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A 10-year review of outpatient skin biopsy results and skin cancer subtypes

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Abstract

The results of skin biopsies over a 10 year period were reviewed from the outpatient dermatology clinic at the Brody School of Medicine in Greenville, North Carolina. This research was conducted because there are very few studies that characterize this information over a long-term horizon. The biopsy rate per patient encounter, the clinical reason for the biopsy, the biopsy outcomes, the distribution of cutaneous malignancies per encounter, and the distribution of the subtypes of basal cell carcinoma, squamous cell carcinoma, and melanoma were analyzed. Biopsy logs from January 1, 2001 to December 31, 2010 were reviewed. Our investigation found that 20% of patient encounters resulted in a biopsy. Of these biopsies, 87.9% were performed to rule out malignancy and 12.1% were completed on patients suspected of having inflammatory skin conditions. The basal cell carcinomas diagnosed in Greenville, NC have more aggressive histologic subtypes compared to other studies, whereas the squamous cell carcinomas and melanomas were less aggressive.

Keywords: Skin, Cancer, Cutaneous, Biopsy, Results, Review

Introduction

Skin biopsies are routinely used in the outpatient dermatology setting as a means to diagnose benign tumors, malignant cancers, and inflammatory skin lesions. They are the link that allows dermatologists and dermatopathologists to collaborate in the treatment of patients. Although biopsies are a standard tool used for the diagnosis of skin lesions, little is known about the biopsy rate per patient or the biopsy results over an extended time period. This study reviews histopathology results of skin biopsies taken in the outpatient dermatology clinic from 2000 to 2010 at the Brody School of Medicine (BSOM) at East Carolina University. The purpose of this study is to evaluate the frequency of biopsies and subsequent results and to review the subtypes of skin cancers at the BSOM dermatology clinic over a ten year period.

Methods

The biopsy logs from January 1, 2001 to December 31, 2010 in the outpatient dermatology clinic at Brody School of Medicine were reviewed. The information was entered into a searchable excel data base. Specific identifying information about the patients' demographics was not available in the data set used in this study. Information from the biopsy logs was recorded was as

follows: Date of biopsy, Patient's medical record number, Pigmented lesion, Melanoma, Type of melanoma, Nevus (yes/no), If dysplastic degree of atypia (mild, moderate, severe, not recorded), Squamous cell carcinoma (yes/ no), Type of squamous cell carcinoma, Basal cell carcinoma, Is it a recurrent lesion (yes/ no), Subtype(s) of basal cell carcinoma, other skin cancer, was the biopsy done for an inflammatory condition.

We reviewed the pathology report in the chart when needed to verify if the subtype of skin cancer had been noted by the pathologist. The information was then tabulated for biopsies done during that 10 year period. We looked at the number of biopsies performed, the clinical indications for performing the biopsy, concern for a pigmented lesion, and the presence of basal cell carcinoma, squamous cell carcinoma, or melanoma. If multiple subtypes of basal cell were recorded, the most aggressive subtype was considered the primary subtype. The order used for aggressiveness from most to least aggressive was: morpheaform, infiltrating, micronodular, nodular, superficial multicentric, and other.

The number of patient encounters for each year was tabulated separately from the electronic medical record. These represent only visits made to the general dermatology clinic for evaluation by a dermatologist. The number of patient visits for the calendar year running from January 1 to December 31 was then matched with the year of the biopsy.

