A Clinicopathological Analysis of Melanocytic Nevi: A Retrospective Series

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Purpose: Melanocytic nevi are common cutaneous lesions. This study aimed to demonstrate the concordance and discordance between clinical and histopathological diagnoses of melanocytic nevi and the importance of histological evaluation in differentiating malignant lesions from diseases with similar clinical manifestations.

Patients and Methods: We studied 4,561 consecutive patients with a clinical diagnosis of melanocytic nevi from 2014 to 2019. We compared the clinical diagnosis with the histopathological diagnosis to establish a histopathological concordance rate and then investigated the effects of clinical characteristics and the reasons for removal on misclassification.

Results: Among 4,561 patients who were clinically diagnosed with melanocytic nevi, the overall histopathological concordance rate was 82.11% (3,745 of 4,561 patients), while the histopathological discordance rate was 17.89% (816 of 4,561 patients). The histopathological concordance included 90.25% common acquired melanocytic nevi (3,380 of 3,745 patients) and 9.75% other benign melanocytic neoplasms (365 of 3,745 patients). The most common diagnostic change was to seborrheic keratosis (n = 470, 10.30%), followed by basal cell carcinoma (n = 64, 1.40%), vascular tumor (n = 53, 1.16%), fibroma (n = 43, 0.94%), epidermoid cyst (n = 34, 0.75%), wart (n = 30, 0.66%), melanoma (n = 24, 0.53%), Bowen’s disease (n = 16, 0.35%), squamous cell carcinoma (n = 4, 0.09%), keratoacanthoma (n = 2, 0.04%), and other neoplasms (n = 76, 1.67%).

Male sex, old age, location of the lesion, and the reasons for removal have a potential effect on misclassification. The percentages of misclassified lesions on the trunk and limbs and the perineum and buttocks were higher than those in lesions without a change in diagnosis. Importantly, locations of lesions on the head and neck were significantly related to a change in diagnosis to non-melanoma skin cancer, while locations on the hands and feet were significantly related to a change in diagnosis to melanoma. In addition to a typical clinical features, removal due to lesion changes or repeated stimulation was significantly associated with a change in diagnosis to melanoma.
INTRODUCTION

Melanocytic nevi are benign tumors of melanocytes; these growths include common acquired melanocytic nevi and other benign melanocytic neoplasms, such as blue nevus, halo nevus, congenital nevomelanocytic nevus, “dysplastic” melanocytic nevus, and Spitz nevus (1–3). Common acquired melanocytic nevi are the most frequent neoplasms. It is unnecessary to remove melanocytic nevi routinely, but they should be removed when any of the following conditions are met: changes in skin lesions, an atypical clinical appearance suspicious for melanoma, cosmetic requirements, or repeated stimulation (4).

In fact, studies have found that common acquired melanocytic nevi are challenging to differentiate in clinical practice from other benign melanocytic neoplasms, such as congenital nevomelanocytic nevus and blue nevus, or even tumors, such as melanoma (5). Moreover, the importance of melanocytic nevi is related to melanoma. A large proportion of melanoma occur in the same area as long-term pre-existing melanocytic nevi (1). Histological examination has shown that approximately 30% of melanoma cases are associated with a residual nevus (6). Therefore, to provide support for clinicians in diagnosing and treating melanocytic nevi, our study focuses on patients with a clinical diagnosis of melanocytic nevi, which are reclassified after a histopathological examination, and assesses whether the clinical characteristics of patients affect the misclassification.

PATIENTS AND METHODS

This is a retrospective review of data from 4,561 consecutive patients with a clinical diagnosis of melanocytic nevi over 5 years, from 2014 to 2019, referred to the Department of Dermatology of Xiangya Hospital, Central South University. All patients in this study had undergone an initial clinical diagnosis, excision, and histopathological diagnosis. The reasons for removal of melanocytic nevi included atypical clinical features, changes in skin lesions, cosmetic requirements, or repeated stimulation (e.g., sites of friction or repeated trauma) (4). To ensure accuracy, two independent dermatopathologists reviewed the hematoxylin- and-eosin-stained slides and made a diagnosis. If there is any disagreement among them, another dermatopathologist reviewed the slide, and the three dermatopathologists made the diagnosis together. Clinical data on each case, including the age and sex of the patient and the location of the lesion, were obtained from the patient records. This study was approved by the ethics committees of Xiangya Hospital of Central South University, Changsha, Hunan, China, and informed consent was obtained from all subjects.

