

## Cutaneous Metastasis of High-Grade Serous Adenocarcinoma: a case report

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# **Introduction & Objectives:**

Skin metastases from gynaecological malignancies are rare but have been described for both ovarian and endometrial neoplasia. The incidence of cutaneous metastasis in ovarian carcinoma ranges from 1.9%- 5.1%. The prevalence of cutaneous metastasis in endometrial carcinoma comprises 0.8%-1.0% of all reported endometrial carcinoma cases.

#### **Materials & Methods:**

We report the case of an 89 year old female presenting with a 7 month history of multiple non-tender, fleshy, skin-coloured nodules with central ulceration and bleeding over the vulva, their diameter ranging from 1cm- 3cm. These were associated with palpable non-tender bilateral inquinal lymphadenopathy.

#### **Results:**

Histological analysis from a skin biopsy showed extensive infiltration of the dermis by a markedly pleomorphic and briskly mitotic population of neoplastic cells exhibiting brisk mitotic activity, variably organized in solid nests, angulated glands and papillary configurations. Extensive ulceration of the overlying skin was evident. Immunohistochemistry showed strong and diffuse expression of PAX8 and EMA, supporting a gynaecological primary. The tumour showed strong expression of both WT1 and p16 and a mutational p53 signature was also observed, with strong nuclear expression. There was no observed oestrogen receptor expression. These findings were in keeping with metastatic high-grade serous adenocarcinoma (HGSC). Blood tests revealed an elevated CA125 of 1278.2U/mL and an elevated Ca19.9 of 386.9U/mL. A computed tomography scan of thorax- abdomen-pelvis confirmed lymph node, liver and lung metastasis. The patient passed away within 3 months of diagnosis.

# **Discussion & Conclusion:**

The commonest site for skin metastasis from ovarian and endometrial carcinoma is the umbilicus, (Sister Joseph's nodule); other reported cutaneous sites include the vulvovaginal area amongst others. HGSC is the commonest primary malignancy of the ovary, thought to derive from the epithelium of the fallopian tube. HGSC may also arise from the endometrial cavity, with this being most frequently seen in the context of endometrial atrophy in the elderly. In this case, both the morphology of the tumour and strong PAX8 expression on immunohistochemical grounds supported a gynaecological primary. A mutational pattern of p53 expression, which may range from strong and diffuse nuclear expression to absent express (null phenotype) or cytoplasmic staining, is seen in virtually all serous carcinomas. The presence of strong and diffuse WT1 staining is usually seen with tubo-ovarian primary tumours, with primary endometrial disease tending to show patchy or absent expression (although a subset of cases may show strong expression). Expression of p16 tends to be diffuse and intense as well in HGSC. HGSC may also show estrogen receptor positivity, although this was negative in our case.

There is no standard treatment for skin metastasis of gynaecological cancer. The prognosis of such cases is very poor, with overall survival time from skin metastasis diagnosis being 4 months (range 2-65 months) for ovarian malignancy, and a mean life expectancy of 4 -12 months for endometrial malignancy. Management should be multidisciplinary, including systemic and surgical treatment were possible, which may help improve survival times. Palliative management should also be incorporated to help with symptom control. 2



# Primary disseminated varicella zoster: A Mimicry of Cutaneous Cytotoxic T-Cell Lymphoma

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# **Introduction & Objectives:**

Varicella-Zoster virus (VZV) is a common skin infection. characterized by multiple painful vesicles typically involving a single dermatome. Histology We present an unusual case of VZV with histological features mimicking a cutaneous cytotoxic T-cell lymphoma..

#### **Case discussion:**

A 64-year-old Chinese woman presented with a three-day history of fever, malaise and widespread painful vesiculopustular eruptions over herskin, oral and vaginal mucosa. She had no significant past medical history. Blood tests revealed elevated hepatocellular transaminases (Alanine transaminase 254U/L, Aspartate Transaminase 191U/L) with leukocytosis (White blood cell count 13.1 x 109/L) and elevated C-reactive protein (153mg/L). Serum immunoglobulin (Ig) M was reactive for VZV while IgG was negative. VZV polymerase chain reaction skin swab was positive. A skin biopsy was performed and showed interface vacuolar change of the epidermis and lymphocytic exocytosis. There was a fairly dense infiltrate of cytologically atypical large T-lymphoid cells in the superficial dermis featuring irregular vesicular nuclei with variably prominent nucleoli and mitoses. The atypical T cells expressed CD3, CD8 and cytotoxic markers, TIA1 and granzyme B. They were negative for CD4, CD56, CD30 and Epstein-Barr virus (EBV)-encoded RNA (EBER). Further T-cell clonality studies were performed - these demonstrated polyclonal TRB and TRG gene rearrangement, supporting a reactive T-cell proliferation. Given these findings, a diagnosis of atypical cytotoxic T-cell cutaneous eruption of primary VZV was made. The patient was treated with 10 days of antivirals with significant clinical improvement.

#### Conclusion:

VZV infection or vaccination is known to elicit an immunogenic response involving helper and cytotoxic T-cells, with case reports of pseudolymphomatous eruption after vaccination in immunocompromised patients. This case highlights an extremely unusual CD8+ cytotoxic lymphomatoid cutaneous reaction in primary VZV infection in an immunocompetent host. Consideration of all clinical-pathological, including molecular diagnostic findings, can help indicate a reactive process and avoid an over-diagnosis of a cytotoxic T-cell lymphoma.



# Predictors of recurrence and progression in poorly differentiated cutaneous squamous cell carcinomas

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**Introduction & Objectives:** Surgery represents the primary treatment option for cutaneous squamous cell carcinoma (cSCC) aiming for complete tumor resection (R0). Recurrence and metastasis significantly affect survival and outcomes, and poorly differentiated (G3) cSCC is associated with a higher risk of recurrence. However, the specific clinical and histopathological features that predict recurrence and progression in G3-cSCC remain unclear.

**Materials & Methods:** A retrospective analysis was conducted on a series of patients with primary G3-cSCC diagnosed at a referral University Hospital between January 2016 and January 2021. After independent histological revision, logistic regression models were used to identify clinico-pathological predictors of cutaneous recurrence, lymph node/metastatic progression, and both types of progression.

**Results:** Among the 161 G3-cSCC patients, 80.1% (129/161) showed no signs of local recurrence or metastatic progression, while 19.9% (32 patients) had progressed. In the univariate logistic regression, tumor clinical diameter, depth of infiltration (DOI), and lymphovascular invasion (LVI) were identified as significant predictors across the various types of progression (p<0.05). In the context of multivariate logistic regression, distinct models proved to be significant. For skin recurrence, a 3-variable model incorporating DOI (OR 1.16, 95% CI 1.01-1.35, p=0.050), LVI (OR 3.61, 95% CI 1.11-11.8, p=0.034), and desmoplasia (OR 3.45, 95% CI 1.25-9.5, p=0.017) was selected. Regarding lymph node/metastatic progression, a 3-variable model combining pT2 (OR 6.10, 95% CI 1.15-32.35, p=0.034), pT3 (OR 14.33, 95% CI 2.79-73.63, p=0.001), and LVI (OR 3.86, 95% CI 1.10-13.62, p=0.036) was identified. Lastly, a 2- variable model for both types of progression consisted of vertical tumor thickness (OR 5.45, 95% CI 1.11-27.32, p=0.039) and LVI (OR 1.15, 95% CI 1.04-1.26, p=0.006).

**Conclusion**: Tumor size, depth of infiltration, and LVI were significant predictors of recurrence and metastatic progression. Notably, the size of histologically defined tumor-free margins did not affect the risk of recurrence, whilst LVI emerged as a key predictor of all forms of progression. Interestingly, the recent EADO-EORTC 2023 guidelines do not mention LVI as a defining feature of high-risk cSCCs. These findings provide insights into risk stratification and suggest that close monitoring and potential adjuvant therapies, such as radiation therapy, may be necessary especially for patients with lymphovascular involvement.

