

Dermatopathological Correlation of Clinically Challenging Cutaneous Lesions: a Single Center Experience of 2184 Cases

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ABSTRACT **Introduction:** Although a trained eye can easily identify typical skin lesions, histopathological examination and clinicopathological correlation are critical in challenging cases.

Objectives: The primary objective is to organize the final diagnoses reached following clinicopathological consensus in clinically challenging cutaneous lesions, identifying the most common diagnostic scenarios encountered by dermatopathologists and discussing their diverse differentials submitted by clinicians. The secondary objective is to investigate how the case profile and clinician decision-making processes evolved during the COVID-19 pandemic.

Methods: Skin and mucosa samples collected by the dermatology department between 2016 and 2020 were classified based on pathology reports. For frequent diagnoses, preliminary diagnoses stated by clinicians on pathology requisition forms were reviewed. The years preceding and following the first nationally reported COVID-19 case were compared to investigate the pandemic's impact on the distribution of dermatology and dermatopathology cases.

Results: One thousand nine hundred and eighty-nine reports were classified into 4 major categories: inflammatory (49.8%), neoplastic (30.1%), other diseases (7.1%), and non-diagnostic (12.8%). We further classified inflammatory diseases based on major tissue reaction patterns and neoplasms based on cell origin. We analyzed the leading diagnoses in each category, discussed their differential

diagnoses, and provided clinicians with clues to reduce errors in practice. Following the pandemic, the overall number of pathology reports and patient admissions dropped dramatically, with significant changes in case profiles.

Conclusions: We presented and discussed the frequently encountered confounding cases to sketch the diagnostic landscape. In the authors' experience, clinicopathological correlation can increase the rate of reaching the diagnosis by up to 75.3%.

Introduction

A trained eye is essential in the identification of skin diseases, yet even common dermatoses can manifest with perplexing lesions [1]. Moreover, a newly formed or regressed rash may not exhibit the classic morphological features [2]. Patients may further complicate the problem by scratching and irritating their lesions, or by self-treating with exogenous and endogenous substances [2]. A skin biopsy is one of the most effective methods for reaching a diagnosis in challenging cases [3].

Histopathological examination, on the other hand, has a different set of limitations to consider. Inadequate sampling, biopsy of an inappropriate location or performing the biopsy at an early or late stage, can result in limited findings [4]. Even with an adequate sample, histopathological examination alone may be insufficient to make a definitive diagnosis and may occasionally reveal findings that contradict clinical information [4]. Another major issue is the clinician's failure to provide sufficient information about the patient or a breakdown in communication between the two departments [5]. A successful final diagnosis is better achieved by linking the clues through clinicopathological correlation [6].

A biopsy requisition form is filled out to transfer the clinical information needed by the pathologist to correctly interpret the histopathological examination [7]. A properly completed form will improve communication between the clinician and the pathologist, allowing for a more accurate diagnosis [6]. Retrospective studies on the consistency of clinical information and pathology results report complete concordance in only 28.3%-68.0 % of cases [3,8-11]. Although these studies emphasize the importance of clinicopathological correlation, they do not provide guidance about the diagnostic dilemmas frequently encountered by dermatologists and dermatopathologists in real-life scenarios.

In this study, we classified the frequently encountered challenging cases and their diagnoses after clinicopathological correlation. All cases were evaluated and concluded on a case-by-case basis in weekly meetings with a dermatologist and a dermatopathologist. We also used clinical information from pathology requisition forms to determine the most frequently considered alternative diagnoses by clinicians prior to biopsy. Finally, we investigated how the COVID-19

pandemic affected dermatology and dermatopathology practice and case distribution.

Objectives

- Organizing the final diagnoses reached after clinicopathological consensus in clinically challenging dermatology cases.
- Identifying and discussing the alternative diagnoses that are more likely to be considered by clinicians prior to biopsy, and providing clues for dermatologists to reduce error in practice.
- Investigating the effects of the pandemic on the case profile of dermatology and dermatopathology departments following the first nationally reported COVID-19 case.

