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doi: 10.46327/msrjg.1.000000000000----.
doi url: <https://doi.org/10.46327/msrjg.1.000000000000---->

*****Published in June, 2023

CORE NEEDLE BIOPSY DIAGNOSIS OF FIBROEPITHELIAL LESIONS OF THE BREAST : ACCURACY AND DIAGNOSTIC CHALLENGES

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Introduction : Breast fibroepithelial lesions (FELs) are biphasic neoplasms consisting of proliferative epithelial and stromal components. It comprises the spectrum of fibroadenomas (FAs) and phyllodes tumors (PTs). Core needle biopsy (CNB) provides a pathological basis, helping in diagnosing fibroepithelial lesions. However, the overlapping spectrum of histological appearance in FELs gives rise to diagnostic problems and may comprise the development of appropriate therapeutic plans. The purpose of this study is to analyze the accordance between CNB and excision diagnoses of FEL patients and evaluate the accuracy of CNB in preoperative diagnoses.

Methods: A retrospective review from the medical records of 68 female patients who underwent preoperative CNB and surgical excision (SE) at university hospital Hassan II in 2022 was performed.

Results: In our study, the concordant rate of diagnosis between CNB and SE is about 50%. Of the FAs diagnosed on CNB (44 %), 90 % showed a complete match with surgical results and 10 % revealed to be a PT. On CNB, 10 % of the cases were diagnosed as PT and showed total concordance with the SE results. We concluded to a FEL in 46 % of the cases. On surgical excision, 60 % revealed to be FA and 40 % revealed to be PT.

Discussion: The differential diagnosis of fibroepithelial tissues in CNB is sometimes challenging. A multidisciplinary approach is a reliable strategy to distinguish between the different FELs. The distinction between the two lesions is challenging sometimes, especially with some FA variants (e.g. cellular FA). The main differential diagnosis of a malignant phyllode is spindle cell metaplastic carcinoma. The treatment is dissimilar. Therefore, it is imperative to differentiate between these lesions. Herein, a comparative table of various studies results :

Maliha latif et al. (2021)	28,8 % patients who had pt at excisional biopsy were diagnosed as fa on biopsy ¹ (vs 10 % in our study).
Gabriel Marcil et al. (2017)	The surgical excision of FEL diagnosed on CNB yield a pathological diagnosis of FA in 62,5 % and PT in 37,5 % ² (vs 60 % FA and 40 % PT in our study).
Resetskova et al. (2010)	In 43 cases of excised fels, 30 % were benign pts, 53 % were fas and 17% were benign cellular fels ³ (vs 60% FA and 40 % PT in our study).

Conclusion : The assessment of histopathological features of FELs on CNB can be subjective. The overlapping spectrum of histological appearance in FEL and sampling limitations of CNB may need more investigation. Immunohistochemistry is helpful but limited. Recent advances in molecular characterisation of FEL appear promising.

Keywords : Fibroepithelial lesion, Core needle biopsy, Breast.

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Competing interests: No competing interest among the authors

COMPARATIVE ANALYSIS OF HER-2 CLONES IN INVASIVE BREAST CANCER: A LITERATURE REVIEW.

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Introduction: The human epidermal growth factor receptor 2 (HER2) gene is an important tumor marker in invasive breast carcinoma (IBC). From 12 to 20% of IBC exhibit HER2 overexpression. The American Society of Clinical Oncology (ASCO) Tumor Marker Guidelines Panel has recommended HER2 research since 2001 as a routine test for newly diagnosed and metastatic breast cancer. Today, it is a standard of care. HER2 status is screened using immunohistochemistry (scored 0 to 3+) and confirmed with in-situ hybridization (ISH) for equivocal (2+) cases. With the era of new therapeutic strategies, the role of pathologists is increasingly crucial, and specific training and special attention during HER2 tests are warranted.

Objective: Several preanalytic factors such as fixation, antigen recovery, antibody clones, enzyme activity, reaction time, temperature and substrate concentration can influence the intensity of HER2 staining. As well, false negative or false positive HER-2 status may lead to inappropriate treatment in IBC patients. The purpose of this work is to study the impact of the choice of the antibody clones on the interpretation of HER2.

Method: We were conducted a literature review, a total of 8 studies published between 2009 and 2022 were analysed (cf. Annex.1) to compare the performance of different HER-2 clones, in particular the interobserving reproducibility and concordance with results of fluorescence in situ hybridization.

Results: This review allowed us to find 2 main clones, HercepTest and 4B5, which are equivalent, and their performance has been improved by automation. We also found other clones that are performing (CB11). Generally, choice of clone left to each laboratory and guidelines of professional societies do not impose a particular clone.

Conclusion: For quality assurance, supplier recommendations should be implemented, in-house blocks are to be developed and a monitor the positivity rate should also be set up as well as an adherence to an external quality assessment system.