	Not recurred/progressed (n=129)	Recurred/progressed (n=32)	p-valu
Sex			0.401
Female	31 (24.1%)	10 (31.3%)	
Male	98 (75.1%)	22 (68.7%)	
Age			0.950
Mean (range)	80.1 (47-96)	79.0 (45-98)	
pT, (%), according to AJCC 8th edition [14]			0.017
pT1	77 (59.7%)	11 (34.3%)	
pT2	33 (25.6%)	9 (28.1%)	
	, ,		
pT3	18 (13.9%)	12 (37.5%)	
pT4	1 (0.8%)	0 (0%)	
Tumor diameter (cm)			0.009
Mean (range)	1.90 (0.4-6)	2.7 (1.0-13.0)	
Anatomical level		1000000	0.004
3	5 (3.9%)	O (0%)	
4	59 (45.7%)	5 (15.6%)	
5	65 (50.4%)	27 (84.4%)	
Vertical tumor thickness (mm)	6.0 (1.4-24)	7.9 (2-40)	0.205
Mean (range)			
<2mm [27]	8 (6.2%)	3 (9.4%)	0.458
>2mm [27]	121 (93.8%)	29 (90.6%)	
Depth of infiltration (mm)	3.9 (1-18)	5.4 (1-15)	0.005
Mean (range)	3.3 (1-10)	5.4 (2-25)	0.003
Tumor horizontal size (mm)	15.3 (3-50)	19.0 (9-45)	0.014
Mean (range)	23.3 (3-30)	15.0 (5-15)	0.014
Perineural invasion (PNI)			0.001
Present	16 (12.4%)	12 (37.5%)	0.001
Absent			
	113 (87.6%)	20 (62.5%)	
Lymphovascular invasion (LVI)			<0.00
Present	7 (5.4%)	10 (31.3%)	
Absent	122 (94.6%)	22 (68.7%)	
Desmoplasia			0.007
Present	18 (14.0%)	11 (34.4%)	
Absent	111 (86.0%)	21 (65.6%)	
Histological distance to lateral margin	3.8 (0.0-22)	3.1 (0.0-8)	0.752
Mean (mm)			
Histological distance to deep margin (mm)	2.3 (0.0-12)	1.8 (0.0-9)	0.064
Mean (range)	210 (010 22)	210 (010 3)	0.004
Ulceration			0.205
Present	95 (73.6%)	27 (84.3%)	0.203
Absent			
	34 (26.4%)	5 (15.6%)	0.400
Immunosuppression*	14/10 00/3	F (4F C0/)	0.483
Yes	14 (10.9%)	5 (15.6%)	
No	115 (89.1%)	27 (84.3%)	
TILs infiltrate grade			0.007
0-1	82 (63.6%)	12 (37.5%)	
2-3	47 (36.4%)	20 (62.5%)	
Follow up time, months			0.082
Mean (range)	33.0 (4-8)	27.5 (6-74)	
Tumor site	H&N: 104 (80.6%)	H&N: 27 (84.3%)	0.877
	Trunk: 11 (8.5%)	Trunk: 2 (6.3%)	0.077
	Extremities: 14 (10.9%)	Extremities: 3 (9.4%)	
Tomple on the localization (2)			0.907
Temple-ear-lip localization [3]	27 (20.9%)	7 (21.9%)	0.907

Legend to table 1. Clinical and histopathological features in our cohort of patients. Statistically significant P-values are highlighted in bold font. TILs (Tumor-Infiltrating lymphocytes) infiltrate is defined according to the Melanoma Institute of Australia (MIA) scoring system: grade 0 (TIL absent), grade 1 (mild multifocal or mild/moderate focal infiltrate), grade 2 (moderate or marked multifocal, marked focal or mild diffuse TIL pattern), grade 3 (moderate or marked diffuse infiltrate). H&N (head or neck localization). \*Immunosuppressed patients were presenting the following conditions: kidney transplant (12), heart transplant (1), liver transplant (1), chronic lymphocytic leukemia (1), diffuse-large B-cell leukemia (1), myelodysplastic syndrome (1), multiple myeloma (1), chronic autoimmune hepatitis (1).

Table 2. Predictors of local recurrence and progression

Progression and analysis type	Parameter	Odds Ratio (95% CI)	p-value
Skin recurrence: univariate LOGIT	•	•	
	pT3	3.30 (1.20-9.30)	0.021
	Tumor clinical diameter	1.35 (1.01-1.81)	0.043
	Depth of infiltration	1.21 (1.05-1.39)	0.008
	Perineural invasion	5.13 (1.96-13.42)	0.001
	Lymphovascular invasion	5.60 (1.87-16.77)	0.002
	Desmoplasia	4.82 (1.85-12.53)	0.001
	TILs > 1	0.32 (0.13-0.81)	0.016
Skin recurrence: multivariate LOGI	Τ		
	Depth of infiltration	1.16 (1.01-1.35)	0.050
	Lymphovascular invasion	3.61 (1.11-11.8)	0.034
	Desmoplasia	3.45 (1.25-9.5)	0.017
Lymph node/visceral progression:	univariate LOGIT		
, ,	pT2	7.17 (1.38-37.29)	0.019
	pT3	18.43 (3.70-91.71)	< 0.001
	Tumor clinical diameter	1.50 (1.06-2.11)	0.022
	Vertical tumor thickness	1.13 (1.03-1.23)	0.007
	Depth of infiltration	1.20 (1.03-1.39)	0.016
	Tumor horizontal size	1.07 (1.01-1.13)	0.023
	Lymphovascular invasion	6.60 (2.05-21.24)	0.002
Lymph node/visceral progression:		,,	
	pT2	6.10 (1.15-32.35)	0.034
	pT3	14.33 (2.79-73.63)	0.001
	Lymphovascular invasion	3.86 (1.10-13.62)	0.036
Skin recurrence and lymph-node/n	netastatic progression: univari	ate LOGIT	•
	pT3	21.75 (2.50-189.49)	0.005
	Tumor clinical diameter	1.44 (1.03-2.03)	0.003
	Vertical tumor thickness	1.15 (1.04-1.27)	0.006
	Depth of infiltration	1.32 (1.10-1.59)	0.003
<u> </u>	Lymphovascular invasion	5.96 (1.29-27.60)	0.023
Skin recurrence and lymph-node/n	netastatic progression: multivo	ariate LOGIT	
	Vertical tumor thickness	5.45 (1.11-27.32)	0.039
	Lymphovascular invasion	1.15 (1.04-1.26)	0.006

 $\textbf{Legend to table 2}. \ Individual \ effects \ of \ clinic opathological features \ on \ local \ recurrence \ and/or \ progression.$ 



## Skin and Syntax: Large Language Models in Dermatopathology

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# **Introduction & Objectives:**

This paper introduces the integration of Large Language Models (LLMs) in dermatopathology, discussing potential benefits, challenges, and prospects. It explores the changing landscape of dermatopathology with LLMs, emphasizing advantages such as automated reporting, continual learning, and patient education. Challenges to the implementation of LLMs in practice include biases and data privacy. Prospects involve LLMs' integration with other AI technologies. The transformative potential of LLMs in dermatopathology is underscored, emphasizing collaboration between AI experts and dermatopathologists for improved patient outcomes.

#### **Materials & Methods:**

The methodology involves a literature review to trace the historical evolution of diagnostic tools in dermatopathology and examine the role of LLMs. Relevant databases were searched for studies and articles related to AI, NLP, and LLMs in dermatopathology. The selection criteria included publications highlighting advancements, applications, and challenges in integrating LLMs into dermatopathology practice.

#### **Results:**

In dermatopathology, LLMs offer several advantages. Firstly, they can revolutionize pathology report generation through automated processes, thereby improving efficiency and addressing the shortage of dermatologists. Additionally, LLMs excel in continual learning, assimilating updated medical knowledge to enhance diagnostic accuracy by staying current with research and advancements. Another notable advantage is their role in patient education, bridging communication gaps by translating complex dermatopathology reports into patient-friendly language, thereby contributing to informed decision-making. The section on case studies and real-world applications further delves into practical uses, including diagnostic support for rare cases, research acceleration, and teaching and training. Notably, the exploration acknowledges potential biases in LLM responses, emphasizing the need for a nuanced understanding of their applications.