RESULTS

Histopathological Review

A total of 4,561 patients were clinically diagnosed with melanocytic nevi according to their skin lesions (Figure 1). The characteristics of the patients are listed in Table 1. There were 1,459 males (31.99%) and 3,102 females (68.01%). The age ranged from 2 to 86 years, with a mean age of 31. The patients were divided into four groups based on age: <20, 20–39, 40–59, and ≥60. The most common age range was 20–39 years (54.70%), followed by <20 years (21.75%), while the least common age was ≥60 years (4.71%). The head and neck (66.24%) were the most common sites of involvement, whereas, the hands (1.43%) and the buttocks (0.75%) were the least common sites of involvement. In addition, the most common reasons for removing melanocytic nevi were cosmetic requirements (48.78%) and atypical clinical features (47.18%).

After a histopathological examination, 3,745 patients were finally diagnosed with melanocytic nevi (overall histopathological concordance rate, 82.11%), while 816 patients

Conclusions: Our study emphasizes the clinical differential diagnosis of melanocytic nevi, especially the possibility of malignant tumors. The occurrence of clinical features associated with clinicopathological discordance should raise the clinical suspect and be carefully differentiated from malignant tumors.

Keywords: melanocytic nevi, melanocytic diseases, melanoma, diagnosis, misclassification
clinically diagnosed with melanocytic nevi were reclassified as other diseases (overall histopathological discordance rate 17.89%; Figure 1; Tables 1, 2).

**Histopathological Concordance and Its Clinical Characteristics**

The histopathologically concordant cases included common acquired melanocytic nevi \((n = 3,380, 90.25\%)\) and other benign melanocytic neoplasms \((365, 9.75\%); \text{Table 1}\). Common acquired melanocytic nevi were divided into intradermal nevus \((n = 2,598, 76.86\%), \text{junctional nevus} \((n = 238, 7.04\%), \text{and compound nevus} \((544, 16.09\%); \text{Table 1}\). The ratio of males to females was roughly the same in all three type-based groups (overall, 981:2,399; 29.02:70.98%). The most common age range was 20–39 years \((61.04\%)\), followed by <20 years \((24.47\%)\). The most common sites of involvement for intradermal nevus and compound nevus were the head and neck \((79.56 \text{ and } 61.58\%, \text{respectively})\), followed by the trunk \((14.43 \text{ and } 13.42\%, \text{respectively}\). However, the most common site of involvement in the junctional nevus group was the feet \((55.04\%)\), followed by the head and neck \((13.45\%)\) and the trunk \((13.45\%)\). The main reasons for removing common acquired melanocytic nevi were cosmetic requirements and atypical clinical features. Interestingly, in the junctional nevus group, 27.73% of the lesions were removed because of repeated stimulation, which was significantly higher than the corresponding rates in the intradermal nevus and compound nevus groups \((0.89 \text{ and } 6.99\%, \text{respectively})\).