Methods

This research was conducted in a referral hospital, serving around half a million people annually. We classified the pathology reports of skin and mucosa samples collected by the dermatology department between 2016 and 2020. All reports indicating a definitive diagnosis were classified under inflammatory, neoplastic, or other diseases. Reports that lacked a diagnosis or a useful clue were categorized as non-diagnostic. Samples that were insufficient or obtained for direct immunofluorescence investigations were excluded.

We further classified inflammatory diseases into six categories based on major tissue reaction patterns, and neoplastic diseases into three categories based on cell origin. The remaining reports diagnosed a wide range of diseases and they were classified as "Other". Reports demonstrating a specific inflammatory pattern without a definitive diagnosis were still considered useful to clinicians and classified under that specific pattern as non-diagnostic (eg, granulomatous pattern, non-diagnostic) (Figure 1).

The three most frequently reported diagnoses by pathologists in each category were compiled. In addition, for each diagnosis, we listed the three most common differential diagnoses submitted by clinicians prior to biopsy.

All comparisons examining the effects of the pandemic were made in the years preceding and following the first nationally reported COVID-19 case. We

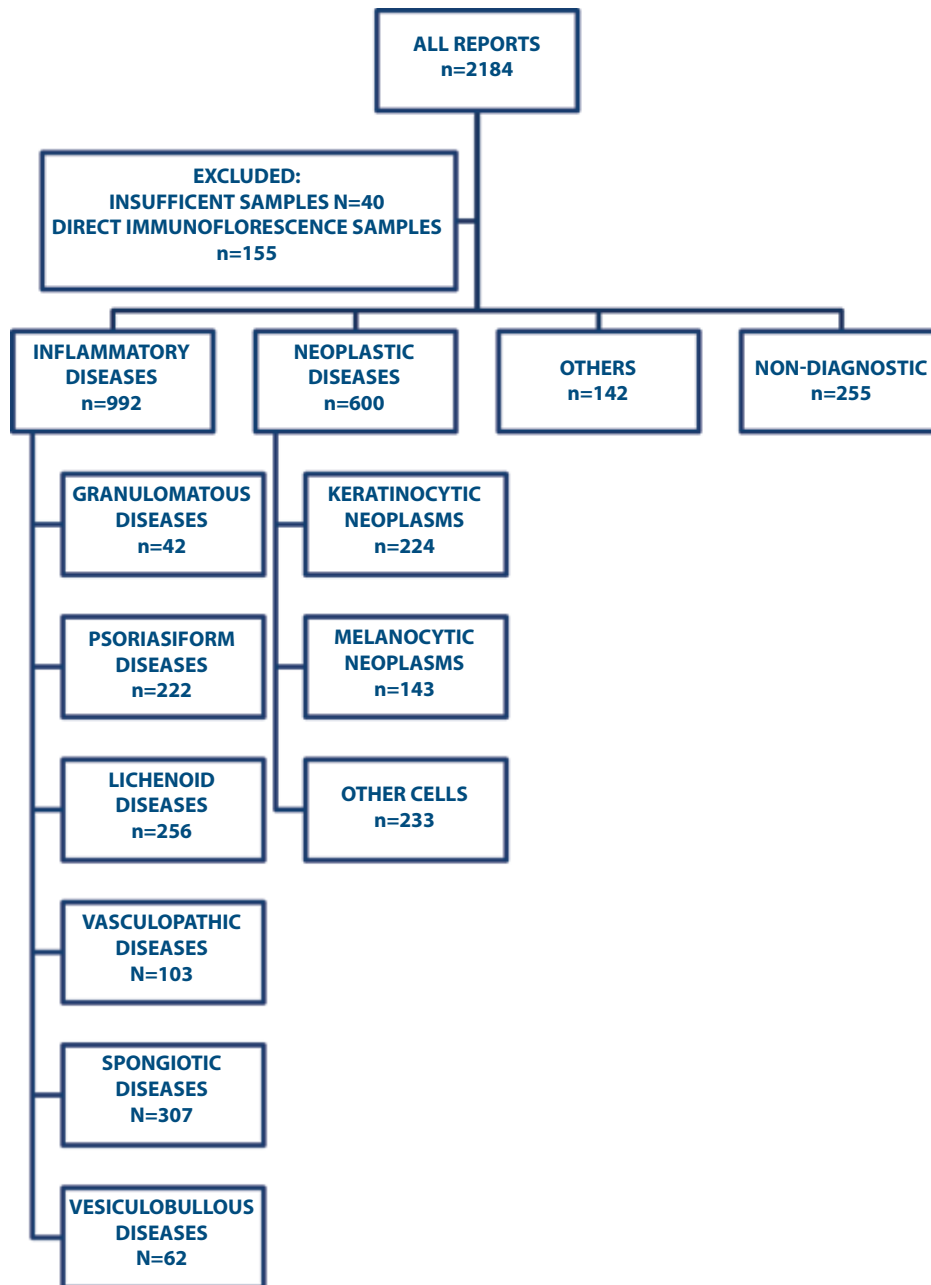


Figure 1. The categorization of pathology reports and the number of cases in each category.

compared the case profiles reached after clinicopathological consensus using the same classification method. We also compared how frequently we biopsied the patients

$\left(\frac{\text{Number of biopsies taken} \times 100}{\text{Total number of clinical examinations}} \right)$, and the percentage

of dermatology department samples sent in $\left(\frac{\text{Number of dermatology samples} \times 100}{\text{Total samples received by pathology}} \right)$. Next, as an

indicator of case diversity, we compared the number of different definitive diagnoses made. Finally, in order to determine the distribution of cases presented in the dermatology outpatient department, we classified the registered ICD-10 codes.

SPSS v.26 was used for statistical analysis. The Chi-square test for proportions or the Fishers' exact test was used,

when appropriate. Statistical significance was determined by p values less than 0.05.

Results