This study also delves into the challenges and limitations associated with the integration of LLMs such as biases, ethics, data privacy, the delicate balance between dependence and assistance, and technical limitations. The discourse advocates for a comprehensive and multidisciplinary approach to ensure the responsible utilization of LLMs in the field.

# **Conclusions:**

Emphasizing future directions, the paper highlights the transformative potential of LLMs in dermatopathology. It calls for increased interdisciplinary collaboration, especially with other AI tools, to enhance diagnostic accuracy and streamline clinical workflows. The future direction also emphasizes the potential utility of LLMs in personalized medicine and their expansion to other pathology sub-disciplines. LLMs may serve in an assistive capacity in the toolset of dermatopathologists. The paper concludes by underscoring the importance of collaboration between AI experts and dermatopathologists for realizing positive changes in practice.



## Case Report of Patient with Eosinophilic Annular Erythema secondary to Rheumatological Disorder

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# **Introduction & Objectives:**

Eosinophilic annular erythema (EAE) is an uncommon benign acute eosinophilic dermatosis of unknown etiology. We present a case for a comprehensive discussion on the prominent histopathological findings and management.

#### **Materials & Methods:**

This study involved analysis of a skin rash of a now 80 year old man upon his visit to the dermatology clinic in 2002. He received an initial diagnosis of psoriasis and received treatment in the form of Dobovet and Enstilar. However, he felt his condition had been unabated since his diagnosis. He returned to the clinic in 2020 where he was noted to have an erythematous, indurated non scaly rash, which was annular in appearance in many areas with central clearing on his trunk and extremities. This presentation was in keeping with Annular Erythema rather than Psoriasis. He was advised to use mometasone 0.1% ointment no more than twice weekly on the areas of the rash to keep it under control and to discontinue Dobovet and Enstilar Foam until there was a proven diagnosis. He was also booked in for a skin punch biopsy. In April 2021 he also received a diagnosis of polymyalgia rheumatica and was put on a course of Predinsolone which was gradually reduced until it was stopped completely.

#### **Results:**

The patient reattended clinic in 2022 and a discussion took place with the patient regarding his histology results. It was noted that his skin condition fit with annular erythema and the results of the histology suggested spongiotic dermatitis with presence of numerous eosinophils consistent with eosinophilic annular erythema. EAE is also associated with rheumatological disorders. This clinical picture added up given his recent diagnosis and treatment of Polymyalgia Rheumatica.

#### **Conclusion:**

EAE is a rare condition in which you can get these changes including lots of eosinophils in the skin biopsy. EAE is also associated with rheumatological disorders. This clinical picture adds up given his recent diagnosis and treatment of Polymyalgia Rheumatica. Dermovate ointment once daily was prescribed to use on all active itchy areas of the rash and as and when required. He had found that the rash had been very well controlled on the small dose of prednisolone he had been taking for the polymyalgia rheumatica.

EAE is characterized by annular, erythematous papules and plaques commonly found on the trunk and the extremities. Virtually all areas of the body can be affected by EAE, including the palms and soles. The lesions evolve with a centrifugal growth pattern with central areas of clearing and are typically either asymptomatic or pruritic. Histologically, EAE is characterized by a dense superficial and deep dermal perivascular and interstitial lymphohistiocytic infiltrate with abundant eosinophils. A limited number of EAE cases in adolescents and adults have been reported to date. Eosinophilia is occasionally a feature of rheumatic disease.

Mild cases of EAE may respond well to topical corticosteroids, which help reduce inflammation and itching. High-potency steroids may be prescribed for more severe cases. Regular use of emollients and moisturizers can help maintain skin

hydration and integrity, reducing the risk of flare-ups and improving overall skin health. For this patient dermovate ointment once daily was prescribed to use on all active itchy areas of the rash and as and when required. He had also found that the rash ahd been very well controlled on the small dose of prednisolone he had been taking for the polymyalgia rheumatica



#### An ambiguous melanocytic lesion

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# **Introduction & Objectives:**

To this day, histopathological examination remains the gold standard for the diagnosis and classification of melanocytic lesions. The distinction between nevus and melanoma has important consequences for the patient. The pathologist is often able to make a clear-cut diagnosis. However, some melanocytic lesions have atypical features that even the most experienced pathologist may have difficulty in classifying. A commonly accepted term for these lesions is MelTUMP, melanocytic tumour of uncertain malignant potential. This category includes mostly benign lesions, but also a minority of melanomas. Due to their uncertain biological behaviour, predicting prognosis and defining optimal treatment remain challenging. As most MelTUMPs have favourable prognosis, treatment should focus on minimizing harm. Complete excision with a 5 mm clinical margin should be undertaken. Even though lymph node involvement is common, distant metastasis and death are rare. Hence, SLNB should not be offered routinely due to its lack of prognostic utility.

# **Materials & Methods:**

We report the case of an otherwise healthy female patient with an atypical melanocytic lesion diagnosed as MelTUMP.

## **Results:**

A 75-year-old female with no relevant medical or surgical history presented with a longstanding asymptomatic cutaneous lesion, located in the right lumbar region. Physical examination revealed a 1x0,7 cm, dark-brown, pedunculated nodule, with smooth surface, firm-elastic consistency and a hypopigmented halo. The lesion has been subject to repetitive trauma. The clinical impression was traumatised dermal nevus.

Dermoscopy revealed a central dark-brown to black structureless area, brown dots, globules and parallel lines at the periphery, scattered on a light-brown structureless area, as well as a few linear vessels at the base.

An elliptical excisional biopsy with narrow (2 mm) margins was performed and the specimen was evaluated by histology and IHC.

Histology presented a dermal proliferation of fusiform cells arranged in a storiform pattern, with elongated nuclei, clumped chromatin and some prominent nucleoli, few mitoses (1/mm2), no maturation with dermal descent, a maximum tumour thickness of 3,6 mm, as well as fibrosis, chronic inflammatory infiltrate and epidermal atrophy. There was no evidence of ulceration, perineural or lymphovascular invasion.

IHC showed positivity for the melanocytic markers MelanA, S100, MITF, diffuse and intense positivity for P16, focal positivity for HMB45 (mainly in the superficial layers), as well as a low KI67 (3%).

A diagnosis of MelTUMP was made. However, in order to exclude melanoma, the pathologist recommended additional molecular tests (NGS).

Given the diagnostic uncertainty and the lack of treatment recommendations, a reexcision with an additional margin of 5 mm was performed, followed by histopathological examination, which came back negative.

Follow-up of 6 months revealed no clinical or dermoscopic evidence of recurrence.

# **Conclusion:**

MelTUMPs are melanocytic lesions that cannot be classified as either benign or malignant due to their ambiguous characteristics. The main differential diagnosis is melanoma and the uncertainty lies in the potential metastatic risk. Little guidance is currently available regarding their management, in particular the optimal excision margins and whether to offer SLNB. Yet, long term clinical follow-up remains the only true evidence of these lesions' biological behaviour.



# Immunosupressive Kaposi's sarcoma and Human herpesvirus type 8 (HHV-8)

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**Introduction & Objectives:** Kaposi's sarcoma (KS)-associated herpesvirus or\*\* Human herpesvirus type 8 (HHV-8) is discovered by PCR using skin samples from patients with Kaposi's sarcoma. This virus is considered a candidate of the etiological factor in this disease.

The aim of the study was detection of the HHV-8 in skin samples from patients with immunosupressive type of KS.

**Materials & Methods:** 10 skin biopsies of patients with histologically confirmed immunosupressive type of KS were examined by PCR. In 5 patients, material was taken from maculoplasty elements, in 3 patients from plaque elements, and in 2 patients from nodular elements.

**Results:** In the group of patients with immunosupressive type of KS, the HHV-8 was detected in all samples (100%). The same patients had the virus detected in their blood (45%) and saliva (17%). Most of the skin samples (72%) were represented by angiomatous histological variant.

**Conclusion:** Thus, in patients with immunosupressive type of KS, HHV-8 is detected with a high frequency (100%) in samples of the affected skin and confirms the viral concept of the disease. The dose and duration of use of immunosuppressive drugs may affect the rate of development of the disease, the phase of development of the virus and its presence in various biomaterials.