The other benign melanocytic neoplasms included congenital nevomelanocytic nevus \((3.04\%)\), blue nevus \((2.40\%)\), lentigo \((1.71\%)\), “dysplastic” melanocytic nevus \((1.04\%)\), recurrent nevus \((0.45\%)\), Spitz nevus \((0.37\%)\), halo nevus \((0.32\%)\), and other melanocytic nevi \((0.40\%)\). We evaluated clinical characteristics that could potentially have an impact on the classification of other benign melanocytic neoplasms. Younger age was significantly associated with the histopathological diagnosis of congenital nevomelanocytic nevus and Spitz nevus, compared with the common acquired melanocytic nevi. The most common age group in the classification of congenital nevomelanocytic nevus and Spitz nevus was <20 years \((54.39 \text{ and } 85.71\%, \text{respectively})\), compared with 20–39 years \((61.04\%)\) in patients with a histopathological diagnosis of common acquired melanocytic nevi (Table 1). Furthermore, the location of the lesion was significantly correlated with the diagnosis of blue nevus, lentigo, and “dysplastic” melanocytic nevus (Table 1). The percentages of blue nevus lesions occurring on the upper limbs and hands, lentigo lesions on the feet, and “dysplastic” melanocytic nevus lesions on the lower limbs were higher than those in patients with a histopathological diagnosis of common acquired melanocytic nevi (Table 1). The reasons for removing melanocytic nevi also influenced the classification of congenital nevomelanocytic nevus, blue nevus, lentigo, recurrent nevus, and halo nevus. In the lentigo and recurrent nevus groups, in addition to atypical clinical features, the percentage of lesions removed due to lesion changes and repeated stimulation was significantly higher for lesions histopathologically diagnosed as common acquired melanocytic nevi (Table 1).

**Clinical Characteristics Have a Potential Effect on Misclassification**

Histopathological review led to a change in diagnosis in a total of 816 of 4,561 patients \((17.89\%; \text{Figure 1 and Table 2})\), including seborrheic keratosis \((n = 470, 10.30\%)\), basal cell carcinoma \((n = 64, 1.40\%)\), vascular tumor \((n = 53, 1.16%)\), fibroma \((n = 43, 0.94\%)\), epidermoid cyst \((n = 34, 0.75\%)\), wart \((n = 30, 0.66\%)\), melanoma \((n = 24, 0.53\%)\), Bowen’s disease \((n = 16, 0.35\%)\), squamous cell carcinoma \((n = 4, 0.09\%)\), keratoacanthoma \((n = 2, 0.04\%)\), and other neoplasms \((n = 76, 1.67\%)\).

We evaluated clinical characteristics that could potentially have an impact on misclassification. Among patients with a clinical diagnosis of melanocytic nevi, male sex was significantly related to a change in diagnosis (overall histopathological concordance vs. overall histopathological discordance, \(p < 0.001; \text{Table 3}\)). In addition, old age was also significantly associated with a change in diagnosis (\(p < 0.001; \text{Table 3}\)). The median age of diagnosis of patients with misclassification was 45 years (range, 2–86 years), compared with 27 years (range, 2–80 years) in patients with histopathological concordance. Interestingly, the location of the lesion was significantly correlated with histopathological discordance (\(p < 0.001; \text{Table 3}\)). The percentages of misclassified lesions on the trunk and limbs and the perineum and buttocks were 40.69 and 7.11%, respectively, compared with 20.00 and 2.22%, respectively, in lesions without a change in diagnosis (Table 3). The reasons for removing melanocytic nevi also influenced the change in diagnosis. The proportion of misclassified lesions removed due to atypical clinical features was 71.81%, compared with 41.82%.
TABLE 1 | Clinical characteristics of 3,745 patients with a clinical diagnosis of melanocytic nevi with histopathological concordance.

### Clinical characteristics of 3,745 patients with a clinical diagnosis of melanocytic nevi with histopathological concordance