In the majority of categories, pathological diagnosis matched the most frequently submitted differential diagnosis by clinicians. The second and third differentials were the most difficult to distinguish clinically. As a result, they were more frequently proposed as alternate diagnoses to pathologists.

Inflammatory diseases accounted for 49.8 % of all reports (Table 1 and Table 2). Looking at the subcategories, we discovered that granulomatous diseases accounted for 2.1% of all cases, psoriasiform diseases 11.1%, lichenoid diseases

Table 1. Granulomatous, psoriasiform, and lichenoid diseases. The pathologist's diagnosis and the three most frequently submitted clinical differential diagnoses prior to biopsy

Number of Cases	Pathologist's Diagnosis	Clinician's Differential Diagnoses
Granulomatous Diseases		
15	1- Granulomatous pattern, non-diagnostic	1- Sarcoidosis 2- Kaposi's sarcoma 3- Mycobacterial infection (tuberculosis, leprosy, etc.)
13	2- Granuloma annulare	1- Granuloma annulare 2- Erythema annulare centrifugum 3- Sarcoidosis
7	3- Sarcoidosis	1- Sarcoidosis 2- Cutaneous lymphoma 3- Pseudolymphoma
Psoriasiform Diseases		
92	1- Psoriasis vulgaris and subtypes	1- Psoriasis vulgaris and other subtypes 2- Lichen planus and variants 3- Contact dermatitis
40	2- Psoriasiform pattern, non-diagnostic	1- Psoriasis vulgaris and other subtypes 2- Contact dermatitis 3- Pityriasis rubra pilaris
30	3- Parapsoriasis	1- Parapsoriasis 2- Mycosis fungoides 3- Nummular dermatitis
Lichenoid Diseases		
71	1- Lichen planus	1- Lichen planus and variants 2- Contact dermatitis 3- Lichenoid drug eruption
47	2- Lichenoid pattern, non-diagnostic	1- Lichen planus 2- Contact dermatitis 3- Drug eruption
21	3- Pigmented purpuric dermatosis	1- Pigmented purpuric dermatosis 2- Mycosis fungoides 3- Contact dermatitis

Table 2. Vasculopathic, spongiotic, and vesiculobullous diseases. The pathologist's diagnosis and the three most frequently submitted clinical differential diagnoses prior to biopsy

Number of Cases	Pathologist's Diagnosis	Clinician's Differential Diagnoses
Vasculopathic Diseases		
47	1- Leukocytoclastic vasculitis	1- Cutaneous small-vessel vasculitis 2- IgA vasculitis 3- Pigmented purpuric dermatosis
23	2- Ulcers of various causes	1- Squamous cell carcinoma 2- Pyoderma gangrenosum 3- Perforating dermatoses
12	3- IgA vasculitis	1- IgA vasculitis 2- Leukocytoclastic vasculitis 3- Not available
Spongiotic Diseases		
102	1- Spongiotic pattern, non-diagnostic	1- Mycosis fungoides 2- Parapsoriasis 3- Psoriasis vulgaris and other subtypes