## PD-L1, PD-1 and CD8 expression in 100 primary invasive cutaneous squamous cell carcinomas

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**Introduction & Objectives:** Squamous cell carcinoma of the skin (SCCs) is the second most common skin cancer with continuously increasing incidence. Programmed cell death ligand 1 (PD-L1), Programmed cell death 1 receptor (PD-1) and CD8 expression in primary SCCs has not been described in many studies. We investigated the association between PD-L1, PD-1, CD8 and clinocopathological prognostic factors for recurrence, metastasis and mortality of SCCs.

**Materials & Methods:** Immunohistochemically stained sections of 100 primary invasive SCCs, divided in two groups, according to macroscopic diameter of the tumors (<20 mm and >20mm) were assessed. Recombinant rabbit Anti-PD-L1 antibody [SP142] - C-terminal, rabbit monocloncal Anti-PD1 antibody [NAT105] and FLEX Mono Mo a Hu CD8, cl C8/144B, RTU were used for immunohistochemical examination.

**Results:** The analysis of the data did not show statistically significant difference for PD-1 and PD-L1 expression and the Breslow depth of invasion of the SCCs: P<0.05 (Actual value P=0.453) and P<0.05 (Actual value P=0.134) respectively.

Analysis of the connection between CD8 expression and depth of SCCs invasion, was also statistically insignificant: P<0,05 (Actual value P=0,146). However, SCCs with major depth of invasion showed higher PD-L1, PD-1 expression and thinner tumors showed higher CD8 expression. Data analysis did not find statistically significant connection between tumor cell differentiation the PD-L1 (P=0,277), PD-1 (P=0,552) and CD8 expression (P=0,889). Data analysis revealed that there was no statistically significant difference between the perineural invasion and the expression of PD-L1 (P=0,284), PD-1 (P=0,710) and CD8 (P=0,327).

Discussion: PD-L1 is a very important co-stimulatory molecule of the immune response which induces immune tolerance in the tumor microenvironment. The PD-L1/ PD-1 bind induces T cell-death and leads to poor prognosis. The higher CD8 expression in SCCs may be a positive prognostic marker. A study by Varki et al. using the SP142 clone of anti-PD-L1 reported positive staining (>5%) in 26% of 66 primary SCCs cases. As opposed to this study, 64% of our PD-L1 positive cases demonstrated expression of 2 – 10% and 36% showed >10% PD-L1 expression in the tumor cells. Our study revealed 98 of the tumors had various inflammatory response but we did not find statistically significant relationship between PD-L1 expression and the inflamation around the primary tumor. Studying the difference between PD-L1 expression in primary SCCs and lymph node metastases, authors in the literature demonstrated higher expression in metastatic tissues. Their results did not show statistically significant connection between the expression of PD-L1 and clinicopathological features, like the analysis of our results. We did not find statistically significant connection between PD-L1/PD-1 expression and histopathological features, such as tumor thickness >6mm, diameter >20mm and poor histopathological grade.

**Conclusion:** According to our results in early stages of SCCs the expression of PD-L1, PD-1 or CD8 is not associated with high-risk clinocopathological factors. Therefore, we suggest that the immunohistochemical examination is more meaningful in advanced SCCs and in metastatic tissues, since they show higher PD-L1/PD-1 expression.



# A retrospective histopathological study of patients with various granulomatous dermatoses attending a tertiary care hospital

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# **Introduction & Objectives:**

Granulomatous dermatoses encompass a wide range of infectious as well as noninfectious conditions. Clinical features of these diseases are overlapping, thus a confirmatory histopathology remains the gold standard for accurate diagnosis.

We aimed to assess the prevalence, demographic distribution, clinical features and histopathology of various granulomatous disorders.

#### Materials & Methods:

This is a retrospective study with inclusion of both indoor and outdoor patients from June 2021 to November 2023. Skin biopsy obtained from patients clinically diagnosed as various cutaneous granulomatous diseases were analysed. Records were maintained in the form of demographic characteristics, morphology of lesions, duration of disease, clinical and histopathological diagnosis.

#### **Results:**

112 cases were included in the study (74 males and 38 females), with a male to female ratio of 1.9:1. Most common common age group affected was 21-30 (n=29; 25.8%). Infectious granulomatous dermatoses (n=106; 94.7%) were more common than the non-infectious ones (n=6; 5.3%). Among the infectious granulomatous dermatoses, leprosy (n=77; 68.75%) remained the major entity followed by lupus vulgaris (n=11; 9.8%). Amongst leprosy cases borderline tuberculoid leprosy (n=40;35.7%) was the most common entity followed by borderline lepromatous leprosy (n=14;12.5%) and least common was mid borderline leprosy (n=2 1.78%). Most common form of lesion was erythematous plaque (n=60;53.5%) followed by hypopigmented patch.

Among the noninfectious granulomatous disorders, granuloma annulare (n=3; 2.6%) was more common followed by sarcoidosis, Crohn's disease and granulomatous cheilitis (n=1, 0.8%) each.

Table showing the frequencies of various granulomatous dermatoses

Disease	Total number of cases	Percentage (%)
Leprosy	77	68.75
Lupus vulgaris	11	9.82
Tuberculosis verrucosa cutis	5	4.46
Granuloma annulare	3	2.67
Papulonecrotic tuberculid	3	2.67
Lichen scrofulosorum	6	5.35
Eumycetoma	2	1.78
Botryomycosis	1	0.89
Granulomatous cheilitis	1	0.89
Crohn's disease	1	0.89
Sarcoidosis	1	0.89

# Table showing comparison of current study with other studies

Disease	Bal A et al (N=586)	Dhar S et al (N=22 )	Zafar et al (N=123)	Kumar VN et al (N=172)	Current study (N= 112)
Leprosy	373 (72.4%)	9 (40.9%)	17 (13.8%)	136 (78.8%)	77 (68.75%)
Cutaneous Tuberculosis	119 (23.1%)	8 (36.3%)	97 (78.8%)	18 (10.5%)	25 (22.3%)
Foreign body granuloma	<b>[</b> -	<b>[</b> -	4 (3.2%)	6 (3.7%)	g-
Fungal granuloma	17 (3.3%)	2(9%)	2 (1.6%)	4 (2.4%)	1 (0.89)
Granuloma annulare	0-	<b>[</b> -	1(0.8%)	3 (1.8%)	3 (2.67%)
Actinomycosis	<b>I</b> -	<b>[</b> -	<b>[</b> -	1 (0.5%)	0-
Post kala azar dermal leishmaniasis	6 (1.16%)	l-	g-	g-	0-
Sarcoidosis	<b>[</b> -	3 (13.6%)	2 (1.6%)	<b>[</b> -	1 (0.89%)
Crohn's disease	<b>[</b> -	<b>[</b> -	<b>[</b> -	<b>[</b> -	1 (0.89%)
Botryomycosis	<b>[</b> -	<b>[</b> -	<b>[</b> -	<b>[</b> -	1 (0.89%)

# **Conclusion:**

Histopathology along with a detailed history and a thorough clinical examination are gold standards for diagnosis and subclassification of cutaneous granulomatous lesions.

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#### Atypical discrete papular localized mucinosis

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# **Introduction & Objectives:**

Papular mucinosis is characterized by the primitive deposition of mucin in the reticular dermis.

We report the case of a patient with discrete atypical papular mucinosis with an unusual localization.

## **Case report:**

A 58-year-old woman with no specific pathological history consulted for a symmetrical papular eruption affecting the face, neck and shoulders, which had been evolving for 6 years. Dermatological examination revealed multiple yellowish-translucent, flesh-coloured papules of 3 to 4 millimetres in diameter on the face, neck and shoulders, with molluscum pendulum in the cervical area; associated with yellowish and whitish deposits in the cavum and above the glottis, and an inflamed mucosa. Histological examination revealed mucin deposits in the dermis on Alcian Blue coloration, discrete vacuolization of the basal stratum, and a moderate inflammatory infiltrate of lymphocytes and plasma cells in a perivascular and periannexal disposition. The final diagnosis was atypical localized papular mucinosis. The patient was treated with dermocorticoids without any real improvement.