Results

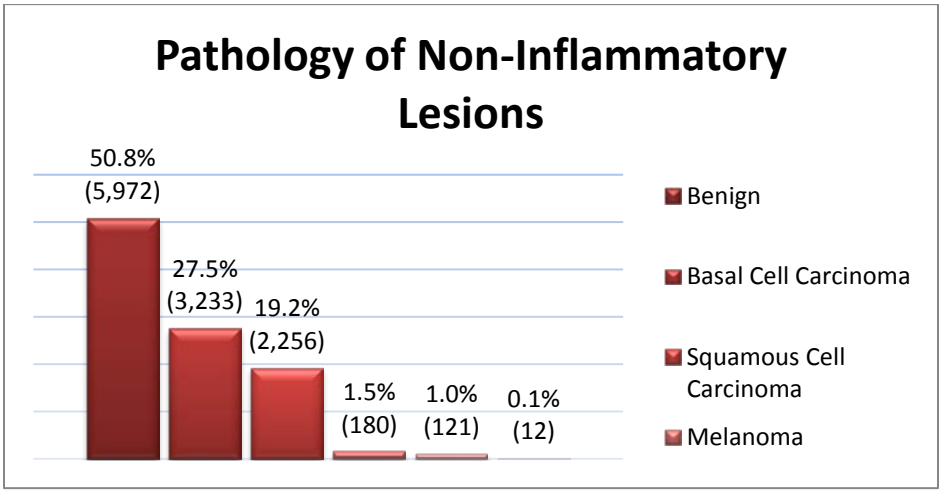

Figure 1. Biopsy results for non-inflammatory lesions from 2001 to 2010

There were 66,967 patient encounters at ECU from 2001 to 2010, and on average, 20% (13,399) of the patient encounters resulted in a skin biopsy. Of these biopsies, 87.9% (11,775) were performed to rule out malignancy and 12.1% (1,624) were completed on patients suspected of having inflammatory skin conditions. There were 11,775 biopsies on suspected keratinocyte proliferations or pigmented lesions to rule out or diagnose malignancy. Of these, 50.8% (5,972) were benign conditions, 27.5% (3,233) were diagnosed as basal cell carcinoma, 19.2% (2,256) were squamous cell carcinoma, 1.5% (180) were melanoma, 1.0% (121) were other cutaneous malignancies, and 0.1% (12) had both a basal and squamous cell carcinoma present in the same specimen (see Figure 1).

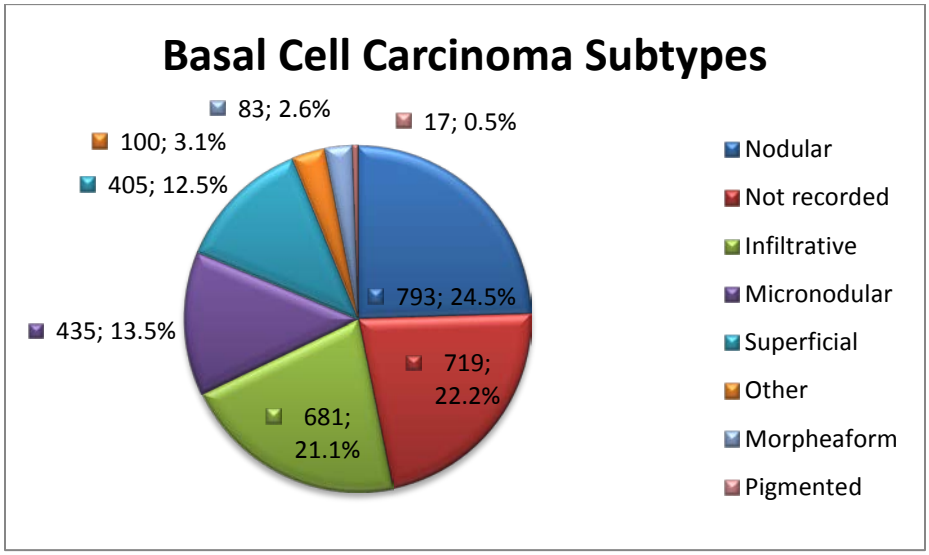

Figure 2. Basal cell carcinoma subtypes from 2001 to 2010

The most common subtypes of the 3,233 basal cell carcinomas were nodular (24.5%, 793), infiltrative (21.1%, 681), micronodular (13.5% 435), and superficial (12.5%, 405). One-hundred (3.1%) BCCs were classified as other. No subtype was reported by the pathologist in 22.2% (719) of biopsy specimens. Less common BCC subtypes include 2.6% morpheaform (83), and 0.5% (17) pigmented. This data is summarized by Figure 2.