| Characteristic | Common acquired melanocytic nevi | Other benign melanocytic neoplasms |
|---------------|---------------------------------|-----------------------------------|
|               | Intradermal melanocytic nevus (N, %) | Junctional melanocytic nevus (N, %) | Compound melanocytic nevus (N, %) | P-value<sup>a</sup> | Blue nevus (N, %) | P-value<sup>a</sup> | Lentigo (N, %) | P-value<sup>a</sup> | "Dysplastic" melanocytic nevus (N, %) | P-value<sup>a</sup> | Recurrent nevus (N, %) | P-value<sup>a</sup> | Spitz nevus (N, %) | P-value<sup>a</sup> | Halo nevus (N, %) | P-value<sup>a</sup> | Other melanocytic nevus (N, %) | P-value<sup>a</sup> |
|---------------|---------------------------------|-----------------------------------|-----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Number        | 4,561                          | 3,745                            | 2,598                            | 238             | 544             | 3,380           | 114             | 90              | 64                 | 39              | 17              | 14              | 12              | 15              |
| Sex           |                                 |                                  |                                  |                 |                 |                 |                 |                 |                                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Male          | 1,459                          | 1,099                            | 739                              | 71              | 171             | 981             | 34              | 30              | 21                 | 509             | 12              | 0.811            | 2               | 0.195            | 4               | 1.000            | 5               | 0.336            | 5               | 0.714            |
| Female        | 3,102                          | 2,646                            | 1,859                            | 167             | 373             | 2,399           | 80              | 55              | 43                 | 27              | 15              | 10              | 7               | 10              |
| Age           |                                 |                                  |                                  |                 |                 |                 |                 |                 |                                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| <20           | 992                            | 968                              | 530                              | 64              | 243             | 827             | 62              | 19              | 9                  | 13              | 6               | 12              | 3               | 7               |
| 20–39         | 2,495                          | 2,250                            | 1,651                            | 144             | 268             | 2,003           | 40              | 50              | 46                 | 24              | 10              | 2               | 8               | 7               |
| 40–59         | 895                            | 481                              | 379                              | 32              | 29              | 440             | 12              | 16              | 8                  | 2               | 1               | 0               | 1               | 1               |
| ≥60           | 215                            | 56                               | 38                               | 8               | 4               | 50              | 5               | 1               | 0                  | 0               | 0               | 0               | 0               | 0               |
| Location      |                                 |                                  |                                  |                 |                 |                 |                 |                 |                                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Head and neck | 3,021                          | 2,628                            | 2,067                            | 32              | 335             | 2,434           | 89              | 38              | 13                 | 16              | 8               | 10              | 4               | 6               | 2               | 10              | 3               | 1                | 8               | 1                | 8               | 1                |
| Upper limbs   | 149                            | 118                              | 61                               | 4               | 27              | 92              | 7               | 15              | 1                  | 2               | 1               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0               | 0                | 0               | 0                |
| Lower limbs   | 169                            | 159                              | 39                               | 8               | 34              | 81              | 4               | 7               | 4                  | 7               | 0               | 2               | 0               | 4               | 4               |
| Trunk         | 763                            | 522                              | 375                              | 32              | 73              | 480             | 12              | 3               | 10                 | 9               | 0               | 1               | 2               | 5               | 4               |
| Perineum      | 108                            | 60                               | 27                               | 10              | 12              | 49              | 0               | 0               | 0                  | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0               | 0                | 0               | 0                |
| Hands         | 65                             | 57                               | 7                                | 21              | 6               | 34              | 0               | 14              | 8                  | 1               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0               | 0                | 0               | 0                |
| Feet          | 253                            | 228                              | 12                               | 131             | 53              | 196             | 2               | 8               | 18                 | 3               | 0               | 1               | 0               | 0               | 0               | 0               | 0               | 0                | 0               | 0                | 0               | 0                |
| Buttocks      | 34                             | 23                               | 10                               | 0               | 4               | 14              | 0               | 5               | 0                  | 0               | 0               | 2               | 0               | 2               | 0               | 0               | 0               | 0                | 0               | 0                | 0               | 0                |
| Reason for removal | 0.002 | 0.001 |<0.001 |0.319 |<0.001 |0.135 |<0.001 |0.135 |0.204 |
| Atypical clinical features | 2.152 | 1.568 | 1.051 |92 | 218 | 1.316 | 67 | 53 | 27 | 20 | 6 | 10 | 12 | 10 | 47.18% | 41.82% | 40.45% |38.66% |40.07% |42.27% |58.77% |58.89% |42.19% |51.28% |35.29% |71.43% |100.00% |66.67% | (Continued)
TABLE 2 | Histopathological diagnosis distribution of 816 patients whose clinical diagnosis was not congruent with the histopathological diagnosis.