#### **Discussion:**

Papular mucinosis is a rare disease, and its pathophysiology remains poorly understood. Diagnostic criteria are sometimes misunderstood, and the classification includes atypical and intermediate forms. Despite the new classification updated by Rongioletti in 2001, papular mucinosis in our patient remains difficult to classify. The closest approximation is papular mucinosis in the "discrete papular" form, but with facial involvement. Our observation is the second case report of an atypical form of papular mucinosis with a cervicocephalic localization. In all cases, treatment is often disappointing.

# **Conclusion:**

papular mucinosis is rare and little-known, and presents a multitude of atypical forms.



# PRAME expression in melanoma is negatively regulated by TET2-mediated DNA hydroxymethylation

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# **Introduction & Objectives:**

Preferentially Expressed Antigen in Melanoma (PRAME) is a promising immunohistochemistry (IHC) biomarker with high sensitivity and specificity for melanoma. 5-hydroxymethylcytosine (5-hmC), a DNA-hydroxymethylation modification produced by the dioxygenase TET2, is an epigenetic hallmark of melanoma and plays a critical role in pathogenesis. Herein, we explore the epigenetic mechanism of DNA-hydroxymethylation of PRAME expression in melanoma.

#### **Materials & Methods:**

PRAME and 5-hmC levels were assessed by IHC and multiplex immunofluorescence (mIF) in an established tissue microarray consisting of benign nevi, primary melanomas, and metastatic melanomas (n=51). Validation cohorts ranging from benign nevi to melanoma also underwent mIF (n=92). Western blot and quantitative PCR detected PRAME and TET2 expression in A2058 melanoma cell lines overexpressing TET2 (TET2OE) vs. vector control. RNA sequencing and hydroxymethylated DNA immunoprecipitation sequencing (hMeDIP-seq) evaluated nevi/melanoma samples and control/TET2OE A2058 cells, respectively.

#### **Results:**

mIF revealed inverse correlations between PRAME expression and 5-hmC levels in benign nevi, dysplastic nevi, precursor regions, melanoma in situ, primary melanomas, and metastatic melanomas (p<0.05 in each category). hMeDIP-seq uncovered decreased 5-hmC in the PRAME 5'-promoter region for melanoma versus nevi. In A2058 cells, PRAME 5'-promoter 5-hmC was restored by over-expression of TET2. In vitro restoration of 5-hmC in A2058 cells significantly decreased PRAME mRNA and protein.

#### **Conclusion:**

We show inverse correlation of PRAME and 5-hmC in melanocytic neoplasms and establish that PRAME is negatively controlled by epigenetic TET2-mediated DNA-hydroxymethylation of the PRAME 5'-promotor. Our findings provide novel insights into the epigenetic underpinnings of aberrant PRAME expression in melanoma.



A case report of benign atypical intravascular CD30 positive T cell proliferation: a reactive lymphoproliferative process and mimic of intravascular lymphoma.

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# **Introduction & Objectives**

Atypical lymphoid cells present in lymphatic or vascular channels are suggestive of intravascular lymphoma; an uncommon entity usually associated with B cell phenotype lymphomas. CD30 is a transmembrane glycoprotein receptor from the tumour necrosis factor receptor family that causes pro-survival effects and is known to be activated in multiple different lymphomas. The finding of atypical CD30 positive atypical lymphocytes within vessels associated with a reactive process rather than neoplastic, although rare, has been previously described in the literature. We present a further case of benign atypical intravascular CD30 positive T cell proliferation in an area of ulceration and inflammation in a patient with a cyst in the groin.

#### **Materials & Methods**

A case report of a 28-year-old female patient who presented to her GP surgery with a cyst in the left groin. She had previously received medical attention for the cyst abroad, requiring antibiotics after the cyst burst. She was referred for excision of the lesion which was sent for histopathological evaluation. Consent and clinical and histopathological pictures were taken.

#### **Results**

Histological assessment of the lesion showed skin with a central area of epidermal ulceration with a mixed inflammatory cell infiltrate. Dilated thin wall lymphatic vessels containing medium to large atypical lymphoid cells were noted. The intravascular lymphoid cells expressed CD2, CD3, CD4, CD5 with partial CD7 expression and loss of CD8. They also expressed CD30. The cells were negative for CD20, TdT and EBER. The case was concluded as benign atypical intravascular CD30 positive T cell proliferation. The case was reviewed at a tertiary center, and the conclusion of the report remained the same.

# Conclusion

Benign atypical intravascular CD30 positive T cell proliferation is a potential diagnostic pitfall for intravascular lymphoma and pathologists must aware of this entity and able to distinguish between the two.



# Axillary Lipomas and supernumerary breasts: a frequent mix-up

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# **Introduction & Objectives:**

The mammary glands emerge on the mammary ridges, which run from the armpit to the inguinal fold during embryonic development. The supernumerary breast is defined by the gland's continued existence on these ridges outside the breast's typical location. Through this case report, we shed light on the possible confusion between bilateral axillary lipoma and supernumerary breasts.

#### **Materials & Methods:**

We report the case of a 32-year-old, Moroccan woman, nullipara nulligravida, with no prior medical history, no use of any hormonal contraceptive, and no family history of breast disorder either. Her general practitioner addressed the patient to the dermatology department for bilateral axillary lipomas evolving for the last nine months, with both tumefactions gradually increasing in volume.

Skin examination revealed a tender non-painful, round, mobile masse with a soft, doughy feel on each axilla suggesting an adipous tissue. Each mass was approximately 12 cm x 5 cm in size. The skin surface was regular with no particular aspect, no dyschromic patches, and no signs of superficial vascularisation either.

An ultrasound exam was ordered, which revealed a lobulated fatty structure separated by septa suggesting the existence of supernumerary breasts. The Gynecology Department operated on the patient. The procedure went on successfully, and the pathological exam showed no sign of malignancy.

#### **Results:**

The prevalence of accessory breast tissue varies according to gender, ethnicity, region, and heredity. The axillary accessory breast may enlarge during adolescence, pregnancy, and breastfeeding. There have been reports linking congenital abnormalities of the circulatory and urogenital systems to accessory breast tissue. It has been found that ectopic breast tissue in patients is a significant cutaneous signal of circulatory system conduction system abnormalities.

We were unable to uncover any congenital anomalies in our patient.

Clinical diagnosis of axillary supernumerary breasts is rarely achieved in the absence of nipple and areola. This explains the frequent confusion of this anomaly with lipomas and axillary lymphadenopathy. Just like normal breast tissue, benign and malignant disorders of accessory breast tissue have been reported.

After suspicion of the diagnosis, it is wise to carry out an ultrasound revealing a breast echostructure with alternation of hyperechogenicity (connective tissue) and hypoechogenicity (glandular and fatty tissue).

Several authors recommend core-needle biopsy in case of doubt, with a pathological study that will find glandular tissue associated with connective and fatty tissue.

# **Conclusion:**

Supernumerary breasts represent a diagnostic challenge mainly and even therapeutic in the event of the presence of a

malignant component in the tumor. In case of doubt, it should be mentioned in any case of a subcutaneous nodule of uncertain diagnosis located on the axillary lactation line by carrying out an ultrasound and a micro biopsy.



## Pseudoxanthoma elasticum-like papillary dermal elastolysis: A mimicker of genetic pseudoxanthoma elasticum

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**Introduction & Objectives:** Pseudoxanthoma elasticum (PXE)-like papillary dermal elastolysis (PDE) is a rare, acquired disorder of the elastic tissue that presents with multiple asymptomatic, nonfollicular yellowish or normochromic papules, with a predilection for the neck of postmenopausal women. The etiology is unknown, but it is speculated that there is a multifactorial pathogenesis, with the contribution of intrinsic aging, exposure to ultraviolet radiation, abnormal elastogenesis, and genetic factors. No systemic involvement has ever been reported. We report a case of PXE-PDE in a postmenopausal woman.