Table 1. Subtypes of Basal Cell Carcinoma

		Secondary Morphology			
		Nodular	**Superficial**	**Infiltrative**	**Micronodular**
Primary Morphology	**Morpheaform**	5	4	9	1
	Infiltrative	244	34	N/A	44
	Micronodular	120	36	8	N/A
	Nodular	N/A	85	0	0

Six hundred and ninety three BCC specimens demonstrated more than one morphology in the biopsy. Table 1 shows the breakdown when multiple subtypes were identified. One hundred and three were not included because the pathology comments, such as pigmented or ulcerated, were not felt to have a biologic impact on the aggressiveness of the tumor.

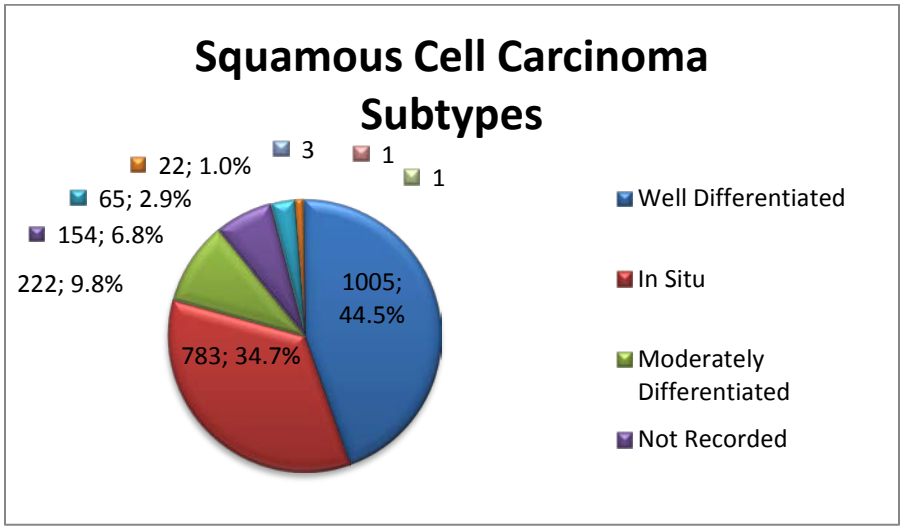

Figure 3. Squamous cell carcinoma subtypes from 2001 to 2010

The most common subtypes of the 2,256 squamous cell carcinomas were 44.5% (1005) well differentiated, 34.7% (783) in situ, and 9.8% (222) moderately differentiated. Less common SCC subtypes include 2.9% (65) poorly differentiated, 1.0% (22) acantholytic, 3 spindle, 1 adenoid, and 1 variable (see Figure 3).