Keywords : Invasive breast carcinoma, HER2 clone, HercepTest , 4B5

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Annex :

Study	Number of samples	Result
Doris Mayr , Sibylle Heim, Cedric Werhan, Evelyn Zeindl-Eberhart, Thomas Kirchner	130	-4B5 seems to be of same reliability like HercepTest with a little better concordance to FISH in this study.
Lester J Layfield , Shellaine Frazier , Magda Esebua , Robert L Schmidt	93	-Interobserver agreement was greater with the HercepTest. -Agreement with FISH results was superior for the 4B5 clone.
Seema Jabbar, MD, Elena Lucas, MD, Yisheng Fang, MD, PhD, Kyle Molberg, MD, Sara Blacketer, Sunati Sahoo, MD	219	-4B5 had a higher concordance with Her2 FISH results than HercepTest.
Lucas, Elena MD; Jabbar, Seema B. MD; Molberg, Kyle MD; Fang, Yisheng MD, PhD; Xie, Xian-Jin PhD; Blacketer, Sara HT (ASCP); Sahoo, Sunati MD.	180	-4B5 significantly reduced the number of equivocal results that require additional testing. It failed to detect 3 cases that were interpreted as positive by FISH.
Chantal Farra , Faysal Fedda , Arafat Tfayli , Ayman Tawil , Ghazi Zaatari , Hanin Ashkar , Grece Issa , Fouad Boulos	154	-Using HercepTest ,all of the false-positive (FISH-negative) breast cancer cases showed some degree of positivity in normal breast epithelium.
Anne-Sofie Schrohl , Hans Christian Pedersen, Sussie Steen Jensen, Signe Lykke Nielsen, Nils Brüner	-	-4B5 clone can bind HER4 peptides and fusion protein. -HercepTest™ antibody showed no cross-reactivity with other HER proteins -CB11 clone weakly detected HER4.
Josef Rüschoff , Michael Friedrich , Iris Nagelmeier , Matthias Kirchner , Lena M Andresen , Karin Salomon , Bryce Portier , Simone T Sredni , Hans Ulrich Schildhaus , Bharat Jasani , Marius Grzelinski , Giuseppe Viale	120	-HercepTest (mAb) had both high specificity (100%) and high sensitivity (100%), with no cytoplasmic staining, and lower background noise than 4B5 clone.
NordiQC (06-DEC-2021)	364 laboratories	-The 4B5 clone provided the highest proportion of optimal results (93%). -The recently launched HercepTest™ GE001, Dako/Agilent, provided a high pass rate of 100%. - For the classical HercepTest™ , a significantly reduced pass rate was observed.

Competing interests: We have no competing interests.

CLINICOPATHOLOGIC ANALYSIS OF 169 CASES OF CUTANEOUS ADNEXAL TUMORS: A RETROSPECTIVE STUDY.

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Background and objectives: Adnexal tumors (ATs) are a heterogeneous entity of primary skin tumors, rarely malignant. Their diagnosis represents a real challenge due to their polymorphism and the locoregional aggressiveness of adnexal carcinomas with their metastatic potential. This study aims to elucidate the morphological and epidemiological characteristics of these tumors through a series of Moroccan patients and to compare them with other series in the literature.

Methods: A retrospective study was conducted over a period of 10 years (2013–2022), including all adnexal tumors of skin diagnosed in the Department of Pathology, University hospital Hassan II of Fez, Morocco. The histological study was performed on formalin-fixed and paraffin-embedded tissue sections. The diagnosis was essentially morphological. Special staining or immunohistochemical complement was rarely used.

Results: Total number of cases that was diagnosed as ATs were 169. There were 135 benign tumors (80%) and 34 malignant tumors (20%). A female predominance was noted with a sex ratio M/F of 0.72. The mean age was 49 yr (5yr-90yr). Most of the cases were in the age group between the 4th and 5th decades (51–60 yr (32/169 cases)). The head and neck are the most often affected areas (74.6%). About 44% of the tumors displayed sweat gland differentiation, 44% hair follicle differentiation, and 12% of the tumors were sebaceous gland tumors. tumors with follicular differentiation were predominant among adnexal carcinomas (58%). Pilomatricoma (16.6%) was the most prevalent tumor of all ATs, followed by chondroid syringoma (13%). Sebaceous Carcinoma (5.6%) was the most common malignant adnexal tumor. The detailed clinicopathological data are shown in the Table.

All of our patients have benefited from a surgical procedure for the treatment of cutaneous adnexal carcinomas. Only 4 patients have been recommended for adjuvant radiotherapy. Following up with our patients allowed us to identify a recurrence in one case in the form of lymph node metastasis and a parotid metastasis in another.

Conclusion: Our findings generally concur with those found in the literature, With the exception of the frequency of carcinomas with follicular origin rather than those with sweat gland origin in other series.

KEY WORDS: Benign, malignant, histopathology, Cutaneous adnexal tumors

		mean age	Sex ratio (M/F)	Localisation
Sweat gland differentiation (44%)	Benign tumors:	46 years		
	Chondroid Syringoma (13%)	34 years	1.75	Head and neck (95%)
	Hidrocystoma (8.9%)	42 years	1.5	Head and neck (73%)
	Syringocystadenoma papillifère (4.1%)	43 years	0.4	Head and neck (100%)
	Hidradénome nodulaire (4%)	51 years	4 women	Extremities (75%)
	Syringoma (3.6%)	47 years	0.5	Head and neck (83%)
	Poroma (2.4%)	52 years	0.33	Head and neck (50%) Extremities (50%)
	Cylindroma (1.8%)	46 years	3 women	Head and neck (100%)
	Hidradenoma Papilliferum (1.8%)	43 years	3 women	Genital tract (100%)
	Hidradenoma (1.8%)	57 years	1.5	Genital tract (67%)
	Spiradenoma (1.2%)	33 years	1	Head and neck (100%)
	Syringofibroadenoma (0.6%)	65 years	1 woman	Extremities
	Malignant tumors :			
	Porocarcinoma (1.2%)	66 years	1	Head and neck (50%) Extremities (50%)
Micrcystic adnexal carcinoma (0.6%)	69 years	1 man	Head and neck	