Table 2 continues

Number of Cases	Pathologist's Diagnosis	Clinician's Differential Diagnoses
101	2- Contact dermatitis	1- Contact dermatitis 2- Psoriasis vulgaris and other subtypes 3- Mycosis fungoides
17	3-Pityriasis rosea	1- Pityriasis rosea 2- Psoriasis vulgaris and other subtypes 3- Erythema annulare centrifugum
Vesiculobullous Diseases		
23	1-Bullous pemphigoid	1- Bullous pemphigoid 2- Pemphigus vulgaris 3- Dermatitis herpetiformis
11	2-Vesiculobullous pattern, non-diagnostic	1- Bullous pemphigoid 2- Pemphigus vulgaris 3- Allergic contact dermatitis
9	3-Pemphigus vulgaris	1- Pemphigus vulgaris 2- Bullous pemphigoid 3- Pemphigus foliaceus

12.8%, vasculopathic diseases 5.1%, spongiotic diseases 15.4%, and vesiculobullous diseases 3.1%.

Reports describing clues that point to a specific inflammatory pattern but do not provide a definitive diagnosis were among the top three in each category. This category was only replaced by ulcers of various causes in the vasculopathic reaction pattern. The ratio of these reports was found to be 0.7% for granulomatous diseases, 2% for psoriasiform diseases, 2.3% for lichenoid diseases, 1.1% for vasculopathic diseases, 5.1% for spongiotic diseases, and 0.5 % for vesiculobullous diseases.

In 30.1% of all reports, a definitive diagnosis of neoplasia was made. Keratinocytic neoplasms accounted for 11.2%, melanocytic neoplasms 7.1%, and other cell-derived neoplasms 11.7% of all reports. Basal cell carcinoma, squamous cell carcinoma, malignant melanoma, and mycosis fungoides were the most common malignant neoplasms reported (Table 3).

Other diseases accounted for 7.1% of total reports after excluding inflammatory and neoplastic diseases. Clinicians needed assistance distinguishing morphea from extragenital lichen sclerosus and mycosis fungoides, verrucas from verrucous carcinoma and squamous cell carcinoma, and dermatophytes from erythema annulare centrifugum and psoriasis in this category (Table 4).

In total, 12.8% of all reports were unhelpful in terms of providing any diagnostic findings. The percentage of reports that provided a single definitive diagnosis was 75.3%. Finally, 11.9% of reports contained diagnostic hints but did not provide a definitive diagnosis.

Following a year of pandemic, the number of reports in each category dropped dramatically. The percentage of cases with spongiotic patterns has decreased, while the percentage of cases with keratinocytic and melanocytic neoplasms has increased (Table 5).

The number of biopsies taken per 100 dermatological examinations was reduced from 2.7 to 2.1. Furthermore, the percentage of skin and mucosa samples received by pathology was reduced from 6.9 percent to 2.7 percent. The case diversity was also reduced from 113 to 60 distinct definitive diagnoses.

Following the first nationally documented COVID-19 case, the number of admissions to the dermatology outpatient department decreased from 16,511 to 5,550 annually. For these admissions, the examining dermatologists registered a total of 21,820 and 6,953 ICD-10 codes, respectively. The total number of diagnoses has decreased in every category except vesiculobullous diseases, where the admission count was the same (81 per year). The incidence of eczematous (including contact, atopic, seborrheic, and nummular dermatitis, among others), infectious (viral, bacterial, fungal, and parasitic), and vesiculobullous diseases (pemphigus and pemphigoid diseases), as well as urticaria & angioedema, and drug-related eruptions, increased significantly. Adnexal diseases (acne, rosacea, hidradenitis suppurativa, hyperhidrosis), papulosquamous diseases (psoriasis, pityriasis rubra pilaris, pityriasis rosea), pigmentation disorders (vitiligo, melasma, post-inflammatory hyperpigmentation among others), and benign neoplasms (seborrheic keratosis, melanocytic nevi, various cyts, etc) all had a significant decrease in incidence (Figure 2).