| Histopathological diagnosis | Clinical diagnosis of melanocytic nevi |
|-----------------------------|--------------------------------------|
|                             | No. of patients | %        |
| Overall histopathological discordance | 816             | 17.89    |
| Seborrheic keratosis        | 470             | 10.30    |
| Basal cell carcinoma        | 64              | 1.40     |
| Vascular tumor              | 53              | 1.16     |
| Fibroma                     | 43              | 0.94     |
| Epidermoid cyst             | 34              | 0.75     |
| Wart                        | 30              | 0.66     |
| Melanoma                    | 24              | 0.53     |
| Bowen’s disease             | 16              | 0.35     |
| Squamous cell carcinoma     | 4               | 0.09     |
| Keratoacanthoma             | 2               | 0.04     |
| Othera                      | 76              | 1.67     |

aOther include nine granuloma, six sebaceous hyperplasia, six scar, four lichenoid keratosis, one Darier disease, two xanthogranuloma, five dermatitis, three blood blister, two venous lakes, one folliculitis, one cutaneous amyloidosis, one mucinosis, one solar keratosis, one trichilemmal cyst, two lichen sclerosus et atrophicus, four fibrous papule of nose, two Fordyce disease, three hamartomas, one mixed tumor, four trichoepithelioma, four pilomatricoma, two syringoma, one poroma, one hidradenoma, one sebaceaoma, one plexiform schwannoma, one xanthoma, three lymphangioma, one clear cell acanthoma, one dermal duct tumor, and one steatocystoma.

among lesions with histopathological concordance ($p < 0.001$; Table 3). Therefore, sex, age, location of the lesion, and reasons for removal all have a potential effect on misclassification.

In further detail, male sex was significantly associated with a change in diagnosis to seborrheic keratosis, basal cell carcinoma, Bowen’s disease, and wart ($p < 0.001$; Table 3 and Supplementary Table 1). However, sex had no effect on the change in diagnosis to melanoma (Table 3). Old age was significantly correlated with changes in diagnosis to seborrheic keratosis, basal cell carcinoma, melanoma, Bowen’s disease, squamous cell carcinoma, keratoacanthoma, epidermoid cyst, and wart ($p < 0.001$; Table 3 and Supplementary Table 1). Furthermore, lesions on the trunk and limbs were significantly associated with a change in diagnosis to seborrheic keratosis (48.51%), lesions on the head and neck were significantly associated with a change in diagnosis to basal cell carcinoma (92.19%), lesions on the hands and feet were significantly associated with a change in diagnosis to melanoma (62.50%), and lesions on the perineum and buttocks were significantly associated with changes in diagnosis to Bowen’s disease (62.50%) and wart (26.67%), compared with 20.00, 70.17, 7.61, and 2.22%, respectively, in patients with histopathological concordance (Table 3 and Supplementary Table 1). More importantly, in addition to atypical clinical features, the percentages of lesions removed due to lesion changes (16.76%) and repeated stimulation (12.50%) were significantly higher among lesions with a change in diagnosis to melanoma than among lesions with a histopathological concordance (0.48 and 3.90%, respectively; Table 3). Therefore, clinical characteristics and reasons for removal have a potential impact on misclassification.
TABLE 3 | Clinical characteristics of patients with histopathological concordance or histopathological discordance.