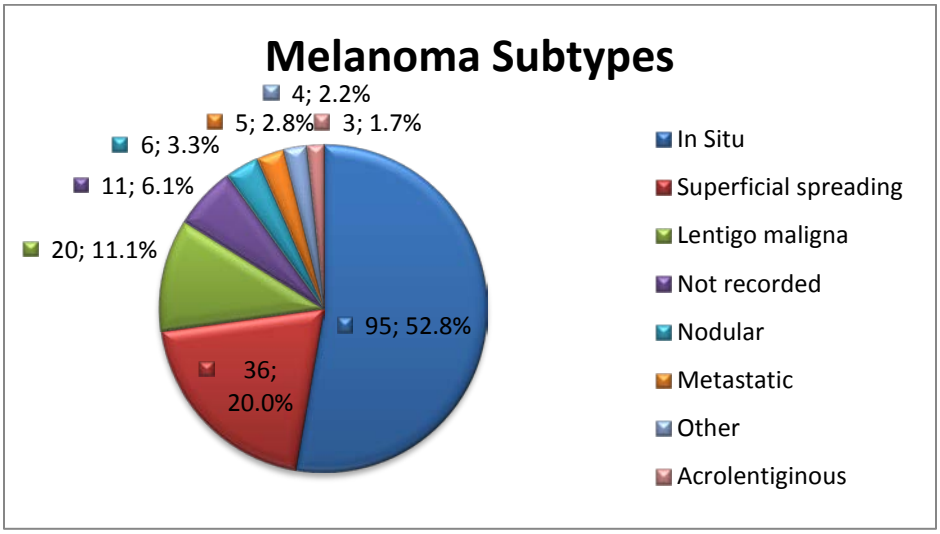

Figure 4. Melanoma subtypes from 2001 to 2010

The most common subtypes of the 180 melanomas were melanoma in situ 52.8% (95), superficial spreading 20.0% (36), and lentigo maligna 11.1% (20). Less common subtypes include nodular 3.3% (6), metastatic 2.8% (5), and acrolentiginous 1.7% (3). Four (2.2%) melanoma biopsies were classified as other. Figure 4 depicts this data.

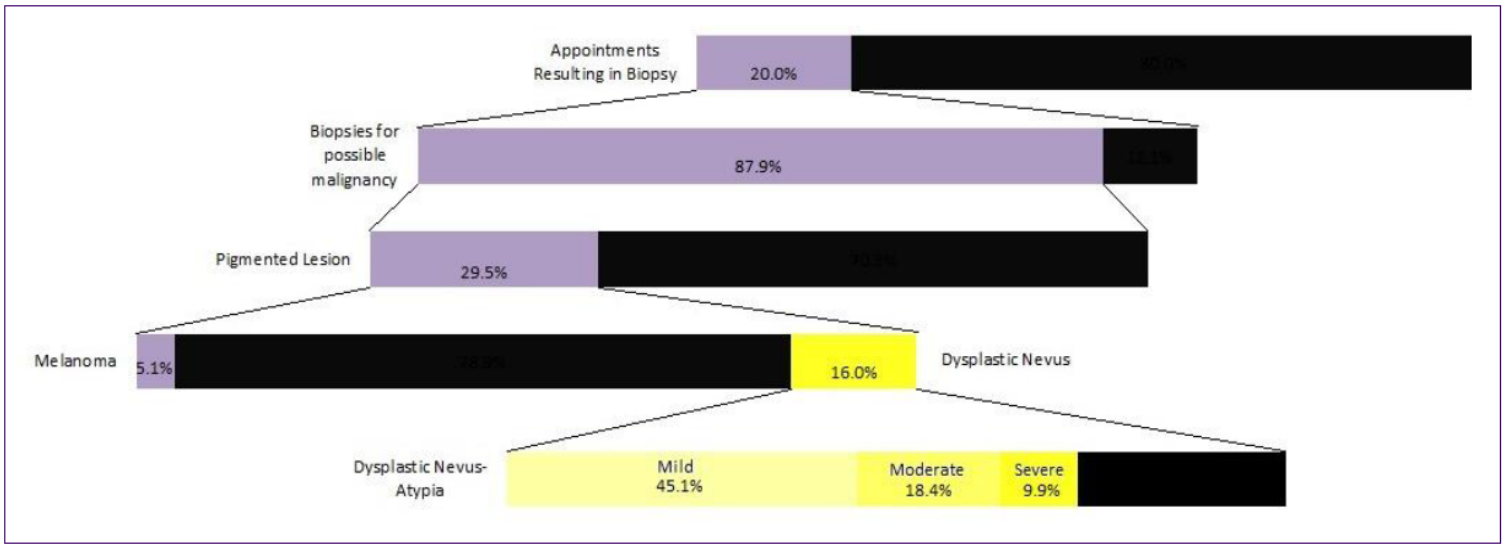

Figure 5. Stratification of pigmented lesion biopsy results

Eighty-eight percent (11,775) of the biopsies from 2001 to 2010 were performed to evaluate possible malignancy. Of these, 70.5% (8,391) were performed to evaluate possible keratinocytic malignancy, whereas 29.5% (3,474) were performed to further analyze a pigmented lesion suspicious for melanoma. Sixteen percent of these 3,474 pigmented lesion biopsies were dysplastic nevi. The identified subtypes of these dysplastic nevi were mild atypia 45.1% (246), moderate atypia 18.4% (100), and severe atypia 9.9% (54). Twenty seven percent (145) went uncategorized. Five percent (180) of biopsies on pigmented lesions were diagnosed as melanoma. Figure 5 summarizes this data.