	Syringoid eccrine carcinoma (0.6%)	65 years	1 woman	Head and neck
Hair follicle differentiation (44%)	Benign tumors:			
	Pilomatricoma (16.6%)	24 years	0.64	Extremities (72%)
	Trichoblastoma (11.8%)	60 years	0.81	Head and neck (90%)
	Trichilemmoma (1.8%)	41 years	2	Head and neck (67%)
	Trichofolliculoma (1.2%)	49 years	1	Head and neck (100%)
	follicular poroma (0.6%)	21 years	1 man	Head and neck
	Malignant tumors :			
	Proliferating trichilemmal tumor (5.3%)	54 years	0.12	Head and neck (89%)
	Trichilemmal carcinoma (3.6%)	48 years	0.5	Head and neck (67%)
Trichoblastic Carcinoma (1.8%)	61 years	1	Head and neck (100%)	
Pilomatrix carcinoma 0.6%)	75 years	1 woman	Head and neck	
Sebaceous gland differentiation (12%)	Benign tumors:			
	Sebaceous Hyperplasia (3.6%)	76 years	3	Head and neck (100%)
	Sebaceous Adenoma (2.4%)	53 years	1	Head and neck (100%)
	Malignant tumors :			
Sebaceous Carcinoma (5.9%)	67 years	0.66	Head and neck (90%)	
Total : 169 patients	Tumeur bénigne : 135 (79.9%)	46 years	0.77	Head and neck (66%)
	Tumeur maligne : 34 (20.1%)	63 years	0.54	Head and neck (85%)

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EXPRESSION OF CYTOKERATIN7, CD10 AND VIMENTIN IN CLEAR CELL RENAL CELL CARCINOMA: SERIES OF 33 CASES

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Introduction: Clear cell renal carcinoma accounts for 70% of all renal cell carcinomas and occurs sporadically in 95% of cases. Immunohistochemistry is still the most used technique for the diagnosis of epithelial renal tumors, although an increasing role of molecular biology is reported, which is sometimes obligatory for some renal epithelial tumor subtypes.

Materials and Methods : In our work, we have aimed to assess any possible correlation between the expression of three immunohistochemical markers : cytokeratin 7 (Ck7), Cluster of differentiation (CD) 10, and vimentin and the different ISUP nuclear grades in clear cell renal cell carcinoma cases. A total of 33 clear cell renal cell carcinoma cases with different ISUP nuclear grades, were analyzed using three IHC markers (Ck7, CD10, and vimentin)

Our results seem to confirm existing data in the literature, namely the fact that although CK7 tends to be negative in clear cell renal cell carcinoma, its positivity is often observed in low-grade cases, and that CD10 and vimentin are inversely correlated with the expression of CK7.

Discussion and Conclusion : Renal epithelial tumors have required in recent years updates and a new classification system, which has become more challenging.

On the immunohistochemical level, no specific marker of clear cell renal cell carcinoma has been described. However, some markers are described as typical for cases of clear cell renal cell carcinoma. These include the carbonic anhydrase IX with a strong and diffuse complete membranous staining, CD10, and vimentin. CK7 is classically negative or only focally positive

According to the literature, no diffuse staining with anti-CK7 antibodies is observed in cases of clear cell renal cell carcinoma. However, different studies reported a wide range of CK7 positivity (0-38%) in these tumors.

CD10 is far from specific, it can help differentiate between clear cell renal cell carcinoma, which shows a sawtooth pattern, and other renal carcinoma subtypes, especially the papillary renal cell carcinoma, which shows a compressed luminal appearance

In many studies, CD10 seems to be inversely correlated with the expression of CK7

Vimentin is classically reported to be more intense in staining high-grade areas. It may be used in the differential diagnosis against cases of chromophobe renal cell carcinoma, especially in the case of the eosinophilic variant of clear cell renal cell carcinoma. This latter shows positive staining with vimentin whereas the former is usually negative

Keywords: Clear cell renal cell carcinoma, ISUP nuclear grade, Cytokeratin 7, Vimentin, CD10

The authors have no conflicts of interest to declare.

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GRANULOMATOUS MYCOSIS FUNGOIDES: REPORT OF THREE CASES AND REVIEW OF THE LITERATURE

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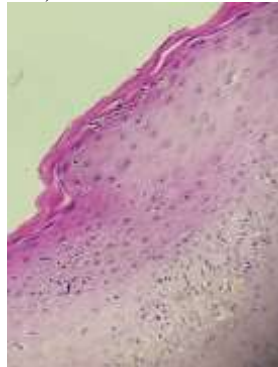
Introduction: Granulomatous mycosis fungoides (GMF) is a rare form of cutaneous T-cell lymphoma that is a major diagnostic challenge.