Conclusions

The majority of diagnostic traffic between dermatology and pathology is driven by inflammatory (49.8%) and neoplastic (30.1%) diseases. The remaining diseases accounted for 7.1% of all reports and covered a broad diagnostic range that could not be classified in either of these two major

Table 3. Neoplasms of keratinocytic, melanocytic, and other cell origins. The pathologist's diagnosis and the three most frequently submitted clinical differential diagnoses prior to biopsy

Number of Cases	Pathologist's Diagnosis	Clinician's Differential Diagnoses
Keratinocytic Neoplasm		
78	1-Basal cell carcinoma	1- Basal cell carcinoma 2- Squamous cell carcinoma 3- Bowen's disease
57	2-Squamous cell carcinoma	1- Squamous cell carcinoma 2- Basal cell carcinoma 3- Actinic keratosis
38	3-Actinic keratosis	1- Actinic keratosis 2- Squamous cell carcinoma 3- Basal cell carcinoma
Melanocytic Neoplasm		
117	1-Melanocytic nevus	1- Melanocytic nevus 2- Atypical melanocytic nevus 3- Malignant melanoma
8	2-Dysplastic nevus	1- Atypical melanocytic nevus 2- Malignant melanoma 3- Melanocytic nevus
5	3-Malignant melanoma	1- Malignant melanoma 2- Atypical melanocytic nevus 3- Squamous cell carcinoma
Neoplasms Caused by Other Cells		
68	1-Acrochordon	1- Acrochordon 2- Melanocytic nevus 3- Not available
31	2- Various cysts	1- Epidermoid cyst 2- Trichilemmal cyst 3- Syringoma
23	3-Mycosis fungoides	1- Mycosis fungoides 2- Parapsoriasis 3- Contact dermatitis

Table 4. The other diseases, excluding inflammatory and neoplastic. The pathologist's diagnosis and the three most frequently submitted clinical differential diagnoses prior to biopsy

Number of Cases	Pathologist's Diagnosis	Clinician's Differential Diagnoses
34	1- Morphea	1- Morphea 2- Lichen sclerosus (extragenital) 3- Mycosis fungoides
25	2- Verruca vulgaris	1- Verruca vulgaris 2- Verrucous carcinoma 3- Squamous cell carcinoma
19	3- Dermatophytosis	1- Tinea incognito 2- Erythema annulare centrifugum 3- Psoriasis vulgaris and other subtypes

categories. In total, 75.3% of cases had a definitive diagnosis after clinicopathological correlation, while 11.9% of cases only had diagnostic clues. Finally, 12.8% of reports yielded no diagnostic information.

In granulomatous diseases, cutaneous sarcoidosis is a frequently investigated diagnosis by both clinicians and

pathologists, and it has a wide range of clinical manifestations, some more specific than others [12]. Although histopathological features are invaluable, it should be kept in mind that classical naked granulomas will not always be encountered [13,14]. Clinically suggestive findings include the disappearance of background erythema with diascopy,

Table 5. Classification of diagnoses reached after clinicopathological consensus in the years preceding (2019) and following (2020) the first nationally reported COVID-19 case

	2019, N (%)	2020, N (%)	Difference (%)	P (Two-tailed)
Inflammatory Diseases				
Granulomatous	12 (1.8%)	3 (2.1%)	0.3	0.737
Lichenoid	91 (14%)	23 (16.5%)	2.4	0.507
Psoriasiform	72 (11.1%)	11 (7.9%)	-3.2	0.291
Spongiotic	96 (14.8%)	9 (6.4%)	-8.3	0.008
Vasculopathic	42 (6.4%)	5 (3.5%)	-2.8	0.238
Vesiculobullous	35 (5.4%)	10 (7.1%)	1.7	0.421
Neoplastic Diseases				
Keratinocytic	68 (10.5%)	21 (15.1%)	4.5	0.139
Melanocytic	21 (3.2%)	12 (8.6%)	5.3	0.007
Other cells	90 (13.9%)	14 (10%)	-3.8	0.270
Other	38 (5.8%)	9 (6.4%)	0.6	0.843
Non-diagnostic	82 (12.6%)	22 (15.8%)	3.1	0.334
Total	647(100%)	139 (100%)		