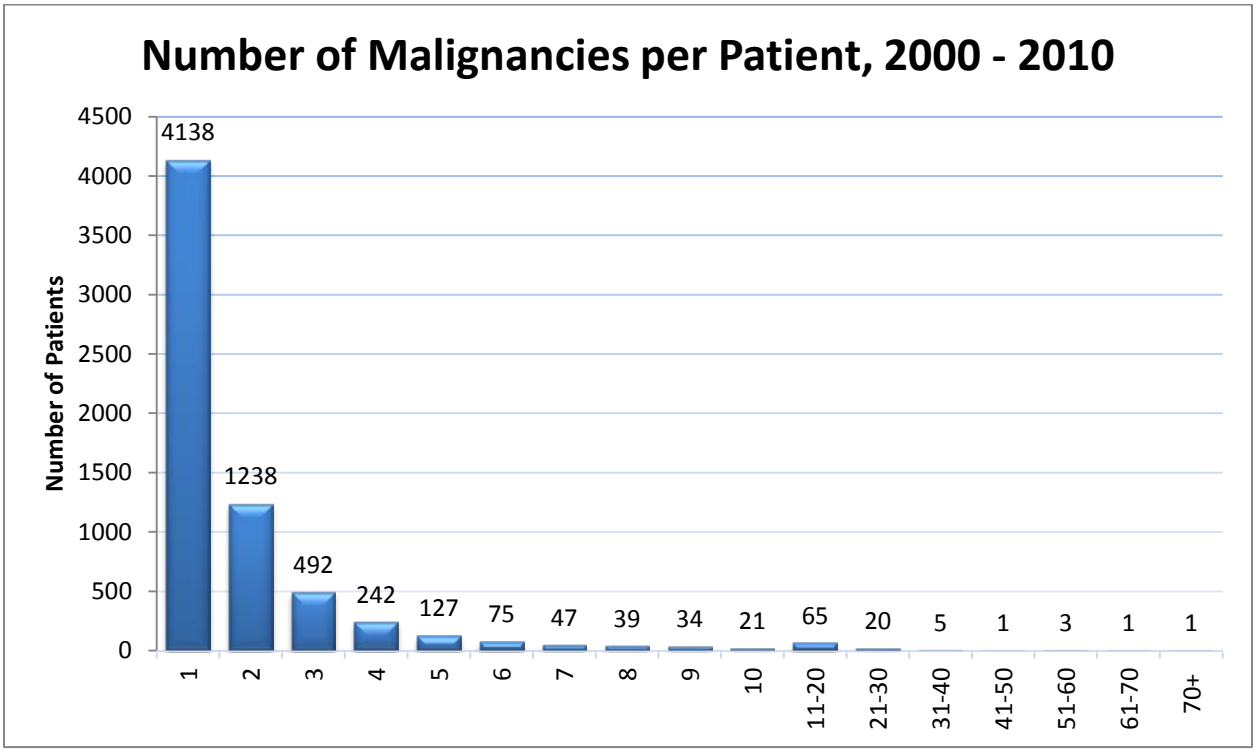

Figure 6. Distribution of number of cutaneous malignancies per patient

The distribution of number of malignancies per patient was also categorized, as seen in Figure 6. There were 6,549 patients who received biopsies. Sixty three percent (4,138) of patients were diagnosed with only one malignancy, 89.6% had three or fewer

tumors diagnosed, 95.2% had five or fewer, and 98.5% had 10 or fewer. Over the course of a decade, 7 patients were diagnosed with more than 35 skin cancers. Sixty two malignancies were seen in one patient, and another had 223 separate tumors.