The objective of this work is to relate the clinical and pathological aspects of this condition and to discuss its differential diagnoses.

Case reports: The cases included 3 patients with GMF, admitted to the dermatology department of Ibn Sina Hospital in Rabat. The first one is a 35 year-old female patient, diabetic, admitted for the management of a slowly growing erythematous plaque formed on the abdomen, which rapidly ulcerated.

The second one is a 46 year-old female, with no medical history, presented with erythematous plaque of the neck, evolving for 3 weeks. The 3rd case corresponds to a 63-year-old male patient, treated since 2013 for Mycosis fungoides.

Résultats: The histological study showed the same findings in the 3 patients, including the exocytosis of atypical lymphocytes in the epidermis and the presence of authentic epithelioid granulomas in the underlying dermis. The immunohistochemical study showed a negative staining of the anti-CD5 antibody (1st case), the anti-CD7 antibody (2nd case) and the anti-CD2 antibody (3rd case). The anti-CD30 antibody was negative in all 3 cases.



Discussion: Granulomatous MF, originally described in 1970 [1, 2], is a rare histological form, constituting 6.3% of MF described in the literature. [3]

The clinical findings are nonspecific and the diagnosis is purely anatomic-pathological. [2]

Histologically, the signs of classical MF are present, namely atypical lymphocytes in the dermis with epidermotropism. The granulomas are sarcoid-like, mixed with Langhans giant cells.

Conclusion: To conclude, MFG is a rare histological form of cutaneous T-cell lymphoma that can histologically mimic infectious or inflammatory dermatosis and cause a delay in diagnosis.

Anatomic-clinical correlation, good morphological analysis and immunohistochemical study help guide the diagnosis.

Key words: Mycosis fungoides, T-cell lymphoma, granulomas.

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MOLECULAR PROFILE OF BREAST CANCER EXPERIENCE OF PATHOLOGY DEPARTMENT UNIVERSITY HOSPITAL OF MARRAKECH BETWEEN 2010 AND 2022

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Breast cancer is the most frequent malignancy among women in Morocco. In this study, we provide an approach on the molecular invasive breast carcinoma subtypes in the region of Marrakesh.

We analyzed 2040 breast invasive carcinoma cases diagnosed at the pathology department of the Mohamed VI University hospital, Marrakesh between January 2010 and June 2022. Molecular subtypes were determined and their associations with the clinico-pathological characteristics of the tumors and prognostic factors were examined.

The mean age at diagnosis was 50,1 years. Invasive ductal carcinoma was the predominant histological type (81,96%), followed by lobular invasive carcinoma (6,57%). Majority of our patients (89,85%) were diagnosed with tumors of more than 2 cm. Histological grade II tumors were the most frequent (69.46%), followed by advanced histological grade (22,7%). Lymph node positive tumors were observed in 61.55% of cases. Most tumors were hormone receptor positive (72,25%) and 22,65% were HER2 positive. Unlike most international molecular profiles Luminal B was the most common molecular subtype (36.39%) followed by Luminal A (18,95%), Triple Negative (12,38%) and HER2 (19,65%). Luminal B subtype had a poorer prognosis than Luminal A, Compared with Triple Negative subtype, HER2 subtype tend to spread more aggressively and are associated with poorer prognosis. Unlike Western countries, breast cancer occurs at an earlier age and is diagnosed at a more advanced stage in Marrakesh. In this region, hormone receptor-positive tumors are predominant and so the majority of breast cancer patients should benefit from hormone therapy. HER2 subtype presents an aggressive tendency, suggesting the importance of anti-HER2 therapy. This study will contribute in developing appropriate screening and cancer management strategies in Morocco.

Keywords : breast cancer, molecular profil, Her2, Ki67.

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PRE-ANALYTICAL PERFORMANCE IN SURGICAL PATHOLOGY: IMPROVEMENT OF THE FIXATION TECHNIQUE AT THE IBN ROCHD UNIVERSITY HOSPITAL OF CASABLANCA MOROCCO

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Background: Pathologists play a crucial role in the management of patients, especially in case of tumor diseases. In order to achieve these missions, adequate course of the pre-analytical phase with all its steps is critical. Fixation is a fundamental part of the pre-analytical process and it is used to protect tissue from decay, making the morphological analysis of tissue and cells possible.

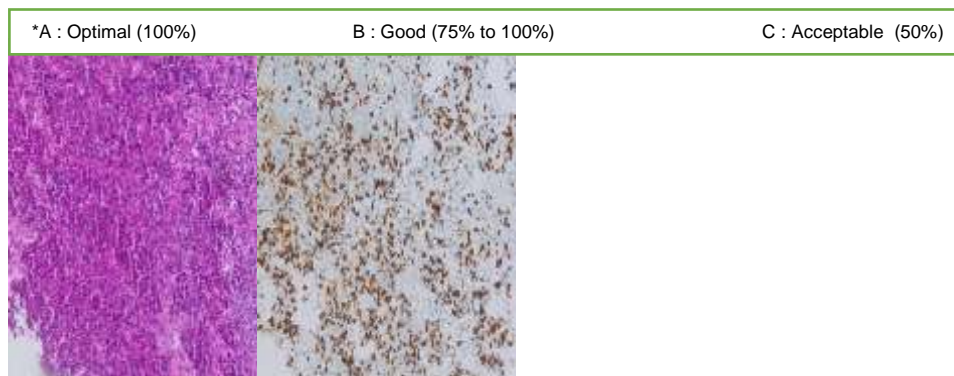
Objective: To improve the fixation process in a central Department of Pathology, serving 4 University hospitals, and to discuss the benefits and drawbacks of each protocol.

