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Management of Residual Spitz Nevus in Surgical Specimens following Biopsy and Excision

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Background: Proper management of Spitz nevi continues to be debated, with treatment ranging from observation to surgery. To better characterize the outcome of surgical procedures performed for incomplete initial excision or biopsy, we sought to ascertain the histopathological presence of residual Spitz nevi in a set of surgical specimens.

Methods: We retrospectively reviewed 123 records with histologically-confirmed Spitz nevus. Data concerning treatment, clinical features, histopathological margin involvement, and presence of residual lesion on subsequent procedural specimens were collected.

Results: Fifty-three percent of lesions (n = 65) were initially sampled by shave or punch biopsy, and the remainder (n = 58) were formally excised without initial biopsy. The rates of re-excision for involved margins were: shave biopsy (92.2%), punch biopsy (78.6%), and formal excision (13.8%). In total, 61.0% of patients who underwent an initial procedure of any kind had involved margins, but only half of those re-excised for involved margins (57.6%) had histologically residual lesion on repeated excision. A significantly higher proportion of initial punch biopsies (90.9%) resulted in residual lesion (in secondary excision specimens) when compared with shave biopsy (48.9%) and formal excision (62.5%; $P < 0.05$).

Conclusions: Findings suggest that clinicians may consider shave biopsy over punch biopsy for diagnosing suspected lesions, when indicated and appropriate. Given the rarity of malignant transformation and the frequency of residual nevus, observation may be reasonable for managing pediatric patients with histologically-confirmed Spitz nevi, who are post initial biopsy or excision despite known histopathological margin involvement. *(Plast Reconstr Surg Glob Open 2020;8:e3244; doi: 10.1097/GOX.0000000000003244; Published online 18 December 2020.)*

INTRODUCTION

In 1948, Sophie Spitz first described nests of large epithelioid or spindled melanocytes observed in children as benign juvenile melanomas.[1] Since that time, the classifications of these spitzoid proliferations have diversified, and now include a spectrum of diagnoses such as classical or benign Spitz nevi, atypical Spitz tumors, and spitzoid melanomas.[2–4] The increasingly complex nomenclature and similarity to melanomas have made the diagnosis and management of spitzoid lesions in the pediatric population historically challenging and controversial.[5–7] In addition to the reported fatalities among patients with spitzoid melanomas and atypical Spitz tumors,[8] there is at least 1 reported death due to metastasis in a child diagnosed with a conventional Spitz nevus, which was originally classified as benign by 6 different pathologists.[9]

However, there is now growing evidence for conservative management, namely the "wait and see" approach, for children aged under 12 years who have been diagnosed with a benign Spitz nevus.[10–12] Despite this evidence, clinical uncertainty and a lack of consensus remain among dermatologists and surgeons regarding the management and surgical intervention for these pediatric benign Spitz lesions.[13,14] One major concern among physicians is the potential for malignancy of partially excised Spitz lesions, prompting surgical re-intervention after an initial biopsy or excision.[13–15] Tlougan et al. report that over half of surveyed dermatologists would recommend re-excision of a benign Spitz lesion if there was residual lesion clinically or histologically, and roughly one-third of dermatologists

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would advise re-excision if the sample extends to the lateral histological margin despite no clinical evidence of residual lesion.[16]

While some advances have been made toward a formal recommendation against surgical intervention,[10] there exists a paucity of data and no definitive protocol for the management of involved margins following initial biopsy or excision. To address this gap in the literature, we aimed to characterize the management, clinical course, and outcomes of pediatric patients who underwent surgical intervention for benign, histologically-confirmed Spitz nevi at our institution—with a specific focus on the management of residual lesion after *secondary* excision.

METHODS

Approval from Boston Children's Hospital Committee on Clinical Investigation was obtained (Protocol number: P00025597), with a waiver of informed consent. We retrospectively identified and reviewed the medical records of 123 patients seen at our institution, a large tertiary pediatric facility, for the management of Spitz nevi from January 2007 through June 2017 using the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes D22 and D23. To meet inclusion criteria, all patients were <18 years of age during consultation, underwent surgical intervention for a Spitz nevus (initially) diagnosed by observation and (subsequently) confirmed by histopathology, and were managed by a pediatric plastic surgeon, a general surgeon, or a dermatologist. Patients with atypical or malignant lesions were excluded.