Discussion

An average of twenty percent of 66,967 patient encounters involved a skin biopsy. The most likely reason for a skin biopsy was to evaluate cutaneous tumors; 5,802 of the 13,399 biopsies (43.3%) resulted in a diagnosis of a cutaneous malignancy.

Basal Cell Carcinoma

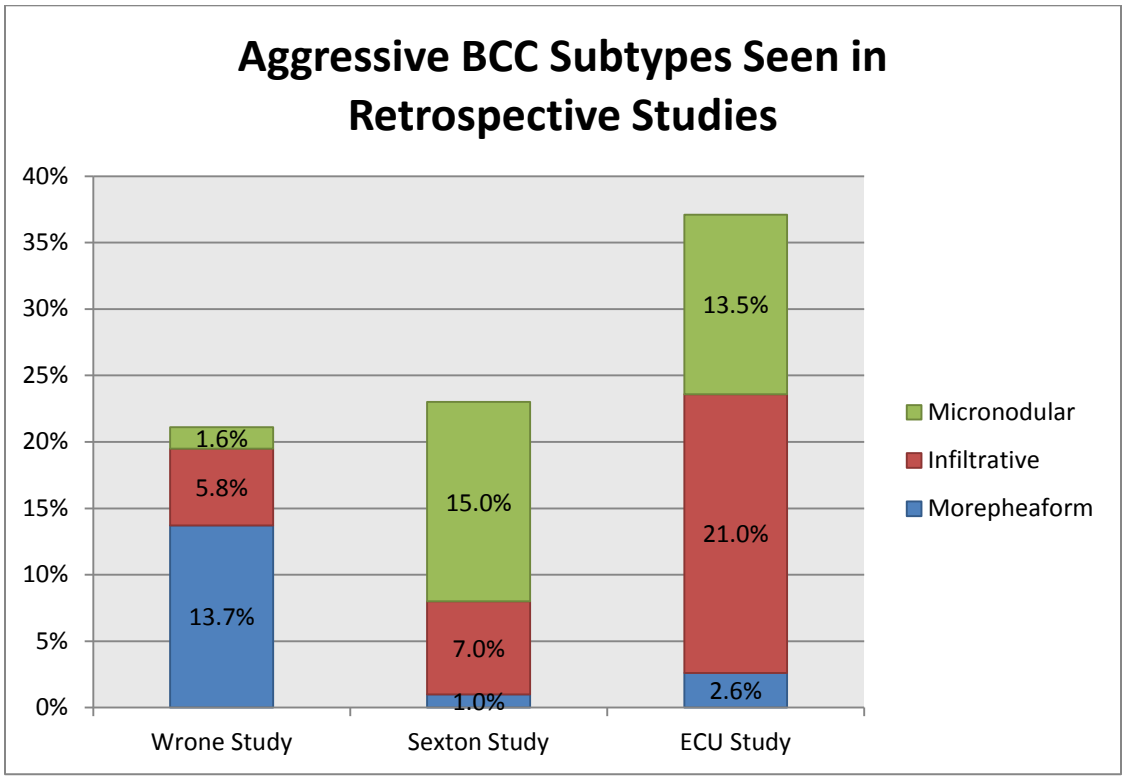

Figure 7. Basal cell carcinoma subtypes seen in retrospective studies

Non-melanoma skin cancers, primarily basal cell carcinoma and squamous cell carcinoma, are the most common cancers seen worldwide and encompass 40% of all malignancies [1]. The basal cell carcinoma subtypes that have a higher clinical risk to invade deeply, recur, or metastasize are morpheaform, infiltrating, and micronodular subtypes [2,3,4,5]. A study by Wrone, et al found that aggressive-growth BCC represent 21.1% of their total BCC seen throughout an 18-month period (13.7% morepheaform, 5.8% infiltrative, 1.6% micronodular) [4]. Another study of 1039 cases by Sexton et al showed that aggressive-growth BCC represented 23% (1% morepheaform, 7% infiltrative, and 15% micronodular) of their total BCC diagnoses [6]. These results are summarized in Figure 7. Our data of over 3,000 cases found that aggressive-growth BCC represent 37.1% of the total BCCs seen over a decade (2.6% morpheaform, 21% infiltrative, 13.5% micronodular).