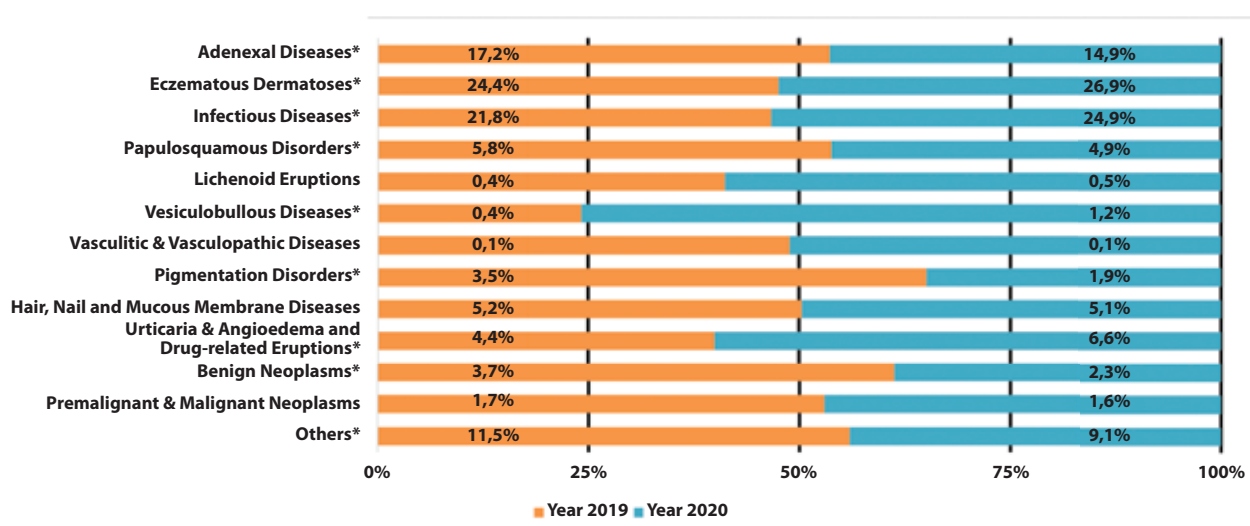


Figure 2. Cases admitted to the dermatology outpatient department in the year preceding (2019) and following (2020) the first nationally announced COVID-19 case.

* P (two-tailed) < 0.05.

revealing an apple-jelly color [15], and the appearance of orange-yellow structureless areas in a focal or diffuse pattern with dermatoscopy [16]. In dermatoscopy, vascular structures may appear as linear or branching vessels, rarely dotted or glomerular. Other less common dermatoscopic findings include dilated follicles, follicular plugs, yellow-white scales, milia-like cysts, white structureless areas and crystalline structures [16].

Lichen planus and its variants can have overlapping clinical presentations with diseases such as psoriasis, contact dermatitis, and lichenoid drug reactions. Clinical and histopathological findings may be insufficient to differentiate between lichenoid diseases and lichenoid reactions (caused by

drugs, metals, foodstuffs, or systemic diseases), particularly in the oral mucosa [17]. Although difficult, establishing a link between exposure and disease, as well as the resolution of lesions when the offending agent is removed, is strongly suggestive, but the regression period may take months [17]. The same holds true for lichenoid skin reactions [18]. Lichenoid skin reactions are characterized by larger, eczematous papules, sometimes with a psoriasiform morphology, and Wickham's striae may be absent [18]. Eczematizing lesions can become widespread, resulting in increased desquamation [18]. It can manifest as a symmetrical (often photo-distributed) eruption on the trunk and extremities, with a tendency to leave post-inflammatory hyperpigmentation [18]. Follicular involvement

and atrophy of the eccrine glands' dermal ducts may result in alopecia and anhidrosis [18].