Medical records were reviewed for patient demographics, Fitzpatrick skin type, age at the time of diagnosis, age at the time of biopsy and excision, biopsy and/or excision method, and patient's family history of melanoma. Lesion characteristics that were collected included: anatomical location, lesion size (longest dimension), clinical presentation, and recurrence status. Due to the retrospective nature of this study, follow-up time was defined as the length of time from initial biopsy or excision to the patient's last clinical visit. The primary outcome was the presence of histological residual Spitz lesion after secondary excision. Secondary excision was defined as a formal excision procedure performed after the specimen of the initial biopsy or excision procedure demonstrated involved margins. Figure 1 outlines the typical clinical pathway and our definition of a "secondary excision." Histopathological records inclusive of fluorescence in situ hybridization and immunoreactivity results were also reviewed.

Statistical analyses were conducted using SPSS (IBM SPSS Statistics for Windows, version 21.0; IBM Corp., Armonk, N.Y.), and SAS 9.2 (SAS Institute Inc., Cary, N.C.). Median age at the time of diagnosis, biopsy, and excision, and median lesion sizes were calculated, with differences compared using the independent-samples median test. Frequency distributions for patient, lesion, biopsy, and excision characteristics were calculated. Fisher's exact testing was used to compare differences in the proportion of patients with residual lesions and clear margins by varying management types, as well as initial method of management and treating specialty. $P < 0.05$ was considered statistically significant.

RESULTS

Demographics and Clinical Features

A total of 123 patients meeting inclusion criteria were identified and included in analyses. Patient and treatment characteristics are presented in Table 1. Roughly half of all patients in our sample were women (51.2%, N = 63). Most patients for which a Fitzpatrick skin type was documented in the chart were types I–II (80.8%, N = 63). No patient had a prior history of melanoma, and 4% (N = 5) of patients reported a family history of melanoma. The most commonly affected anatomical sites were the head/neck area (45.5%, N = 56), followed by the lower (24.4%, N = 30) and upper limbs (21.1%, N = 26), and trunk (8.9%, N = 11). Lesion size was skewed right with a median (interquartile range) diameter of 8 (5) mm at the widest point (Table 2).

Clinical Course

Approximately three-fourths (76.4%, N = 94) of all patients were managed by a plastic surgeon, with the remaining patients treated by either a dermatologist (17.9%, N = 22) or a general surgeon (5.7%, N = 7). Lesions initially managed with excision were significantly larger than those undergoing punch biopsy ($P = 0.02$; Table 3). However, the size of lesions undergoing punch and shave biopsy was comparable ($P = 0.78$). The method

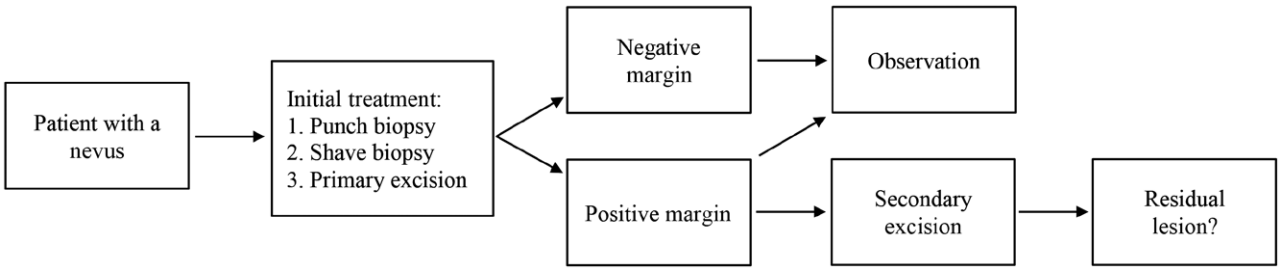

Fig. 1. The clinical course of a typical patient who presented with a suspected Spitz nevus. If margins were involved ("Positive margin"), most (but not all) underwent a secondary excision procedure. The outcome of interest was the presence of histopathologically-confirmed residual lesion on this secondary specimen.