Methods: We carried out a prospective study in the Department of Pathology of the Ibn-Rochd University Hospital, Casablanca, Morocco. We evaluated the quality of fixation by buffered formalin compared to unbuffered formalin on surgical breast specimens collected from the Oncology-gynecology Department over a period of 3 months. We evaluated slides reading and current recommendations.

Results & Conclusions: A total of 145 specimens were examined and 5 pathologists participated in this study. Each case was analyzed by two pathologists. We summarized our results in the table 1, below.

Table.1 – Summary of the main findings

Specific process		Specific criteria	Fixers used	
			Unbuffered formalin	Buffered formalin (ph=7.1)
Quality of cuts		Adequate thickness	B	A
		Presence/absence of tears, creases, streaks, dye stains, delaminations	C	B
		Presence/absence of contamination	B	A
		Montage	B	A
Quality of routine staining	Nuclear components	Clear and blue/purple chromatin	B	A
		Well identified nucleolus	B	A
		Well defined nuclear membrane	B	A
	Cytoplasmic features	Well delimited cytoplasm	B	A
		Well defined cytoplasmic granules	B	A
		Well defined mucus	B	A
	Extracellular matrix components	Bright red hematies	B	A
Quality of fibers		B	A	



The **Breast HE X200** form **Breast Ki-67 X200** le and reproducible fixation, a better preservation tissue, a relatively short period of fixation and better morphological analysis.

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Keywords: Preanalytic, Quality, fixation process, buffered formalin

Conflicts of interest: None
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PROGNOSTIC IMPACT OF TUMOR BUDDING ON MOROCCAN GASTRIC CANCER PATIENTS

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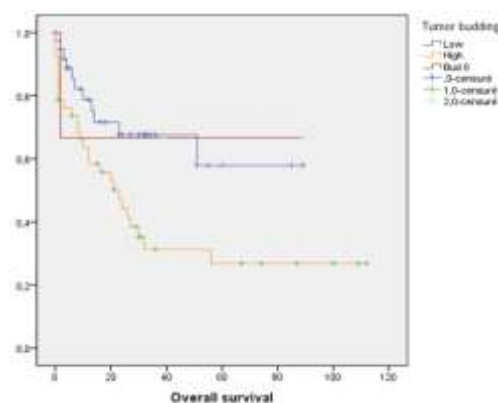
Background: Tumour budding (TB) has been defined as an independent prognostic factor in many carcinomas like colon adenocarcinoma, but its prognostic impact on gastric cancer patients remains not well established. In the present study, we aimed to highlight the correlation of tumor budding with clinico-pathological features and predict its survival outcomes in gastric cancer patients for the first time in the Moroccan population.

Methods. This study was conducted on 83 patients who underwent surgery for gastric adenocarcinoma from 2014 to 2020. The patient's clinico-pathological characteristics were obtained from the pathological and clinical records of each patient. Tumor budding was assessed on HES slides, according to the 2016 International Tumor Budding Consensus Conference criteria. The association of tumor budding grades with categorical and continuous variables were respectively assessed by the χ^2 -test and the unpaired t-test. Survival analysis was performed by the Kaplan-Meier method, the log-rank test.

Results. Patients consisted of 65.1% of men and 34.9% of women with a median age of 61,3 years. Histologically, the majority of the tumors were adenocarcinoma (65,1%). Among all cases, 3.6% (3/83) were classified as Bud 0, 14.5% as Bud1 (12/83), (27/83) 32.5% as Bud 2, and 49.4% (41/83) as Bud 3 grades. High-grade tumor budding (BUD 3) was found to be significantly associated with special clinicopathological features including older age (P=0.02), Unradical resection (R1/R2) (P=0.03), and the presence of vascular invasion (P=0.05), and perineural invasion (P=0.04). Furthermore, tumors with high-grade tumor budding were significantly associated with a low rate of resected lymph nodes (P=0.04) and advanced TNM stage (P=0.02). Among all stages, high-grade tumor budding was correlated with shorter overall survival in univariate and multivariate analysis (P=0.04). Patients with high- tumor budding had worse relapse-free survival compared with patients with low- tumor budding grade and those without tumor budding (P=0.01).

Conclusion. According to our study, the high-tumor budding grade was correlated with unfavorable clinicopathological features and poorer survival. The present study findings suggest that Tumor Budding should be considered in the treatment and prognosis of gastric cancer patients.

Figure 1 : Kaplan–Meier curves demonstrating associations between tumour budding and overall survival (P=0.03).



Keywords: Gastric cancer. Tumor budding. Survival.

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RET REARRANGEMENT IN PAPILLARY THYROID CARCINOMA

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Introduction: Papillary thyroid carcinoma accounts for 80% of all cases. The only documented risk factor for PTC is exposure to ionizing radiation. The prognosis is generally excellent. During the last 2 decades numerous studies on genetic alterations have demonstrated the pathogenic role of RET (rearranged during transfection) proto-oncogene rearrangements in PTC.