Previous studies have shown that superficial BCC is unique in both body location and age of presentation. Nodular BCC, pigmented BCC, and the aggressive BCCs (micronodular, infiltrative, and morepheaform) are more likely to occur on the face, whereas the superficial BCC subtype is more likely to occur on the trunk. [7, 8, 9]. The mean age of superficial BCC is 58.8 years, which is much lower the average age of the rest of the BCC subtypes which range between a mean of 62.9 years to 66.1 years [8].

The BCCs with aggressive histology are most likely to occur on the face, and there is a risk of incomplete excision. Therefore, Mohs micrographic surgery is the treatment of choice for high risk lesions. By examining 100% of the tumor margin, Mohs surgery achieves the lowest recurrence rate compared to other treatment modalities [10]. Mohs is also the treatment of choice for recurrent BCC [11]. Radiotherapy is the treatment of choice of high risk BCC in patients who are unable to undergo surgery [12, 13]. Surgical excision has been found to be superior to radiotherapy for both the cure of cancer (99.3% vs. 92.5%) and satisfactory cosmetic outcome (87% vs 69%) [14]. One study recommends that patients with high risk BCC should be followed the dermatology clinic for 5 years post-operatively for recurrence at the surgical site [15].

Squamous Cell Carcinoma

Poorly differentiated squamous cell carcinomas are more aggressive than other subtypes of SCC, as the metastatic rate is almost three times greater than well differentiated lesions. The local recurrence rate is also more than double [16, 17]. A report by Mullen et al, that excluded in situ SCCs and Mohs cases, showed that 24% of their squamous cell carcinoma biopsies were moderately differentiated and 13% were poorly differentiated [18]. Our data (which includes in situ SCCs and ones that may have gone to Mohs surgery) shows much lower percentages with 15% of the SCCs being moderately differentiated and 4.4% being poorly differentiated.

Mohs micrographic surgery is the treatment of choice for high risk squamous cell carcinomas in cosmetically sensitive or critical areas [16, 19]. Risk factors for SCC include poor differentiation, size greater than 2cm, depth greater than 4mm (or beyond subcutaneous fat), recurrence, location (ear, lip, anogenital, scars), and previous radiation therapy [20]. Additional risk factors to be noted by the pathologist include perineural invasion, Clark level V, small tumor nests/strands, acantholysis, and single-cell infiltration [17]. Patients with high-risk SCC should also be considered for sentinel node biopsy. Local lymph node evaluation enables early detection of metastasis, provides staging information, and allows the appropriate adjunct treatments to be initiated [17]. Radiation therapy can be used for inoperable tumors [20]. Patients with high-risk SCC should be evaluated by a dermatologist every 3-6 months for up to five years because both 95% of metastasis and local recurrences are found within this time [21].

The skin cancer patients at BSOM Dermatology clinic typically are people from the surrounding farming and coastal communities, many who work on farms, on the water, or other outdoor labor. Given the type 1 – 3 skin prevalent in our patient population and sunny mid-Atlantic weather of the region, the fact that ten patients were diagnosed with over thirty cutaneous malignancies over the course of a decade is not surprising. The individual that had 223 separate tumors was a solid organ transplant recipient.

Melanoma

The second most common reason for biopsies listed on surgical pathology reports is clinical suspicion of melanoma [22]. This study showed a 5.1% detection rate for melanoma in the analysis of pigmented lesions. This is comparable to a previous report showing a melanoma rate of 7.6% in shave biopsies of pigmented lesions over a two year period [22]. Recommendations for proper assessment of pigmented lesions include regular use of dermoscopy, as well as annotated assessment on all pathology submissions of patient age and gender, lesion size and anatomic location, biopsy type performed, and overall diameter of lesion in comparison to biopsy site [22, 23]. These methods are known to impact the impression of the pathologist when interpreting potentially ambiguous dysplasia or cellular irregularities. Additional clinical information that can be used to assess pigmented lesions includes ABCDE criteria, a clinical photograph, and presence of macroscopic satellitosis. Skin biopsies for clinical suspicion for melanoma should be completed with an excisional biopsy of the entire lesion with a 1 to 3 mm margin [23]. Incisional biopsy may be considered for facial or acral lesions, if clinical suspicion for melanoma is low, and for very large lesions [24].