**Results:** We present a 63-year-old female patient,\*\* Fitzpatrick skin type III, with a history of ankylosing spondylitis medicated with adalimumab. Referred to the Dermatology clinic due to slowly progressive appearance of asymptomatic non-follicular papules, located on the neck, with one year of progression. The patient denied history of marked solar exposition or trauma on the affected areas. There was no family history of similar lesions. The physical examination of the skin revealed the presence of multiple skin-colored and yellowish papules, with a cobblestone appearance, sized 1–6 mm, symmetrically distributed on the lateral region of the neck (Figure 1). We performed a punch biopsy for histopathologic examination which showed a normal epidermis, with a slight perivascular lymphocytic infiltrate in the papillary dermis. Orcein and Verhowff stains revealed an absence of elastic fibers in the papillary dermis (Figure 2). No calcifications were observed on Von Kossa stain. Based on the clinical and histological findings, the diagnosis of PXE-PDE was made.

**Conclusion:** PXE-PDE is a mimicker of inherited PXE, but it differs histologically and lacks the ophthalmologic and cardiac manifestations of PXE. Clinicopathologic correlation is critical as hematoxylin-eosin staining is nonspecific and elastic tissue stains are necessary to make the correct diagnosis. It is probably underestimated, which reinforces the importance of better clinical and histologic identification to distinguish it from inherited PXE.



## Epidemiological aspects and clinical-histopathological correlations in cutaneous squamous cell carcinoma

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**Introduction & Objectives**: Cutaneous squamous cell carcinoma (SCC) is the second most common cancer after basal cell carcinoma, but the incidence in the Caucasian population is increasing. The occurrence of de novo or on pre-existing lesions and their evolution as in situ or invasive forms explain the clinical variability of SCC and the existence of numerous histological subtypes. The authors aim to highlight epidemiological characteristics and study clinical-histopathological concordance in patients diagnosed with SCC.

**Materials & Methods**: We performed a retrospective study between 01.01.-31.12.2023. The group was distributed according to age, sex, environment, location of tumors, and the result of histopathological examination. We identified histopathological subtypes of cutaneous SCC and noted certain histopathological parameters considered important prognostic factors: depth of cutaneous invasion (subhypodermic invasion), lesions larger than 2 cm, and perineural invasion.

Results: The studied group included 37 patients (18 women, 19 men) diagnosed histopathologically with cutaneous squamous cell carcinoma. There were 13 patients from rural areas (35.13%) and 24 from urban areas (64.87%). The median age was 71.54 years, ranging from 45 to 87 years. The topography of lesions was as follows: cephalic extremity 25 cases (67.56%), upper limb 6 cases (16.22%), lower limb 2 cases (5.40%), anterior thorax 3 cases (8.11%), vulvar 1 case (2.71%). We encountered the following clinical diagnoses: squamous cell carcinoma 9 cases (clinical-histopathological concordance 24.32%), keratoacanthoma 7 cases (18.91%), basal cell carcinoma 10 cases (27.02%), mixed carcinoma 1 case (2.70%), actinic keratosis 5 cases (13.51%), seborrheic keratosis 2 cases (5.40%), Jadahson nevus 1 case (2.70%), hyperkeratotic papilloma 1 case (2.70%), cutaneous horn 1 case (2.70%). The histopathological examination reveals the following subtypes of SCC: Bowen's disease 1 case, carcinoma in situ of the lower lip 1 case, SCC developed on actinic keratosis – 4 cases (carcinoma in situ, microinvasive, well or moderately differentiated), SCC Keratoacanthoma type 8 cases (SCC microinvasive 4 cases, well-differentiated 2 cases, moderately differentiated 2 cases), metatypical carcinoma 7 cases (well and moderately differentiated), vulvar verrucous carcinoma 1 case, invasive SCC 15 cases (microinvasive 4 cases, well-differentiated 3 cases, moderately differentiated 5 cases, and undifferentiated 3 cases). Considering keratoacanthoma as a particular clinical form of SCC, the percentage of concordance between clinical and histopathological diagnosis increases to 43.24%. In the studied group, we did not encounter subhypodermic invasion, 1 single case had neural invasion, and tumors were not over 2 cm in size.

**Conclusion**: Efficient management of this tumor consists primarily of early diagnosis and correct staging, with histopathological examination being essential in approaching these cases. The correlation of clinical prognostic factors with certain histopathological parameters allows the identification of cases with an increased risk of local recurrence or risk of metastasis.



# Primary Disseminated Varicella Zoster: A Mimicry of cutaneous cytotoxic T-cell lymphoma.

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# **Introduction & Objectives:**

Varicella-Zoster virus (VZV) is a common skin infection characterized by multiple painful vesicles typically involving a single dermatome. We present an unusual case of VZV with histological features mimicking a cutaneous cytotoxic T-cell lymphoma.

#### **Case discussion:**

A 64-year-old Chinese woman presented with a three-day history of fever, malaise and widespread painful vesiculopustular eruptions over her skin, oral and vaginal mucosa. She had no significant past medical history. Blood tests revealed elevated hepatocellular transaminases (Alanine transaminase 254U/L, Aspartate Transaminase 191U/L) with leukocytosis (White blood cell count 13.1 x 109/L) and elevated C-reactive protein (153mg/L). Serum immunoglobulin (Ig) M was reactive for VZV while IgG was negative. VZV polymerase chain reaction skin swab was positive. A skin biopsy was performed and showed interface vacuolar change of the epidermis and lymphocytic exocytosis. There was a fairly dense infiltrate of cytologically atypical large T-lymphoid cells in the superficial dermis featuring irregular vesicular nuclei with variably prominent nucleoli and mitoses. The atypical T cells expressed CD3, CD8 and cytotoxic markers, TIA1 and granzyme B. They were negative for CD4, CD56, CD30 and Epstein-Barr virus (EBV)-encoded RNA (EBER). Further T-cell clonality studies were performed - these demonstrated polyclonal TRB and TRG gene rearrangement, supporting a reactive T-cell proliferation. Given these findings, a diagnosis of atypical cytotoxic T-cell cutaneous eruption of primary VZV was made. The patient was treated with 10 days of antivirals with significant clinical improvement.

#### Conclusion:

VZV infection or vaccination is known to elicit an immunogenic response involving helper and cytotoxic T-cells, with case reports of pseudolymphomatous eruption after vaccination in immunocompromised patients. This case highlights an extremely unusual CD8+ cytotoxic lymphomatoid cutaneous reaction in primary VZV infection in an immunocompetent host. Consideration of all clinical-pathological, including molecular diagnostic findings, can help indicate a reactive process and avoid an over-diagnosis of a cytotoxic T-cell lymphoma.



## Acute eczema on patches of vitiligo: Unusual Wolf's isotopic response

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# **Introduction & Objectives:**

Wolf's isotopic response occurs when a dermatosis appears in a region previously affected by another unrelated and already healed skin disease. The term was first introduced by Wolf et al in 1995. In most cases, infection with varicella-zoster virus (VZV) or herpes simplex virus (HSV) is the most common pre-disposing skin disorder for an isotopic response. Different cutaneous diseases may develop on the same site, most commonly granulomatous, lichenoïd reactions, malignancies, and infections.

#### **Materials & Methods:**

We report an unusual manifestation of allergic contact eczema on vitiligo patches.

#### **Results:**

A 64-year-old woman with a history of hypothyroidism and systemic lupus erythematosus presented with achromic plaques on the face and extremities that had been evolving for 3 months. The diagnosis of active acrofacial vitiligo was made and the patient was treated with weekend corticosteroid therapy and topical corticosteroids for 2 months without improvement. Furthermore, following the start of work in a fish market, the patient developed very itchy erythematous, scaly, and fissured plaques located only over the achromic plaques on the back of the hands and forearms, sparing the normal skin. A biopsy of these lesions was performed. Histopathologic examination showed in addition to the disappearance of melanocytes, spongiosis of the epidermis associated with focal hyperkeratosis and a moderate dermal infiltrate made up of lymphocytes and eosinophils. Hence, the diagnosis of acute eczema on patches of vitiligo was made. Patient was treated with topical steroids with favorable outcomes.