Pigmented purpuric dermatosis is a capillaritis characterized by petechiae, purpura, and brown-red discoloration [19]. Mycosis fungoides is a T-cell cutaneous lymphoma with various clinical presentations [20]. Clinically, the skin manifestations of these two diseases can sometimes overlap [21]. According to some studies, pigmented purpuric dermatosis is a type of cutaneous lymphoma [22], and persistent cases may be a precursor to mycosis fungoides [23]. Mycosis fungoides should be suspected when there are generalized purpuric lesions that extend beyond the lower extremities and are accompanied by pruritus [24], as opposed to pigmented purpuric dermatosis, which is asymptomatic [25]. Additional studies, such as repeated biopsies, immunopathologic, cytogenetic, and gene rearrangement studies, should be performed in doubtful cases [24].

Histopathological and immunofluorescent studies remain the gold standard in the diagnosis of vasculitic [26] and autoimmune bullous diseases [27]. They are correlated with clinical history, physical examination, and other investigations to distinguish from similar diseases and confirm the diagnosis. There is significant overlap between small vessel vasculitides, making it difficult to distinguish these diseases from skin lesions alone [28]. The presence of gastrointestinal (nausea, vomiting, abdominal pain, melena), renal (nephrotic and nephritic syndrome), joint (arthritis, arthralgia) symptoms, and IgA accumulation in skin or kidney biopsies should raise the possibility of IgA vasculitis [28,29]. Although IgA vasculitis is most common between the ages of 3 and 15, it can occur at any age between 5 months and 89 years old [28,29]. IgA vasculitis in adults is typically limited to the skin [29]. However, all patients should be monitored for long-term systemic involvement [28,30].

To distinguish between autoimmune bullous diseases, histopathological, direct and indirect immunofluorescence methods are used in addition to clinical features [31]. Pemphigus vulgaris is distinguished by flaccid bullae and painful mucosal and skin erosions, as well as a positive Nikolsky sign [32]. Although the Nikolsky sign is also positive in pemphigus foliaceus, mucosal lesions are uncommon. Small flaccid bullae are occasionally encountered, but crusts and erosions are more common [31]. Bullous pemphigoid, on the other hand, is characterized by tense bullae that develop after extremely itchy erythematous urticarial patches and plaques that can last for weeks to months, with mucosal involvement ranging from 10% to 30% [31,32].

Finally, contact dermatitis is a great imitator, presenting with erythematous or purpuric patches, edematous plaques, vesicles, bullas, crusts, papules, scales, lichenification, and other lesions [33,34]. Despite its origins as a spongiotic disease, it is frequently used as a differential diagnosis in our

study for a variety of inflammatory diseases. The most crucial aspect of making a diagnosis is combining the history (particularly occupational) with the distribution of the lesions. Although patch testing is the gold standard in allergic contact dermatitis, potential allergens should be evaluated in terms of clinical significance. The diagnosis of irritant contact dermatitis is usually made by exclusion [35].

In neoplastic diseases, the biopsies were mostly performed to either differentiate between premalignant (actinic keratosis, Bowen's disease) and malignant (basal and squamous cell carcinoma, malignant melanoma, mycosis fungoides) lesions or to confirm the diagnosis and guide the treatment. Thus the diagnostic spectrum is straightforward. The relatively low number of dysplastic nevus and malignant melanoma cases could be explained by the fact that this study only used data from the dermatology department, and patients are referred to surgery in doubtful cases to ensure careful control of surgical margins. Excision of small lesions, typically less than 5mm in size, accounts for the high number of benign melanocytic nevi. The various neoplasms caused by other cells are mostly overshadowed by the abundance of benign proliferations (acrochordons and cysts) that are mostly submitted for legal concerns.

The remaining reports diagnosed a wide range of diseases, with the most common goal being to distinguish morphea from extra-genital lichen sclerosus, verruca vulgaris from verrucous or squamous cell carcinoma, and dermatophytosis from erythema annulare centrifugum or psoriasis.

Circumscribed morphea appears as an oval plaque on the trunk with an ivory sclerotic center and erythematous-violaceous borders [36]. It is associated with dyspigmentation (usually hyperpigmentation) and an increase in local temperature [36]. Extragenital involvement is seen in 6%-20% of lichen sclerosus patients [37]. The inner thighs [38] and submammary region [37,38] are frequently affected. Circumscribed plaques or clustered guttate lesions are distinguished by pale atrophic skin and follicular plugging [37]. It is worth remembering that these two diseases share a common pathogenetic basis and can coexist in the same patient [39].