Our work aims to investigate RET rearrangements in a series of papillary thyroid carcinoma.

Materials and methods: This is a series of randomly selected cases of histological papillary thyroid carcinoma diagnosed at the laboratory of anatomy and cytological pathology of the CHU Ibn Rochd of Casablanca. To evaluate RET rearrangements, we performed FISH analysis on formalin-fixed and paraffin-embedded tissues using a RET gene break apart probe reagent.

Results : A total of 12 cases of papillary carcinoma were collected. The average age of our patients was 48.8 years and all were female. The tumor size was variable with extremes between 15mm and 55mm long axis, and multifocal in 5 cases (41.7%).

Among the histological subtypes, the vesicular and classical variants were the most frequent. Indeed, 4 cases (33.3%) of the vesicular variant and 4 cases (33.3%) of the classical variant were found, followed by the high cell variant in 2 cases (17%). Finally, the oncocyctic variant was present in 1 case (8.7%) and the combination of vesicular and oncocyctic variants also in 1 case (8.7%). Vascular emboli were present in 83.3% (10 cases) and extra-thyroidal extension in 5 cases. RET rearrangement was observed in 2 cases (16.7%) whose epidemiological and histological characteristics are described in the table.

	Case 1	Case 2
Age (years)	47	49
Sex	F	F
Tumor size	15 mm	42mm
Uni/Multifocal	Unifocal	Unifocal
Histological types	Classic	Oncocyctic
Vascular invasion	-	+
Capsular invasion	+	+
Extra thyroid extension	-	-
TNM	pT1b	pT3a

Conclusion: The search for molecular alterations in iodine-refractory thyroid carcinoma is desirable especially in view of the availability of systemic treatments and targeted therapies with promising results.

Keywords : papillary thyroid carcinoma, RET rearrangement, targeted therapy.

Conflict of interest statement : None

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TdT POSITIVE IN BLASTIC DERMAL INFILTRATE: THINK OF BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM

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Background: Terminal deoxynucleotidyl transferase (TdT) is a DNA polymerase expressed in lymphoblastic lymphomas/leukemias but also in other undifferentiated tumors. An expression of Tdt in a blastic dermal infiltrate may constitute a diagnostic pitfall.

Methods: We present here a case diagnosed in our institution illustrating this diagnostic difficulty.

Results : We report the case of an 81-year-old man, with no particular medical history, who had consulted for a purplish nodular dorsal mass accompanied by several diffuse infiltrated papular lesions that had evolved over several months.

The biopsy showed a diffuse tumor infiltrate in the dermis, made of medium-sized cells with reduced cytoplasm and dense chromatin and separated from the epidermis by a grenz zone (Figure 1).

The initial immunohistochemical study showed absence of CD3, CD8 and CD20 expression and expression of CD4, CD56 and TDT (Figure 2). Other lymphoid markers were requested to rule out lymphoma/lymphoblastic leukemia (PAX5, CD79a, CD5) as well as myeloid markers to rule out myelomonocytic leukemia (MPO, CD34, CD68, CD15), cytotoxic markers to rule out NK lymphoma (granzyme B and TIA1) and epithelial and neuroendocrine markers to rule out Merkel carcinoma. These markers were all negative, pointing to a blastic plasmacytoid dendritic cell neoplasm.

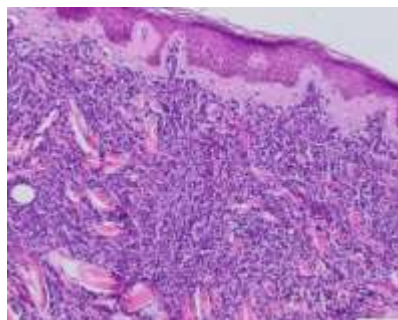


Figure 1: HEx20

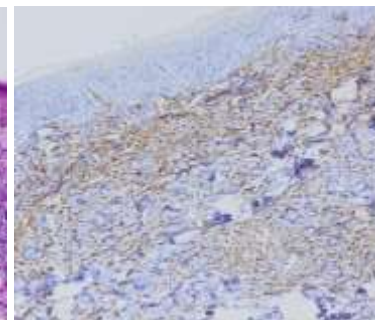


Figure 2: Tdt

Conclusion: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy with usually poor outcomes and high risk of progression to acute leukemia. Histological diagnosis is challenging and immunohistochemical analysis is mandatory. This entity represents a diagnostic challenge for pathologists given its rarity and possible TdT expression.

Keywords: Terminal deoxynucleotidyl transferase, blastic dermal infiltrate.

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THE CLINICOPATHOLOGICAL FEATURES AND PROGNOSTIC IMPACT OF HER2-LOW BREAST TUMORS SUBTYPE. NEW OPPORTUNITY FOR UNTREATED PATIENTS.

