Spitz/Reed nevi: proposal of management recommendations by the Dermoscopy Study Group of the Italian Society of Dermatology (SIDeMaST)


GUIDELINES

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Spitz nevus is a benign melanocytic neoplasm mostly appearing in the pediatric age and clinically consisting of a single, pink, red or brown papule, mainly observed on the face and limbs and characterized by an initially rapid growth. Reed nevus is the pigmented variant of Spitz nevus, which appears more frequently on lower limbs and has equally dynamic morpho-evolutive aspects.

Histopathologically, both Spitz and Reed nevi are typified by a proliferation of large epithelioid and/or spindle-like melanocytes. Therefore, the 2 entities will hereafter be referred to under the “umbrella” term “Spitz/Reed nevus”.

The diagnosis of the most typical variants of Spitz/Reed nevus does not generally pose any problems of interpretation, especially in the pediatric age. On the other hand, the diagnosis of atypical forms is more complex, due to the morphologic overlap with atypical Spitz/Reed tumor and Spitzoid melanoma. The latter is particularly relevant for Spitz/Reed nevi arising in adults.

Recent advances in the histopathologic classification of Spitz/Reed nevi have improved the reliability of microscopic diagnosis, narrowing the interpretative “grey areas”. Furthermore, the gradually acquired experience in the use of dermoscopy and videodermoscopy along with data provided from longitudinal studies concerning the evolution of Spitz/Reed nevi facilitated the more accurate
diagnosis and appropriate management of pediatric Spitz/Reed nevi.\textsuperscript{12-14}

By combining the existing evidence and our own experience, our purpose was to provide a comprehensive summary on the clinical and dermoscopic characteristics of Spitz/Reed nevi, aiming to allow clinicians better diagnosis and management of Spitzoid lesions.

A still open debate

Spitzoid lesions are generally characterized by an extremely dynamic clinical and dermoscopic evolution in the course of time. Their rapid morphologic alterations often force clinicians to excise the lesions in order to resolve their diagnostic uncertainty by histopathologic examination. The introduction of confocal microscopy may constitute a valuable and promising alternative to histopathologic examination, even if its use is still limited to a restricted number of Italian hospitals. Despite the improvement of histopathologic and immunohistochemical techniques and the experience that pathologists have acquired in evaluating Spitzoid lesions, the debate about the accurate classification of Spitzoid neoplasms is still open. In fact, several attempts to reach a consensus on the “grey areas” – constituted by Spitzoid lesions of more complex interpretation – has so far resulted in the suggestion of a “case by case” evaluation, integrating clinical and histopathologic information.

Spitzoid lesions represent an articulate complex of entities with different biologic behavior, with the completely benign Spitz/Reed nevus at the one edge and Spitzoid melanoma at the other, while the malignant potential of atypical Spitzoid lesions that lay in between is uncertain and controversial. This causes significant difficulties in their interpretation and results in a great heterogeneity of management strategies.

A recent paper\textsuperscript{15} has shown that 95.8% of American dermatologists consider Spitz/Reed nevus a benign entity and recommend classification up in about 50% of cases. However, the criteria warranting excision were not clearly discussed, not allowing the development of a management plan applicable in the clinical practice.

Our suggestions are based on existing evidence, as well as on the experience our research team has acquired over the years. Our aim was not to thoroughly review the controversial topic of histopathologic criteria, but mainly to focus on the “clinical” issue, providing clinicians practical recommendations on the interpretation of the clinical and dermoscopic characteristics of Spitzoid lesions and on the management decision.

Age is crucial

As strongly supported by existing data, the most crucial parameter in the evaluation of Spitzoid lesions is age. Specifically, the possibility that a Spitzoid-looking lesion is a melanoma linearly increases after puberty, while it is extremely low before 12 years of age. This has led to the recommendation that a Spitzoid-looking lesion developing in the postpubertal age should be excised to exclude melanoma. The threshold of 12 years is supported from statistical and epidemiological considerations. Particularly, by applying Bayes’s rule to differentiate between Spitz/Reed nevus and melanoma, Vollmer \textit{et al.}\textsuperscript{16} showed that the a priori possibility to diagnose Spitz/Reed nevus vs melanoma is high in subjects under 12 years of age, sharply decreasing after this threshold.

Actually, the discrimination of patients with Spitzoid lesions in 2 age groups is also supported by different clinical and dermoscopic characteristics between them. In detail, Spitzoid lesions in prepubertal children usually exhibit a more typical morphologic aspect and clinical course. Nevi deviating the typical morphologic criteria or undergoing unexpected evolution and, thus, prompting clinicians to excise them, are uncommon in this age group. In contrast, Spitzoid lesions in individuals after puberty are often more troublesome to interpret from a clinical and dermoscopic point of view. Surgical excision of Spitzoid lesions is the rule in the latter age group, but even histopathologic examination may be insufficient to establish an accurate diagnosis.