Table 1. Patient and Treatment Characteristics

Characteristics	Patients (N = 123)
Gender	
Men	63 (51.2%)
Women	60 (48.8%)
History of melanoma, N (%)	0 (0%)
Family history of melanoma, N (%)	5 (4.1%)
Median (IQR) age at biopsy, y	7.3 (4.9)
Median (IQR) age at initial excision, y	6.6 (6.0)
Median (IQR) time from biopsy to excision, mo	2.5 (3.1)
Median (IQR) time from excision to re-excision, mo	3.5 (3.5)

Table 2. Lesion Characteristics

Characteristics	Lesions (N = 123)
Median (IQR) diameter at widest point, mm	8.0 (5.0)
Anatomic location, N (%)	
Head/neck	56 (45.5%)
Lower extremities	30 (24.4%)
Upper extremities	26 (21.1%)
Trunk	11 (8.9%)

of initial management did not significantly vary by treating specialty ($P = 0.11$).

Over half of all patients (52.8%, N = 65) underwent a biopsy (shave or punch) following a clinical diagnosis of a suspected Spitz nevus, with a median (interquartile range) age of 7.3 (4.9) years. A total of 7 patients who had initial biopsy did not require further surgical management due to uninvolved/clear margins. Of all subjects in our sample who had a secondary excision, 65.2% (N = 43/66) underwent general anesthesia and 34.8% (N = 23/66) underwent local anesthesia. Figure 2 summarizes the clinical outcomes of patients in this sample.

Shave biopsies were the most frequently performed biopsy in our sample (78.5%, N = 51), and most shave biopsies had margin involvement confirmed by pathology (98.0%, N = 50). Three patients with margin involvement after shave biopsy did not undergo re-excision, and were told to follow up in case of recurrence. Ninety-two percent (N = 47) of lesions undergoing shave biopsy were subsequently excised (secondary excision procedure). In these formal excisions, 23 (48.9%) specimens demonstrated residual lesion on histopathology. Clear margins were achieved in 93.6% (N = 44/47) of cases requiring secondary excision; the 3 patients with margin involvement underwent repeat excision with subsequent clear margins.

Punch biopsy was performed in one-fifth (N = 14) of all patients in our sample who underwent a biopsy. Pathology reported margin involvement in roughly 80% (N = 11) of these biopsies, and all of these patients underwent secondary excision procedures. In these formal excisions, 10 (90.1%) specimens demonstrated residual lesion on histopathology. Two patient specimens exhibited margin involvement, prompting repeat excision that led to clear margins.

A total of 58 excisions were performed *without* initial biopsy and most of these specimens exhibited uninvolved margins (75.9%, N = 44). Of those patients with margin involvement (N = 14), 6 were followed clinically with no evidence of recurrence, and 8 were re-excised (secondary excision) with subsequent clear margins. In these 8 formal re-excisions, 5 (62.5%) specimens demonstrated residual lesion on histopathology.

Overall, after any kind of initial procedure that resulted in positive margins, only 57.6% of secondary excision specimens demonstrated histologically-confirmed residual lesion. These results are summarized in Table 3.

The likelihood of having involved margins was higher after any form of biopsy when compared with formal (initial) excision (93.8% versus 24.1%, respectively, $P < 0.001$). A significantly higher proportion of initial punch biopsies resulted in residual lesion (in secondary excision specimen) when compared with shave biopsy and formal excision ($P = 0.04$). Additionally, shave biopsy was superior to punch biopsy in avoiding the presence of residual lesion after subsequent formal excision (51.1% versus 9.1%, $P = 0.02$).

Management and Follow-up

The median follow-up time for the entire cohort was 13.8 (IQR: 52.2; minimum: 0; maximum: 154.0) months. No patients exhibited signs of metastases at the time of diagnosis and during their follow-up appointments. Currently, all patients in this sample are alive with no evidence of melanoma or recurrent disease.

