lesions, in a post-renal transplant patient: report of unusual case and literature review. American Journal of Dermatopathology 2005; 27: 217 – 223
15 *Boudova L*, *Kazakov DV*, *Jindra P* et al. Primary histiocyte and neutrophil-rich CD30$^+$ and CD56$^+$ anaplastic large cell lymphoma with prominent angioinvasion and nerve involvement in the forehead and scalp of an immunocompetent woman. The Journal of Cutaneous Pathology 2006; 33: 584 – 589
16 *Massone C*, *El-Shabrawi-Caelen L*, *Kerl H* et al. The morphologic spectrum of primary cutaneous anaplastic large T-cell lymphoma: a histopathologic study on 66 biopsy specimens from 47 patients with report of rare variants. The Journal of Cutaneous Pathology 2008; 35: 46 – 53
17 *Kong YY*, *Dai B*, *Kong JC* et al. Neutrophil/eosinophil-rich type of primary cutaneous anaplastic large cell lymphoma: a clinicopathological,

immunophenotypic and molecular study of nine cases. Histopatology 2009; 55: 189 – 196
18 *Papalas JA*, *Mater DV*, *Wang E*. Pyogenic variant of primary cutaneous anaplastic large cell lymphoma with a predilection for the immunocompromized and the young. The American Journal of Dermatopathology 2010; 32: 821 – 827
19 *Kempf W*, *Pfaltz K*, *Vermeer MH* et al. EORTC, ISCL, and USCLC consensus recommendations for the treatment of primary cutaneous CD30 positive lymphoproliferative disorders: lymphomatoid papulosis and primary cutaneous anaplastic large-cell lymphoma. Blood 2011; 118: 4024 – 4035
20 *Diamantidis MD*, *Papadopoulos A*, *Kaiafa G* et al. Differential diagnosis and treatment of primary, cutaneous, anaplastic large cell lymphoma: not always an easy task. Int J Hematol 2009; 90: 226 – 229
21 *Kadin ME*. Current management of primary cutaneous CD30+ T-cell lymphoproliferative disorders. Oncology 2009; 23: 1158 – 1164
22 *De Olivera LSR*, *Nobrega MP*, *Monteiro MG* et al. Primary cutaneous anaplastic large cell lymphoma – Case report. Anais Brasileiros de Dermatologia 2013; 88: 132 – 135
23 *Krishnan J*, *Tomaszewski MM*, *Kao GF*. Primary cutaneous CD30$^+$ ALCL. Report of 27 cases. Journal of Cutaneous Pathology 1993; 20: 193 – 202
24 *Goodlad J*, *Calonje E*. Cutaneous lymphoproliferative diseases and related disorders. Calonje E, Brenn T, Lazar A et al., eds. Mckee's pathology of the skin with clinical correlations (4th Ed). New York, USA: Elsevier; 2012: 1311 – 1420
25 *Lui HL*, *Hoppe RT*, *Kohler S* et al. CD30$^+$ cutaneous lymphoproliferative disorders: the Stanford experience in lymphomatoid papulosis and primary cutaneous anaplastic large cell lymphoma. Journal of the American Academy of Dermatology 2003; 49: 1049 – 1058
26 *von den Driesch P*, *Bivolarevic I*, *Peters KP* et al. Cutaneous pleomorphic large cell lymphoma. Cutis 1992; 50: 294 – 298