Although age represents a crucial parameter in the interpretation of Spitzoid lesions, this should not mislead clinicians to underestimate cases of prepubertal melanoma. Pediatric melanoma, albeit uncommon, does exist and its early diagnosis and appropriate management have a substantial impact on patient’s health. Effectively, the dual goal of clinicians when evaluating spitzoid lesions under the age of 12 is not to miss the rare cases of melanoma,
while minimizing the rate of nevi misinterpreted and managed as melanoma. The latter is particularly relevant since melanoma management includes surgical procedures with significant burden on patient’s health, such as the complete lymph node dissection following a positive sentinel lymph node biopsy. Especially in childhood, both under- and over-diagnosis of melanoma result in important physical, social, ethical and legal consequences.

**Dynamic of Spitzoid lesions**

The benign natural evolution of Spitz/Reed nevus is well-documented, while few described cases of metastatic diffusion with deadly outcome were more likely melanoma not accurately diagnosed. Typically, after a rapid growth phase, Spitz/Reed nevus stabilizes and gradually enters an involutive process. This evolution characterizes both pigmented and amelanotic forms and partially explains the reason why Spitz/Reed nevi are uncommon in adults, making the detection of a Spitzoid lesion in the adult age even more alarming. Effectively, given that a Spitz/Reed nevus showing “typical” aspects in prepubertal age is likely to regress spontaneously, only follow-up should be deemed necessary. A surgical excision should be considered only in case of peculiar clinical and/or dermoscopic characteristics that do not fit the typical aspect of a Spitz/Reed nevus. Avoiding unnecessary surgical procedures is particularly useful in children, considering that the pediatric patient generally shows little compliance to surgery, often requiring general anesthesia or sedation. Moreover, surgery entails the risk of complications and unaesthetic scars that may turn out to be problematic in the adult age. Postsurgical complications might be significantly more severe in case of sentinel lymph node biopsy, which may result positive in Spitz/Reed nevi, and especially in case of completion lymph node dissection. Finally, legal consequences cannot be ruled out if the surgical procedures were based on no other indication than the diagnosis of a typical Spitz/Reed nevus.

**Size of the lesions**

The decision to excise a Spitzoid lesion in the pediatric age should be based on the presence on morphologic or evolutional parameters that exceed standards of “relative normality”.

The first factor reported is the size, with lesions exceeding 8 mm of larger diameter warranting excision. The diameter of Spitz/Reed nevi is usually equal to or less than 6 mm, while a growth beyond 10 mm has been reported in the literature as uncommon and suspicious. An intermediate value of 8 mm constitutes an acceptable threshold and has been considered a valid discriminant dimensional factor in previous studies.

**Palpability**

Nodular spitzoid lesions merit special attention. A nodular lesion of recent onset is by definition suspicious, especially when it dermoscopically lacks the characteristic regular distribution of monomorphous dotted vessels that typifies Spitz/Reed nevi. Although large irregular, polymorphous and asymmetricaly distributed vessels have also been described in the context of Spitz/Reed nevi, the presence of the latter criteria is generally suggestive of melanoma. The presence of micro ulcerations is an additional warning sign, as they indicate a thinning of the epidermis due to the rapid proliferation of the underlying lesion.

**Dermoscopic patterns**

Dermoscopically, Spitz/Reed nevi display two predominant patterns, namely globular and starburst. The former is more frequently associated with Spitz nevi while the latter characterizes Reed nevi, even though this distinction, as explained above, might be practically irrelevant. Less common dermoscopic patterns include the homogeneous black pattern, the homogenous pink pattern (characterized by dotted or irregular vessels), and the inverse network pattern. The latter is characterized by interconnected hypopigmented serpiginous lines which form a network that circumscribes irregular pigmented globular-like structures or dotted vessels and which can be associated with crystalline or chrysalis structures. However, in about 20% of cases, Spitz/Reed nevi may dermoscopically exhibit a multicomponent or atypical pattern, characterized by an asymmetric distribution of structures and colors and by pigmentation...
structures similar to the white-blue veil. The evidence of asymmetric growth is often considered an indicator of histopathologic atypia.