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Introduction: The emergence of a new tumor entity called HER2-low breast cancer leads us to reconsider therapeutic indications in patients whose tumors were considered as HER2-negative. HER2-Low subtype was defined as HER2 1+ and HER2 2+ FISH not amplified. The development of antibody-drug conjugates (ADCs) allows using HER2 as a vector of a cytotoxic drug with significant clinical efficacy and less side effects in breast cancer with HER2 low expression. Herein, we aimed to evaluate the differences in clinicopathological characteristics and prognostic factors between HER2-Low breast carcinoma and those with HER2-negative cancer, according to HR profile.

Methods: We conducted a 10-years bicentric cohort study on 1955 invasive breast tumors of Moroccan patients, collected at two Moroccan centers between 2012 and 2022.

Results: Out of 1955 BC patients, 49,3% were classified as HER2-Low; of which 80,7% were hormone receptors positive. The clinicopathological features indicate that HER2-Low subtype behave much more like HER2-positive than HER2-negative tumors. The survival analysis showed that the HER2-Low subtype-belonging patients present significantly the poorest prognosis in disease free survival ($p=0,003$). Hormonal dependent tumors show a significant difference according to HER2 subtypes in DFS ($p<0,001$). Moreover, patients with HR+/HER2-Low tumors subgroup present a significantly good prognosis in OS compared to the ones with hormonal negative tumors ($p =0,008$).

Discussion: The introduction of the concept of HER2-low BC has extended the benefit observed with novel anti-HER2 agents to a much larger number of patients with BC from 15% to 70%. Several studies reported incidences of 31% to 59,7%, based on data from The Cancer Genome Atlas and clinical trial dataset. HER2-low tumors were frequently found within HR-positive BCs compared to HR-negative cancers. These findings are strongly similar to our results. Early and metastatic BCs characterized by a larger tumor size, more LN metastasis and slightly higher grade in her2-low BC compared to her2 negative, which is similar to our study. According to PAM50 intrinsic classifier, there was a significant difference between her2-low and her2 zero in HR negative group while there is no difference in HR positive group, in particular, HER2 enriched represented 13.7% in HR-/HER2 Low vs 1.6% IN HER2-ZERO. This intrinsic heterogeneity of HER2-Low group, reflected already on clinical outcome, highlights the importance of considering HR status in the HER2-low BCs.

Conclusion: HER2-low breast cancer is now distinct subgroup of BCs of which is necessary to consider the HR status. To select HER2-low patients, pathologist must adhere to guidelines and maintain accurate performance and consistent interpretation of test results. Finally, Future prospective analysis and deeper understanding of HER2-low breast cancer requires to allow personalized treatment and avoid under or over treatment.

Key words: HER2 low, breast cancer, hormone receptors, survival.

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THE HISTOPROGNOSTIC VALUE OF TERTIARY LYMPHOID STRUCTURES IN ENDOMETRIAL CANCER

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Introduction: In postmenopausal women, endometrial adenocarcinoma is the most prevalent malignant uterine tumor [4]. Endometrial adenocarcinomas are currently classified into four subtypes, listed from best to worst prognosis: ultramutant POLE, hypermutant with microsatellite instability, low copy number, and high copy number. This classification has recently been incorporated into the ESGO guidelines [5][3] to stratify prognostic groups and guide further treatment. Tertiary lymphoid structures, also known as ectopic lymphoid structures, have emerged as a new prognostic factor.

Materiel et methods: A retrospective descriptive study was conducted over a one-year period, from January , 2022 to December, 2022, on 27 cases of endometrial cancer that had been histologically confirmed and were being treated at the Hassan II University Hospital in Fez. We reviewed the 27 cases to determine the presence of secondary lymphoid structures, and we will go over the key clinical and histoprognostic data in relation to secondary lymphoid structures.

Results: There were 26 women with endometrial cancer, with an average age of 56.9 years and ages ranging from 37 to 76.

Endometrial tumors were classified into four histological subtypes: 57.69% of endometrioid adenocarcinomas, 11.53% of serous adenocarcinomas and 11.53% of poorly differentiated carcinomas According to the FIGO classification, nearly 73.03% of endometrial cancer cases were diagnosed at an early stage [I,II], while 26.92% were diagnosed at a late stage [III, IV].

In 30.76% , we found tertiary lymphoid structures at the tumor invasion front and in the myometrium. Vascular emboli were found in 65.38% of the cases .

These results could be used to establish correlations between tertiary lymphoid structures, vascular emboli, TILS, histological type . The histological subtype most frequently connected to tertiary lymphoid tissues was endometrioid adenocarcinoma grade II (26.66%). Tertiary lymphoid structures were detected in early stages (I, II) in 40%, vascular emboli (EV3) in 62.5%, and the presence of TILS in 83.33% of cases.

Discussion: Tertiary lymphoid structures (TLS) are ectopic lymphoid structures that form in and around cancers. They are lymphoid cell aggregates organized in the form of follicles, with a zone of T cells and a zone of B cells [1]. TLSs have been found in a variety of solid tumors, including non-small cell lung cancer, head and neck squamous cell carcinoma, ovarian cancer, breast cancer, and hepatocellular carcinoma [2].

Conclusion: The prognostic value of tertiary lymphoid structures has only been partially explained. Extensive analyses will be required to comprehend and characterize these structures .

Keywords : Endometrial adenocarcinoma , Tertiary lymphoid structures , Prognostic Groups ,B CELLS.

Conflict of interest statement The authors declare that they have no conflicts of interest.