DISCUSSION

There has been recent momentum toward a singular treatment protocol for benign Spitz nevi in children in whom observance and reassurance are the primary methods of management.[10,12] Despite these recommendations, benign Spitz nevi continue to be surgically managed in a subset of pediatric patients and clinical uncertainty remains regarding the necessity of re-excision when clear margins are not achieved. Anecdotal and official reports of pathologically confirmed benign Spitz nevi metastasizing[17] have made physicians apprehensive to simply observe previously excised benign Spitz nevi. This study aimed to elucidate the outcomes of re-excised histologically-confirmed, benign Spitz nevi in children and to understand

Table 3. Incidence of Histopathological Residual Lesion on Surgical Specimens after Secondary Excision

	Initial Management			
	Punch Biopsy (N = 14)	Shave Biopsy (N = 51)	Formal Excision (N = 58)	Total (N = 123)
Median (IQR) diameter at widest point, mm	8.0 (5.0)	6.0 (5.0)	9.5 (5.0)	–
Margin involvement	11/14 (78.6%)	50/51 (98.0%)	14/58 (24.1%)	75/123 (61.0%)
Residual lesion in secondary procedure specimen	10/11 (90.9%)	23/47 (48.9%)	5/8 (62.5%)	38/66 (57.6%)

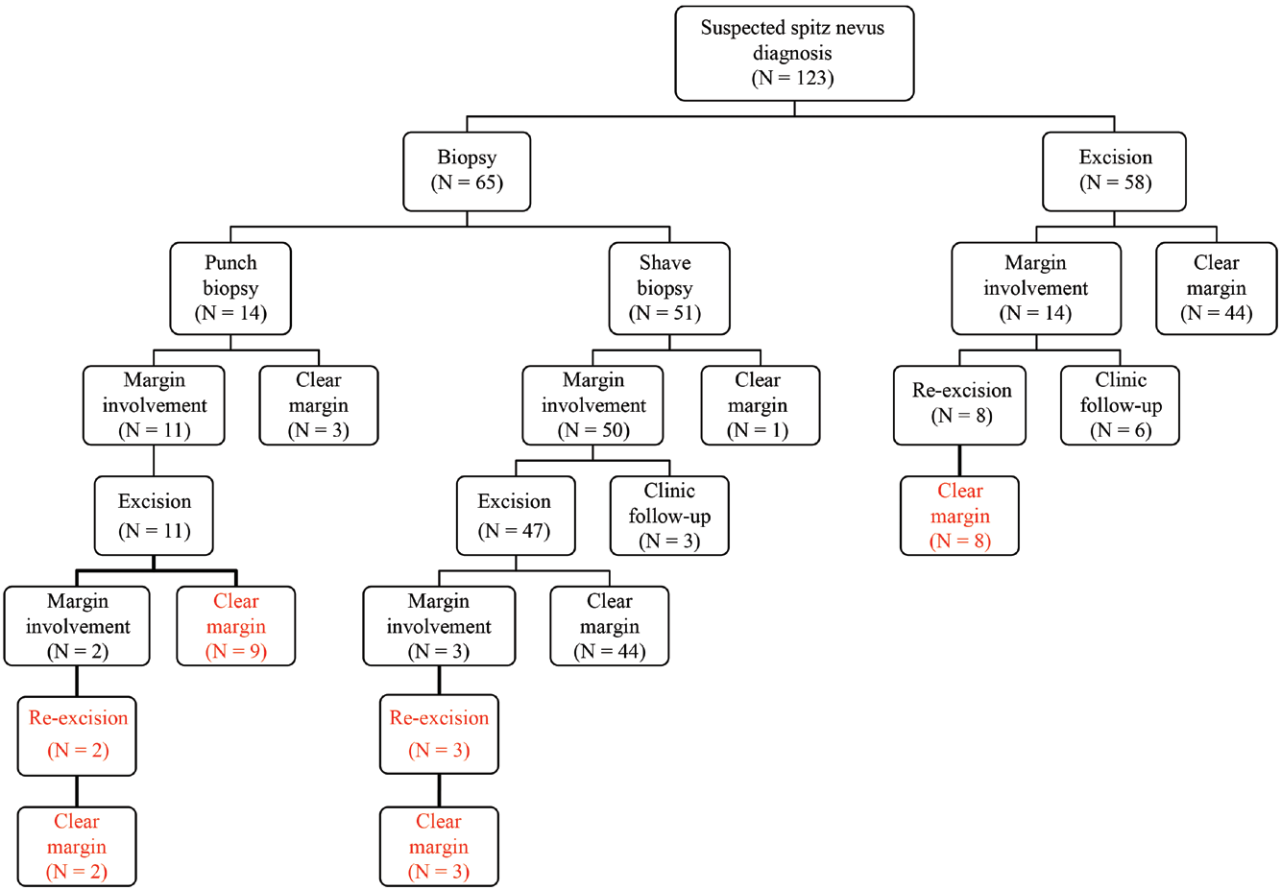

Fig. 2. Summary flow diagram of patient outcomes.

the incidence and management of residual lesion in secondary excision specimens when the initial biopsy/excision specimen demonstrated involved margins.