Nodular melanoma is more aggressive and has been shown to be a larger contributor to death from melanoma compared to other subtypes. For example, patients may have a 1.5 times greater risk of death from nodular melanoma compared to the superficial spreading type [25]. Nodular melanoma, as well as acral lentiginous melanoma, often presents at a more advanced stage of disease and this adds to the increased risk of mortality [26]. According to Garbe et al in a study of 69,962 cases of melanoma, the incidence of nodular melanoma and acral lentiginous melanomas were 20.6% and 4.2%, respectively [27]. The National Cancer Data Base report from 1985-1994 found nodular melanoma represented 18.9% and acral lentiginous represented 2.1% of the total cutaneous melanomas in over 77,000 cases [26]. A third study of 5,775 cases of invasive melanoma by Mar et al found 14% nodular and 1% acral lentiginous subtypes [25]. Our data, excluding melanoma in situ, demonstrates a lower incidence of the aggressive nodular melanoma subtype at 7% and a comparable incidence of acral lentiginous melanoma at 3.5%.

The hallmark of clinical management of primary cutaneous melanomas is early detection and treatment with surgical resection before the melanoma develops a vertical growth phase and metastasizes [28]. Non-surgical treatments of the lesion, such as topical imiquimod or radiation therapy, generally are not recommended as primary therapy. However, inferferon-alpha treatment can be used as an adjuvant therapy for stage II and III melanomas thicker than 1.5 mm, because this treatment increases the relapse-free survival [29]. Baseline imaging studies and blood tests are not generally recommended for asymptomatic patients with localized cutaneous melanoma of any thickness [23]. Treated melanoma patients should be followed-up on at least an annual basis with examination of the skin, lymph nodes, liver, and spleen [30]. Patients should also be counseled to self-exam their skin every month [31].

Inflammatory Skin Conditions

One of the less common reasons for a skin biopsy is to clarify the nature of inflammatory conditions. In this study, 12.1% of the skin biopsies were performed for this reason. This is consistent with a prior study which showed 12.1% of 6,816 biopsies completed by dermatologists over a two year period were to evaluate papulosquamous eruptions [32]. However, another study of 589 biopsies performed by primary care physicians showed that only 1.5% of pathology submissions assessed inflammatory processes. This lower percentage may be owing to the fact that primary care physicians manage fewer patients with inflammatory skin conditions and will refer these patients to dermatologists for treatment.

Finally, clinicians should be aware of several potential errors in biopsy selection and processing, which can contribute to decreased accuracy between clinical suspicion and pathological interpretation. These errors include difficulties collecting proper sample size and depth, challenges with selecting a representative area of lesion that is devoid of artifact, issues with fixation and transportation to a pathology laboratory, and lack of proper communication between clinician and pathologist [32, 33]. Diagnostic accuracy can be augmented by using a dermatoscope when choosing the site of biopsy, especially for pigmented lesions [34].

Conclusions

This report summarizes the biopsy data for patients seen at the dermatology clinic at the Brody School of Medicine, located in the region of Eastern North Carolina. Only an average of one of five patient encounters involved a biopsy and the vast majority of them were to evaluate a possible malignancy. Almost half of the skin biopsies done resulted in a diagnosis of a malignancy. Each of the three common skin cancers may present with more aggressive histological subtypes. A brief review of the management of aggressive skin cancers, the challenges of taking biopsies, and methods to accurately evaluate lesions have also been discussed. This study provides a long-term review of biopsy results to provide clinicians a better perspective about the expected outcomes from biopsies.

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