| Characteristic                      | Overall histopathological concordance (N, %) | Overall histopathological discordance (N, %) | P-value | Seborrheic keratosis (N, %) | Basal cell carcinoma (N, %) | Melanoma (N, %) | Bowen's disease (N, %) | Squamous cell carcinoma (N, %) | Keratoacanthoma (N, %) | P-value |
|------------------------------------|--------------------------------------------|--------------------------------------------|---------|-----------------------------|-----------------------------|--------------------------|-----------------------------|--------------------------------|-----------------------------|---------|
| Number                             | 4,561                                     | 3,745                                     |         |                             |                             |                          |                             |                                |                             |         |
| 82.11%                             | 17.89%                                    | 10.30%                                    | 1.40%   | 0.53%                       | 0.35%                       | 0.09%                    | 0.04%                       |                                |                             |         |
| Sex                                |                                            |                                            |         |                             |                             |                          |                             |                                |                             |         |
| Male                               | 1,459                                     | 1,099                                     | <0.001  |                             |                             | 0.031                    | 0.077                       |                                |                             | 0.721   |
| 31.99%                             | 29.35%                                    | 44.12%                                    | 42.77%  | 57.81%                      | 45.83%                      | 81.25%                   | 50.00%                      | 50.00%                         |                             | 1.000   |
| Female                             | 3,102                                     | 2,646                                     | <0.001  |                             |                             |                          |                             |                                |                             | 0.007   |
| 68.01%                             | 70.65%                                    | 55.88%                                    | 57.23%  | 42.19%                      | 54.17%                      | 18.75%                   | 50.00%                      | 50.00%                         |                             |         |
| Age                                |                                            |                                            | <0.001  |                             |                             |                          |                             |                                |                             |         |
| Mean                               | 31                                        | 27                                        | 45      | 48                          | 55                          | 50                       | 43                          | 49                            | 63                          |         |
| Range                              | 2–60                                      | 2–80                                      | 2–86    | 2–86                        | 21–80                       | 17–73                    | 25–69                       | 34–64                         | 50–76                       |         |
| <60                                | 4,346                                     | 3,689                                     | 657     | 376                         | 28                          | 14                       | 12                          | 2                             | 1                           |         |
| ≥60                                | 215                                       | 56                                        | 159     | 94                          | 25                          | 10                       | 4                           | 2                             | 1                           |         |
| Location                           |                                            |                                            | <0.001  |                             |                             |                          |                             |                                |                             | 0.723   |
| Head and neck                      | 3,021                                     | 2,628                                     | 393     | 218                         | 59                          | 1                        | 1                           | 4                             | 2                           | 1.000   |
| 66.24%                             | 70.17%                                    | 48.16%                                    | 46.38%  | 92.19%                      | 4.17%                       | 6.25%                    | 100.00%                     | 100.00%                        |                             |         |
| Trunk and limbs                    | 1,081                                     | 749                                       | 332     | 228                         | 3                           | 6                        | 3                           | 0                             | 0                           |         |
| 23.70%                             | 20.00%                                    | 40.69%                                    | 48.51%  | 4.69%                       | 25.00%                      | 18.75%                   | 0.00%                       | 0.00%                         |                             |         |
| Perineum and buttocks              | 141                                       | 83                                        | 58      | 18                          | 2                           | 2                        | 10                          | 0                             | 0                           |         |
| 3.09%                              | 2.22%                                     | 7.11%                                     | 3.83%   | 3.13%                       | 8.33%                       | 62.50%                   | 0.00%                       | 0.00%                         |                             |         |
| Hands and feet                     | 318                                       | 285                                       | 33      | 6                           | 0                           | 15                       | 2                           | 0                             | 0                           |         |
| 6.97%                              | 7.61%                                     | 4.04%                                     | 1.28%   | 0.00%                       | 62.50%                      | 12.50%                   | 0.00%                       | 0.00%                         |                             |         |
| Reason for removal                 |                                            |                                            | <0.001  |                             |                             |                          |                             |                                |                             | 0.018   |
| Atypical clinical features         | 2152                                      | 1566                                      | 586     | 328                         | 54                          | 16                       | 13                          | 4                             | 2                           | 0.094   |
| 47.18%                             | 41.82%                                    | 71.81%                                    | 69.79%  | 84.38%                      | 66.67%                      | 81.25%                   | 100.00%                     | 100.00%                        |                             |         |
| Changes in skin lesions            | 30                                        | 18                                        | 12      | 3                           | 4                           | 4                        | 4                           | 0                             | 0                           |         |
| 0.86%                              | 0.48%                                     | 1.47%                                     | 0.64%   | 6.26%                       | 16.67%                      | 0.00%                    | 0.00%                       | 0.00%                         |                             |         |
| Cosmetic requirements             | 2225                                      | 2015                                      | 210     | 139                         | 6                           | 1                        | 3                           | 0                             | 0                           |         |
| 48.78%                             | 53.81%                                    | 25.74%                                    | 29.57%  | 9.38%                       | 4.17%                       | 18.75%                   | 0.00%                       | 0.00%                         |                             |         |
| Repeated stimulation               | 154                                       | 148                                       | 8       | 0                           | 0                           | 0                        | 0                           | 0                             | 0                           |         |
| 3.38%                              | 3.90%                                     | 0.98%                                     | 0.00%   | 0.00%                       | 12.50%                      | 0.00%                    | 0.00%                       | 0.00%                         |                             |         |