The frequency of different dermoscopic patterns of Spitz/Reed nevi and their histopathologic correlation was investigated by Ferrara et al. The authors found a higher frequency of the globular pattern in the “classic-desmoplastic” Spitz nevus, while the starburst pattern was more typical of pigmented Spitz nevus, Reed nevus and Spitz/Reed nevus. An important finding of the latter study was the high frequency of the “multicomponent” pattern among histopathologically atypical Spitz nevi. Pellacani et al. investigated the correlation among dermoscopic, histopathologic and confocal microscopic findings of Spitz nevus, Clark nevus and melanoma. According to their results, the most frequent dermoscopic patterns of Spitz nevi were the starburst, the globular, and the multicomponent, followed by the reticular/homogeneous and the inverse network pattern. Of note, a reticular/homogeneous or a multicomponent pattern was observed mostly in lesions suggestive of melanoma by means of confocal microscopy.

Location

Although there is no evidence that the risk of melanoma depends on the anatomical site, the management of Spitzoid lesions might also be influenced by their localization on specific body sites. First, we recommend the excision of lesions located on anatomical sites not typical for a Spitz/Reed nevus according to what has been reported in the literature and observed in the clinical practice (head, neck, lower limbs). Our recommendation is in agreement with other investigators suggesting excision of scalp, acral and genital Spitzoid lesions, because they are often associated with cytologic and architectural atypias. Furthermore, in our experience, Spitzoid lesions on special body areas often deviate the usual dermoscopic features of Spitz/Reed nevus, complicating the clinical diagnosis and management. For instance, the specific anatomic architecture of the acral skin might result into an atypical dermoscopic pattern of an acral Spitz nevus, posing significant problems in its accurate diagnosis and regular follow-up.

In addition, early surgical excision of Spitzoid lesions located on surgically troublesome body sites, such as the nose or the eyelids, might also be recommended. This suggestion is based on the experience of our group and aims to prevent more complicated surgical interventions that would be required if the lesion grows during follow up.

Special variants

Finally, we recommend excision of lesions whose clinical and/or dermoscopic characteristics are suggestive of a “special” Spitz variant (i.e., verrucous, desmoplastic, and angiomatoid). The clinical management of these subtypes might be troublesome, as they often deviate from the “standard” diagnostic criteria and natural course of Spitz/Reed nevus. In a previous study, we excised a verrucous nevus showing several typical criteria (dotted vessels, inverse network) but displaying a global architecture not fitting the diagnosis of Spitz/Reed nevus. Similarly, a combined lesion consisting of a Spitz/Reed nevus and a common nevus described by Duncan et al. was histopathologically characterized by a high degree of cytologic atypia, increased cellularity, loss of symmetry and an increase of mitotic figures.

Conservative approach in children

According to our recommendations, a conservative management strategy should be applied in the vast majority of Spitzoid lesions in childhood. However, we strongly recommend their regular follow-up in order to enable the detection of spitzoid melanomas that may appear small and morphologically regular at baseline visit, but exhibit signs of irregular or excessive growth during monitoring. In line with previous evidence, we suggest a 3 to 6 month period as the optimal follow up interval.

An excessive dimensional growth (beyond 8 mm), a tendency not to stabilize (typically, the appearance of globules of different dimension and color), or the detection of one or more of the previously described morphologic features at any time during follow-up, should warrant excision of the lesion.

As mentioned above, the expected evolution of Spitz/Reed nevi includes a stabilization phase followed by a slow involution until their disappearance. Therefore, in children younger than 12, a Spitz nevus showing “typical” aspects should be dermoscopically monitored until its stabilization, which often
Conclusions

Spitzoid lesions are a diagnostic challenge for dermatologists, since they represent a group of morphologically similar entities whose biological behavior ranges between the benign Spitz/Reed nevus and the potentially lethal spitzoid melanoma. The studies carried out in the last few years have only partially clarified the discrepancies on interpretation of atypical Spitzoid lesions. The advances of immunohistochemical and biomolecular techniques have so far been able to shed light to the controversy and provide clinicians with useful information for the diagnostic approach and appropriate management of Spitzoid tumors.

Based on existing evidence and our experience, we aimed to provide decision-making criteria that could enhance clinicians to adopt a more homogeneous diagnostic and management path of Spitzoid tumors.

Management flow-chart

Summarizing the aforementioned recommendations, which are based on existing evidence and the experience of our group of experts, we present a management flow-chart for Spitzoid lesions (Figure 1). Taking into account the subject’s age, history and the lesion’s clinicodermoscopic morphologic characteristics, the chart could represent a practical guide, helping dermatologists in the management of Spitzoid lesions in daily practice.

It should be further underlined that, in order to be useful in daily practice, our recommendations should often be adjusted by the clinician in the context of each individual patient.
References


Conflicts of interest.—The authors certify that there is no conﬂict of interest with any ﬁnancial organization regarding the material discussed in the manuscript.

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