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THE PROGNOSIS AND PREDICTIVE VALUE OF ESTROGEN NEGATIVE/PROGESTERON POSITIVE (ER-/PR+) PHENOTYPE.

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Background: Breast cancer is a serious worldwide public health problem and is currently the most common cancer overall. Its endocrine therapy is related to the expression of the steroid hormones (ER/PR). Breast cancers can be presented under multiple profiles of steroid hormones. 2–8% of all breast cancers express only PR (ER-/PR+) which is an abnormal phenotype, with less known about their behaviors and outcomes.

Methods: We collected a large and well-characterized database of primary breast cancer from 2012 to 2019, including 1159 cases. These cases were divided according to ER and PR expression, we focused ER-/PR+/HER2+ and ER-/PR+/HER2- subgroups, to highlight their clinicopathologic features.

Results: 94 patients (8%) had ER-/PR+ profile, while 676 (58.4%) had ER+/PR+, 88 (7.6%) had ER+/PR-, and 164 (14.2%) had ER-/PR- profile. The ER-/PR+ group was statistically correlated with a high risk of recurrence and death in midway between the double negative and double-positive HR. According to HER2 status, a low DFS was observed in patients ER-/PR+/HER2-, which was closer to the DFS of TNBC cases but worse than ER+/PR any. On the other hand, the ER-/PR+/HER2+ showed also a poorer DFS closer to the HER2+ subgroup between TNBC and ER+/PR any. The clinicopathological features of the ER-/PR+/HER2- and ER-/PR+ HER2+ have distinguished the patients into two groups with a difference in some clinicopathological characteristics: both groups had closer OS estimation, which was worse than ER-/PR any and better than TNBC and HER2. On the other hand, the ER-/PR+/HER2+ seems to increase the risk of death more than ER-/PR+/HER2- in comparison with ER+/PR any.

Discussion: In our study, 8% of patients had presented the ER-/PR+ phenotype; this is consistent with the previously published cohort using ER and PR IHC. Our findings are similar to those already published such as younger age at diagnosis, poorly differentiated tumor and larger tumor size. On the other side, the separation into intrinsic subtypes by PAM50 test revealed that the vast majority of cases were of the basal subtype (53–65%), followed by the luminal A subtype (15–27%). It shares molecular features with TNBC. 90% of ER(-)/PR(+) tumors are characterized by low predicted endocrine sensitivity by the sensitivity to endocrine therapy (SET) gene signature, especially in “high-risk” cancers.

Conclusion: ER-/PR+ BCs really exist and it's different from others subgroups BCs, its clinical molecular feature and behaviors midway between those of double positive and double negative, moreover, these distinction seems more important in the subgroup HER2 negative which is slightly similar to TNBC. So the question is treat or not treat with ET single PR+ BC, the response to this requires prospective studies and clinical trials in order to optimize the breast cancer's treatment in the era of precision medicine.

Key words: breast cancer; immunohistochemistry, estrogen negative/progesteron positive phenotype, prognosis.

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WHAT PROGNOSTIC IMPACT OF NECROSIS IN COLIC ADENOCARCINOMA?

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Background: Colon cancer is a real public health problem.(1) Tumor necrosis has been proposed as an independent prognostic marker for colon cancer following a number of similar studies reporting necrosis as a marker of poor prognosis in renal, breast and lung carcinomas.(2,3) The mechanisms underlying the relationship between necrosis and cancer survival, however, are unclear(3).

The aim of this work is to analyze the prognostic value of tumor necrosis in colonic adenocarcinomas by comparing our results with those of the literature.

Methods: This is a retrospective study of 100 cases of colonic adenocarcinoma diagnosed in the pathological anatomy and cytology department of CHU Hassan II in FES. The diagnosis was made after histological study. Tumor sections were made and the presence of necrosis was split into 2 groups: more than 50% or less than 50%. Correlations have been made between the presence of necrosis and its extent and the various histoprognostic factors and patient survival.

Statistical analysis was performed using SPSS software and a correlation is considered significant if $p < 0.05$.

Overall survival was assessed using the Kaplan Meier method.

Results : 100 cases of colonic adenocarcinoma were included in our work. Average age: 57 (29 and 89). Gender: MIF: 1117. Most common location: right colon. The most common histological type: moderately differentiated adenocarcinoma. The follow-up of our patients: 43 months and 5 months (average: 47 months). The extent of tumor necrosis: less than 50% (73%) and more than 50% (27%). 56% of patients with >50% necrosis also had vascular emboli.

Discussion: Previously, tumor necrosis has shown prognostic value in a variety of solid organ tumors including renal, breast, lung, pancreatic, and colorectal.(3,4) It appears from these and similar studies that necrosis is not an isolated pathological feature but is strongly related to other aggressive features, including tumor size, grade, and pathological stage.(3,5)

In our series, the presence of necrosis was associated with an advanced stage, weak differentiation and vascular invasion. The lack of a significant relationship between necrosis and survival may be explained by the limited numbers of patients in our sample.

Conclusion: Our results show that tumor necrosis has a negative impact on patient prognosis and survival and should be included as a histoprognostic factor in pathology reports.

Keywords: necrosis, carcinoma, colon.

Competing interests: we declare no conflict of interest

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