*aDemographic comparison was made between the overall histopathological concordance group and histopathological discordance group.*
**DISCUSSION**

Melanocytic nevi are the most common benign neoplasms of the skin and are also the most easily misdiagnosed skin disease (5). Our study collected excised lesions clinically diagnosed as melanocytic nevi in a Chinese population over 5 consecutive years. The results showed that the consistency of the clinical and histopathological diagnoses of melanocytic nevi was 82.11% after the histopathological examination. Among them, 90.25% were common acquired melanocytic nevi, and 9.75% were other benign melanocytic neoplasms, such as congenital nevomelanocytic nevi, blue nevi, and lentigo. More importantly, 17.89% of patients were reclassified as having other diseases after the histopathological examination. The most common diagnostic change was to seborrheic keratosis, followed by basal cell carcinoma. Overall, 24 (0.53%) patients were reclassified as having melanoma. In addition, clinical characteristics, such as sex, age, and location of the lesion, and the reasons for removal have a potential impact on misclassification.

Morphologically, common acquired melanocytic nevi are challenging to distinguish from other benign melanocytic neoplasms (8). Our study found that, among the cases with histopathological concordance, 9.75% were other types of benign melanocytic neoplasms. In addition, the results showed that younger age was significantly associated with the histopathological diagnosis of congenital nevomelanocytic nevus and Spitz nevus, compared with common acquired melanocytic nevi. The reason for the clinical significance of congenital nevomelanocytic nevus (CMN) is the risk of malignancy (9). The malignancy potential of CMN is well-characterized in congenital melanocytic giant nevi (10). However, the possibility of melanoma development has also been clearly verified for medium and small nevi (11). Spitz nevus is predominantly observed in children and adolescents. In children, a Spitz nevus presents as isolated, dome nodules with a smooth surface and a bright red to brown color. In adults, a Spitz nevus is usually dark in color with brown to black papules, nodules, and nodes (12–14). Because of the difficulty of the clinical diagnosis of Spitz nevus, histopathological examination is necessary (15, 16). Therefore, patients should be asked for a detailed medical history, and lesions in younger patients should be differentiated from congenital nevomelanocytic nevus and Spitz nevus. “Dysplastic” melanocytic nevus, also known as atypical melanocytic nevus, is unusually large and variable in form and shows atypical asymmetry, size, borders, and coloration (7). Moreover, “dysplastic” melanocytic nevus is challenging to distinguish from common acquired melanocytic nevi and melanoma (17). Importantly, it has been reported that melanoma can develop in “dysplastic” melanocytic nevi with a probability of 1:200 to 1:500 and that the presence of several “dysplastic” melanocytic nevi increases the melanoma risk (3). Our data found that the percentage of “dysplastic” melanocytic nevus lesions occurring on the lower limbs was higher than that in patients with a histopathological diagnosis of common acquired melanocytic nevi. Therefore, lesions on the lower limbs with atypical clinical features should be given a detailed physical examination and carefully differentiated from common acquired melanocytic nevi.