Shave and punch biopsies are two of the most commonly recognized biopsy techniques for Spitz nevi, with complete excision representing the most aggressive initial treatment. In the present study, about half of all lesions underwent an initial shave or punch biopsy (53%) and almost all had margin involvement (94%). All other lesions underwent an initial excision and roughly one-quarter had margin involvement (24%). These findings confirm those of previous pediatric and young adult studies.[10,18] Often times these residual lesions are re-excised due to concern for initial misdiagnosis, potential metastasis, or recurrence, particularly when recurrent lesions are irregular in form or confined within a subsequent scar.[19] To date, there exists no evidence that re-excision can reliably achieve clear margins, but the belief that re-excision can reduce the possibility, albeit small, of malignant or fatal outcomes by achieving clear margins remains pervasive among physicians.[12,13]

In this present study, we observed that roughly half of all re-excised shave biopsies had residual, histologically-confirmed lesions, while the great majority of initial punch biopsies (91%) had confirmed residual Spitz lesions. It is possible that inflammatory healing responses eliminated viable remaining cells from the wound beds that had involved margins on the initial specimens, but regardless, these findings suggest that shave biopsy is superior to punch biopsy with respect to total removal of the initial lesion. Nevertheless, we would be remiss not to note the important diagnostic advantage of punch biopsies over shave biopsies: punch biopsies can more reliably excise a full-thickness specimen with preserved architecture of the lesion in question, providing the most clarity on the malignant potential of a lesion, or the presence of atypical Spitz tumor in these cases.[20]

Finally, the prognostic value of residual lesion or involved margins following the initial surgical management of a benign spitzoid lesion in the pediatric population has not been verified. Although it is likely that the a priori presence of residual lesion portends a higher likelihood of recurrence, it is not clear whether this predisposes to pre-malignancy. It must be noted that malignancy and lesion reoccurrence were not observed in any subject during the present study's follow-up period. Given the observed 42% incidence of no residual lesion in wound beds which initially had margin involvement, and the low incidence of malignant or atypical Spitz nevi in children under 12 years and low recurrence rates of classical Spitz lesions,[10–12] clinicians may observe biopsied or primarily excised lesions with involved margins when appropriate—especially if there is no clinically visible lesion remaining. Additionally, physicians should consider the benefits and

risks of a secondary procedure because many of these lesions occur in the aesthetically-sensitive head and neck areas, often pose the additional risks of general anesthesia, and are not guaranteed to achieve clear margins.

The current study is retrospective and, as such, has several limitations. The results of this study may not be generalizable because subjects were recruited from a single large, tertiary-care facility. Additionally, the included patients were identified by their assigned ICD-10 codes, potentially limiting the selection of relevant cases. Although we did not discern any demographic differences in the subjects, confounding could not be controlled. Color could not be ascertained and stratified. There was also no indication of whether there was visible lesion after the initial excision or biopsy and before the secondary excision, and this information would have been very useful to correlate with histopathological residual lesion. It is possible that the absence of visible lesion decreases the pretest probability that histological residual lesion remains, and thus tilts the scale toward observation. Finally, the median follow-up time for the cohort was relatively short (approximately 1 year), and future studies are needed to explore long-term outcomes in this population.

CONCLUSIONS

Benign Spitz nevi in the pediatric population are commonly managed with observation alone. However, a subsection of these cases are treated with surgical intervention. Concern for recurrence and potential malignancy have driven clinicians to re-excise classical Spitz nevi in pediatric patients to achieve clear margins. Our findings suggest that observation post initial biopsy and excision may be a reasonable treatment course for pediatric patients with histologically-confirmed Spitz nevi. As such, we urge physicians to fully consider the risks and benefits of secondary excisions of classical Spitz nevi in children.

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