# **Conclusion:**

Our case illustrates a non-previously described manifestation of the Wolf's isotopic response. The pathophysiology of this phenomenon remains poorly understood. The possible hypotheses formulated to explain this phenomenon include viral, neural, immunological and vascular factors.

The time interval between primary and secondary dermatosis can vary from a few weeks to months or even years.

Eczema has not been reported as a secondary dermatosis, particularly on vitiligo. Only one case report of lichen planus patterns on non-segmental mucocutaneous vitiligo has been reported in the literature. This supports the hypothesis suggesting the role of neuro-hormonal modulation of local immunity in response to different types of dermatoses, especially as this phenomenon seems to extend to other dermatoses, notably dysimmunity.

However, continued investigation should be performed to understand the pathogenesis of this phenomenon in order to make an early diagnosis and ensure appropriate treatment.



# Atypical Histophatologial finding in lichen planus; Case report.

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# **Introduction & Objectives:**

Lichen planus is a pathology with multiple clinical presentations, so its adequate description is important to improve the diagnostic and therapeutic approach. In the case presented, classic epidemiological characteristics of lichen planus are observed, but clinical and histological findings are not so frequent, which is why it is important for us to present these findings as a reinforcement of the typical and atypical scenario of lichen planus.

#### **Materials & Methods:**

A 60-year-old female patient from Mexico City, presents with a significant background of Diabetes Mellitus, Systemic Arterial Hypertension and Hepatitis C Infection without current treatment. Viral load is unknown.

Patient reported starting with dermatosis a year earlier with papulo-pustular lesions on the lower extremities that were pruritic with increased itching after bathing.

On physical examination we found a single dermatosis located on lower extremities bilateral symmetrical with predominance in the anterior tibial area, polymorphic consisting of erythematous-violaceous papules with a tendency to converge in plaques, some with white center and signs of excoriation with scabs, pruritic with a chronic evolution.

It was decided to take a punch biopsy. The histopathological result showed epidermis with corneal plugs and vacuolar degeneration of the basal stratum with formation of subepithelial clefts. In the dermis there are numerous dilated blood vessels, melanophages and lymphocytic inflammatory infiltrate, which in some areas are forming a band.

Therefore, the diagnosis of lichen planus is concluded.

#### **Results:**

Our patient falls into the classic epidemiological group of lichen planus, a 60-year-old female with risk factors such as hepatitis C infection. Her dermatosis follow the rule of the 4Ps of lichen planus: Small, polygonal, purpuric papules; however, her lesions contain whitish spots with pustular characteristics that are not typically described in this pathology. The literature does not describe them as a finding, so it was decided to take a biopsy, in which traditional signs of lichen planus were found, such as lymphocytic infiltrate with a band distribution, basal vacuolar degeneration and Max-Joseph spaces, as well as corneal plugs. which we associate with the whitish central lesions that are observed macroscopically and with dermatoscope.

#### **Conclusion:**

Lichen planus is a pathology with low incidence characterized by small polygonal purpuric papules. Our case presents an atypical clinical characteristic with whitish dots in the papules associated with keratin or corneal plugs in the biopsy. The objective is to present the findings to raise awareness of this clinical and histopathologic presentation.



## Gouty tophus in an 18-year-old Filipino female with Takayasu arteritis: A case report

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# **Introduction & Objectives:**

Gout is a chronic inflammatory condition caused by the deposition of monosodium urate crystals in the joints, bone, skin, or soft tissues, attributable to hyperuricemia. Historically, gout has been predominantly associated with older, overweight men, and is extremely rare in the pediatric population, especially in girls. However, chronic states of hyperuricemia in children, especially in the background of cardiovascular or kidney disease, can lead to the accumulation of urate crystals in soft tissues progressing to gout, similar to that seen in adults.

#### **Materials & Methods:**

This is a case of an 18-year-old Filipino female diagnosed with Takayasu arteritis, chronic kidney disease stage 2 from bilateral renal artery stenosis, and congestive heart failure from severe aortic and mitral regurgitation secondary to aortopathy from Takayasu arteritis, who presented with a 2-month history of multiple progressive nonpruritic, nontender, firm to hard small tan-white round papules coalescing to form nodules, on the bilateral elbows and right calf. The cutaneous lesions are associated with arthralgia of bilateral hands and feet, flexion contractures of the 3rd and 5th digits of the right hand, and an inability to flex bilateral wrists fully. The patient is overweight using the WHO Asian Body Mass Index Classifications. The primary working impression was calcinosis cutis.

#### **Results:**

A 4-mm skin punch biopsy of a firm white nodule on the right elbow was performed. However, the biopsy revealed nodular aggregates of amorphous deposits of pale basophilic material in the dermis consistent with gouty tophus. Her uric acid upon workup was 6.9 mg/dL. The patient was started on allopurinol, a uric acid-lowering agent, to control the disease.

# **Conclusion:**

Despite its rarity in young females, gout should be considered in juvenile patients presenting with firm white papules and nodules in the skin associated with peripheral arthritis, especially when concomitant metabolic, cardiovascular, and renal comorbidities are also present. A confirmed case of pediatric gout should be managed promptly using uric acid-lowering agents to avoid permanent joint deformities.



# Comparative analysis of tissue BRAFV600E detection in melanoma: Immunohistochemistry versus PCR?

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**Introduction & Objectives:** The mutated BRAFV600 is the most known predictive tissue marker allowing the application of the BRAF inhibitor targeted treatment in melanoma patients. The DNA-based polymerase chain reaction (PCR) techniques are the gold standards for identifying the BRAF mutation in melanoma malignum. However, there are limitations of the PCR techniques indicating solutions in the detection of the BRAF state. As the targeted drug acts on the mutated BRAFV600E protein, the in situ immunohistochemical (IHC) detection of the BRAFV600E protein within the melanoma tissue gives a potential opportunity for a short time prediction and for the urgent start of the BRAFV600E targeted therapy in advanced melanoma cases.

**Materials & Methods:** In this IHC validation study, we included 94 patients which had melanoma tissue available, aiming to focus on (1) the clinical significance of inhomogeneous positive BRAF staining in the melanoma diagnostics, and (2) to investigate the differences between BRAFV600E mutated protein validated by IHC (clone VE1 – BRAFV600E mutation specific antibody) and the DNA-based BRAF mutation analyzed by Sanger sequencing. Based on the heterogeneous BRAFV600E staining of the samples, groups of negative, diffuse positive and focal positive cases were annotated. The mismached IHC-PCR paires were revalidated by qPCR.

**Results:** From the 94 cases 8 harbored BRAFV600K, 1 case displayed BRAFK601 mutation, 2 samples presented BRAFV600R mutations and 32 cases showed BRAFV600E mutation, the rest of the samples (n=51) proved wild type of BRAF identified by Sanger PCR.

Compared the two techniques, we observed a significant mismatch between the PCR and the IHC (Pearson Chi2 p <0.05) mainly resulted from the IHC false positive results, as 8 and 11 cases showed diffuse and focal IHC BRAFV600E positivity among the PCR negative cases (n=51). For the validation of the Sanger PCR, further detailed qPCR sequencing revealed one positive case of BRAFV600E which previously was diagnosed as PCR negative indicating possible dilution artefact of the mutated DNA. One false positive IHC case was also identified at the BRAFV600K mutation group showing a diffuse BRAFV600E IHC expression pattern. As far as the IHC sensitivity considered, all of the BRAFV600E positive melanoma cases diagnosed by PCR showed variable extent of positive IHC. Interestingly, none of the BRAFV600E positive PCR cases displayed focal tissue IHC expression.

**Conclusion:** Our study results highlighted (1) the disparities between the two validation technique, the limitations of the (2) routine PCR sequencing (dilution artefact), (3) of the IHC (false positive results) and (4) underscored the potential significance of focal positive BRAF cases in melanoma histopathology as well. Although BRAFV600E IHC has been proven a very fast and relatively cheap method for the routine diagnostic histopathology practice the study also pointed out the combined usage of the two (PCR and IHC) techniques.