In this study, 17.89% of lesions were reclassified as other diseases after the histopathological examination. The most common diagnostic change was seborrheic keratosis, a common benign epidermal tumor (18). Seborrheic keratosis is generally a roundish, scaly, reddish to brownish lesion; it is most common in individuals over 50 years old (19, 20). Clinically, seborrheic keratosis can mimic the appearance of melanocytic tumors (21). Our study found that male sex, older age, and location of the lesions on the trunk and limbs have a potential impact on the misclassification of seborrheic keratosis. Thus, skin lesions with the above-mentioned characteristics should be differentiated from seborrheic keratosis. More importantly, after the histopathological examination, 1.89% of patients were reclassified as having non-melanoma skin cancer (NMSC), including 64 with basal cell carcinoma, 16 with Bowen’s disease, four with squamous cell carcinoma, and two with keratoacanthoma. NMSC is the most common human cancer, and sun exposure is an important risk factor for this disease (22). In addition, it has been reported that the incidence of NMSC is higher in men than in women, and 80% of cases occur in people aged 60 years and older (23). Basal cell carcinomas are usually small and have a translucent or pearly appearance (24, 25). Approximately 80% of all basal cell carcinomas occur on the head and neck. Unlike basal cell carcinomas, squamous cell carcinomas can have precursor lesions, such as actinic keratosis and Bowen’s disease (26), and typically develop on sun-exposed sites. These studies support our findings. Our study found that male sex was significantly associated with changes in diagnosis to basal cell carcinoma and Bowen’s disease. Old age and sun-exposed sites (head and neck) have a potential impact on the misclassification of NMSC, except for Bowen’s disease. Lesions on the perineum and buttocks were significantly related to a change in diagnosis to Bowen’s disease. Therefore, melanocytic nevi-like lesions in elderly and/or male patients and on sun-exposed skin should be carefully differentiated from basal cell carcinoma and squamous cell carcinoma, and lesions on the perineum and buttocks should be differentiated from Bowen’s disease.

The most important task in the diagnosis of melanocytic nevi is to differentiate these lesions from melanoma. We found that 24 patients were reclassified as having melanoma after the histopathological examination. Sex had no effect on misclassification. However, older age and lesions on the hands and feet were significantly related to a change in diagnosis to melanoma, which might be related to the characteristics of melanoma in China. The incidence of cutaneous melanoma is rising faster than that of any other solid tumor (27, 28). Superficial spreading melanoma is the most common type of cutaneous melanoma in Caucasians (29). However, acral melanoma is a common subtype of melanoma in Chinese patients, while it is rare in Caucasian patients (30–33). Melanoma can develop from pre-existing nevi in approximately 20–40% of cases (34). Early diagnosis is the key to improving the survival rate (35). The ABCDE rules (asymmetry, border irregularity, color variegation, diameter, and evolution) are useful for the early identification of melanoma (36). In addition, dermatoscopy
improves diagnostic accuracy, particularly in the differential diagnosis between benign and malignant melanocytic tumors. Furthermore, the results showed that, in addition to atypical clinical features, the percentage of lesions removed due to lesion changes and repeated stimulation was significantly higher in lesions whose diagnosis was changed to melanoma than in lesions with histopathological concordance. Therefore, our study shows that melanocytic nevi should be differentiated from melanoma in elderly patients when the lesions are in load-bearing and friction-prone sites or in the event of changes or repeated stimulation.

In summary, our data demonstrate that histopathological review results in a change in diagnosis in 17.89% of patients with clinical characteristics that raise the clinical suspect and be carefully differentiated from malignant tumors.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the ethics committees of Xiangya hospital of Central South University, Changsha, Hunan, China. Written informed consent to participate in this study was provided by the participants’ legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

PL performed the study design, data analysis, and manuscript writing. XZ, MC, XC, JL, and CP contributed to data collection and validation. YK, MC, and XC performed the clinical diagnosis and samples collection. JS, YK, and WZ were clinical experts and performed the manuscript revision. All authors read and approved the final version of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2021.681668/full#supplementary-material

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