Although the diagnosis of viral warts is usually straightforward, slowly growing large exophytic lesions with a papillomatous or verrucous surface and a tendency to compress deep tissues should be considered for verrucous carcinoma, a subtype of squamous cell carcinoma [40]. These lesions are more common in older men and can be found in the oral mucosa, anogenital region, or plantar region [40,41]. The presence of verruca vulgaris in a high number of pathology reports could also be explained by therapeutically excised samples being submitted for legal reasons.

Dermatophytosis infections can change clinically as a result of drug use, particularly topical corticosteroids, and can be confused with other papulosquamous diseases. Although

dermatophytoses can be diagnosed through direct examination and culture of skin samples, the low sensitivity [42] may have necessitated a second pathology opinion.

The importance of clinicopathological correlation has been highlighted in a number of studies in the literature. According to a study on inflammatory skin diseases, pathologists could only diagnose 55% of cases based on a histopathological examination alone, but when given clinical information, they could diagnose 78% of cases correctly [43]. Another study found that in 78% of cases, the correct diagnosis was already included in the clinician's pathology requisition form [44]. A 5-year study in Tanzania looked at the case distribution and found a similar diagnostic spectrum, with the exception of the relatively high number of Kaposi's sarcoma and leprosy cases [45]. In addition to these two diseases, a similar study in Ethiopia reported high rates of cutaneous tuberculosis and leishmaniasis [46].

The total number of pathology reports was reduced by 77.4% as a result of the shift in clinical decision making to balance patient care and prevent viral transmission. The biopsy rate for clinically benign presentations was reduced, and others were prioritized in order to rule out malignancy. Despite a decrease in the overall number of cases, the rate of pathology reports diagnosing keratinocytic and melanocytic neoplasms increased, while the rate of spongiotic diseases decreased. The frequency of reports involving neoplasms other than keratinocytic and melanocytic cells has also decreased.

Following the pandemic, the total number of patients applying to the dermatology outpatient department decreased by 33.6%, and several differences in case distribution were observed. There was an increase in eczematous diseases, which could be attributed to increased hand washing and disinfectant use. Because patients receiving immunosuppressive treatments required close monitoring during this time period, the number of patients admitted with autoimmune bullous diseases increased. An increase in patients who self-medicate without consulting a doctor may have led to an increase in admissions for urticaria, angioedema, and drug-related eruptions. Moreover, admission rates for infectious skin diseases (primarily bacterial and fungal) increased during this time period. Admissions for adnexal diseases (primarily acne and rosacea), papulosquamous diseases (psoriasis, pityriasis rubra pilaris, and pityriasis rosea), pigmentation disorders (vitiligo, melasma), and benign neoplasms (nevus, seborrheic keratosis, and various cysts) were significantly reduced.

Several studies examine the post-pandemic period from various perspectives and report similar findings. Admissions to dermatology outpatient departments [47–50], samples submitted to pathology [51] and cytology [52,53] laboratories, and elective surgical procedures performed [54,55] all decreased; however, the distribution of cases varied depending on the region where the study was conducted.

One significant limitation of this study is that the results are dependent on a variety of factors such as the study's time period and location, the practice habits of the participating physicians, and the available patient population. Another major limitation is the difficulty in classifying diseases both dermatologically and pathologically. To address this limitation, we took a broader approach, excluding variations and subtypes of the same diseases in order to represent cases across a broader spectrum.

The study's strengths include the fact that it was carried out with a large number of cases over a 4-year period in a dermatopathology referral center, and that when new findings are obtained, they are thoroughly discussed over weekly meetings to ensure strong clinicopathological correlation. The rate of non-diagnostic cases remained stable throughout the COVID-19 year, as clinicopathological correlation of cases was continued through online channels rather than weekly meetings.

A trained eye and open mind is essential in the diagnosis of skin diseases, but additional investigations may be required for some challenging cases. While histopathological techniques are extremely useful, it should be noted that they, too, have limitations and cannot always produce a definitive diagnosis alone. Maintaining clinicopathological correlation and continuous communication between dermatologist and pathologist, in our experience, can increase the likelihood of reaching a diagnosis by up to 75.3%.

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