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## Vulvar mass revealing cellular angiofibroma: Case report

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#### Introduction

Cellular angiofibroma of the vulva represents a rare benign mesenchymal tumor typically observed in middle-aged women, with its initial description dating back to 1997. While it predominantly manifests in the vulvar region, isolated cases of extravulvar cellular angiofibromas have also been documented. Herein, we present a case of vulvar localization in a 58-year-old woman, successfully managed through complete excision

#### **Case observation:**

A 58-year-old multiparous woman, menopausal for eight years and with no history of oral contraceptive use, presented with a painless vulvar mass that had been progressively developing over one year, causing discomfort while walking.

Upon physical examination, a well-defined mass spanning the left labia majora, measuring 7 cm in length, was noted. The mass exhibited mobility in the superficial plane but adherence to the deep plane, firm consistency, and lacked inflammatory signs. Palpable lymph nodes were free, and pelvic examinations were unremarkable

Pelvic MRI revealed a tumoral process centered on the left labia majora, devoid of locoregional metastases. Skin biopsy demonstrated a tumor proliferation of spindle-shaped cells without atypia, alongside a stroma containing numerous small to medium-sized vessels with thickened walls.

Immunohistochemical analysis revealed positive labeling of tumor cells with anti-CD34 antibodies, while staining with anti-protein S100, anti-desmin, and anti-smooth muscle actin antibodies was negative.

A diagnosis of cutaneous cellular angiofibroma was confirmed, and the patient underwent complete excision.

Postoperatively, the patient experienced significant symptom relief without any complications and is currently under regular outpatient follow-up

# **Discussion:**

Cellular angiofibroma is a rare benign mesenchymal tumor found in the genitourinary tract of both sexes, primarily in the vulvovaginal region in women and the inguinoscrotal region in men. It typically manifests earlier in women, around age 50, compared to men, who typically develop it around age 70.

Clinically, it presents as a small, painless mass that grows slowly within the superficial soft tissue, often leading to delayed consultation, as observed in our case where the patient sought medical attention a year after the tumor appeared. However, there are exceptional cases of early symptomatic disease. It may be misdiagnosed as a Bartholin's cyst.

Histologically, cellular angiofibroma comprises monomorphic spindle cells and small to medium-sized prominent vessels with mural hyalinization, consistent with the findings in our case. Sarcomatous transformation is rare.

Immunohistochemically, tumor cells typically stain positive for vimentin, and CD34 expression is observed in 60% of cases. However, they do not express S-100 protein, desmin, or smooth muscle actin, as seen in our case.

Treatment involves complete local excision with healthy surgical margins, and local recurrence is uncommon.

#### **Conclusion:**

We present a case of painless vulvar angiofibroma, where the mass developed over one year before the patient sought consultation. Due to its extremely benign nature and low recurrence risk, surgical excision was chosen as the treatment approach. Despite its rarity, early identification is feasible, potentially averting symptoms associated with a larger mass, as demonstrated in the case under study



# Dermatological emergencies: a Moroccan prospective case series over a period of one year

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# **Introduction & Objectives:**

Although dermatology is generally regarded as an ambulatory clinical practice characterized by non-acute, non-fatal conditions

4% to 12% of all emergency room visits are due to symptoms related to dermatological disorders.

This demand for urgent consultation is growing, and may correspond to an acute dermatosis or to a non-urgent dermatitis (in 49-82%) in order to obtain a shorter consultation time.

The aim of our study is to identify the main dermatological emergencies consultations and establish a demographic and clinical profile of the reasons for dermatological consultations.

#### **Materials & Methods:**

We conducted a prospective study in the dermatology department of the Ibn Sina University Hospital in Rabat between June 01, 2022, and May 31, 2023. 1321 patients were included by receiving telephone calls via the dermatological emergency number during 24-hour shifts, 7 days a week, then collecting patient information, and this information was transcribed into a "dermatological emergency register".

Excel and Statistical Package for the Social Sciences (SPSS Inc., version 15.0 for Windows) were used for data entry and analysis.

#### **Results:**

1,321 urgent dermatology consultations were received during this period (4 patients/day), with more patients on Mondays (257 patients) and fewer on weekends (177 patients). 46.8% of consultations were requested in the morning vs. 37.6% in the afternoon and 15.6% in the evening. The sex ratio was 0.89, with a slight female predominance, and the average age was 45.6 years (01months-95years).

37% of patients consulted emergency departments, 43% hospital departments, 7% of patients referred from the private sector for urgent consultation, and 7% of staff consulted for urgent dermatological conditions.

The reasons for consultation were: infectious pathologies in 47% (Erysipelas in the lead), inflammatory pathologies in 24%, toxidermia in 7%, autoimmune bullous dermatosis in 4%, tumor pathologies in 3%, and others in 15% of cases.

Management was by emergency hospitalization in 5.9%, scheduled hospitalization in 10%, and outpatient treatment in 84.1% of cases.

"Dermatological emergency" is defined as any acute dermatological disorder that develops and worsens in less than 5 days. True dermatological emergencies" are: Infectious dermatosis, inflammatory dermatosis Toxidermia and Autoimmune bullous dermatosis.

Fewer than 20 studies have been published in the literature concerning urgent dermatological consultations. Our results concur with those of the literature concerning the average age of patients and the main reasons for consultations, with

erysipelas in the lead.

# **Conclusion:**

The pathologies encountered in dermatological emergencies are very diverse. However, the majority of patients do not require an emergency consultation.

This research project is an educational guide to the main dermatological emergencies in Morocco, aimed at residents and other healthcare professionals.



# atrophoderma of pasini and pierni: a case report

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Introduction & Objectives:

Atrophoderma of Pasini and Pierni (APP), is a rare disease of which fewer than 100 cases have been reported in literature until today. Pasini first described it in 1923 under the name of "progressive idiopathic atrophoderma" and Pierini et al further suggested its link to morphea in 1936. Classically APP presents with well demarcated, hypo- or hyperpigmented depressed patches with 'cliff-drop' borders and no obvious inflammation distributed over the trunk and limbs.

# Case Summary:

A 22-year-old young man presented with a three-year history of 'bruise-like changes' over his skin, initially bilaterally over the lateral aspects of the abdomen, and then becoming more widespread to involve the back and upper arms. On closer inspection, the lesions were multiple round areas of marked subcutaneous tissue loss and hyperpigmentation, albeit, without any 'cliff-drop' borders. A 6-week reducing course of prednisolone, starting at 30 mg once a day, trialed the year before had shown to stop the skin changes progressing before the lesions became more widespread. The patient was systemically well. An ultrasound performed to assess the depth of lesions was non-specific, as was a skin biopsy.

Following a 6-year loss to follow up, change of healthcare provider, and plateauing of lesions, the patient presented again at the age of 28 with evolving skin lesions. Blood tests including a vasculitic screen, immunoglobulin electrophoresis, complement levels, and streptolysin O titre levels were negative. A special interest meeting was held, morphea (or limited cutaneous scleroderma), Atrophoderma of Pasini and Pierni, and interstitial granuloma annulare were considered as differentials, and a repeat biopsy was planned.

An incisional skin biopsy with subcutaneous fat was performed on the left hip which had been left untreated with topical steroids. The epidermis was within normal limits on the section of skin biopsied. Superficial and mid dermis showed moderate perivascular and periadnexal lymphohistiocytic infiltrate, eccrine ducts were high up in the dermis, and at one end of the biopsy the dermal collagen was thickened with marked eosinophilia and loss of intervening spaces. The changes to dermal collagen extended deep with widening of fibrous septa in subcutis. The features of the biopsy were most in keeping with morphea. Given the clinical presentation the diagnosis of Atrophoderma of Pasini and Pierni, was made.

The patient is currently being teed up for methotrexate treatment.

### Conclusion:

This case presents an atypical presentation of an already rare and poorly understood cutaneous syndrome. The lack of classical features like "cliff-drop' borders made us consider other differentials. However, the age of the patient, distribution and progression of lesions, absence of inflammation, and a biopsy indicating eosinophilic dermal collagen thickening extending deep into the subcutis clinched the diagnosis of Atrophoderma of Pasini and Pierni.