Successful treatment of adult-onset auricular agminated Spitz nevi with cryotherapy: A case report with an 11-year follow-up and literature review

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INTRODUCTION

Spitz nevus is a commonly acquired melanocytic neoplasm that typically appears on the face and extremities. Multiple Spitz nevi are rare and can be classified as agminated/clustered or disseminated.[1] Agminated Spitz nevi (ASN) represent multiple grouped and localized Spitz nevi, often observed on the face and arms.[1,2] Genetic anomalies associated with ASN include mosaic mutations and oncogene translocations.[3] Given the absence of recommendations for treating adult-onset ASN, we reviewed the literature on treatment options and present a case of adult-onset auricular ASN successfully treated with cryotherapy.

Abbreviation used:

ASN: agminated Spitz nevi

CASE REPORT

A 21-year-old healthy Chinese woman presented with multiple pruritic erythematous round papules on the right side of the superior auricular region that gradually appeared over 20 months. On examination, there was an indurated erythematous plaque, measuring 5.5 × 4.2 cm, with irregular and poorly defined borders involving the right superior helix, helical crus, and antihelix (Fig 1, *A*). Within the plaque, some of the dome-shaped papules had verrucous surfaces.

Histopathology of the 2 verrucous lesions revealed dermal nests composed of spindle-shaped cells with occasional melanin pigments and minimal cellular atypia (Fig 2, *A-C*). Immunohistochemical analysis revealed strong positivity for S100 and p16, weak positivity for Melan-A, and scattered but minimal positivity for HMB-45. The Ki-67 index was approximately 1%. Accordingly, ASN was diagnosed.

After discussion, the patient underwent cryotherapy treatment every 2 weeks for 8 treatment sessions. During each session, cryotherapy was performed with liquid nitrogen using cotton-wool swabs until a 1-2−mm frozen halo appeared around the base of the lesion (usually after 4-6 s). Multiple freezing cycles (up to 2-3) were performed in each session, and thawing was achieved between sessions. The procedure was well tolerated, except for mild pain. The patient was then followed up every 6 months for 2 years, followed by annual visits. The papules largely disappeared 4 months after treatment (Fig 1, *B*). At the 11-year follow-up, there was no clinical evidence of recurrence, with only mild postinflammatory dyschromia observed (Fig 1, *C*). The patient was highly satisfied with the outcome.

DISCUSSION

ASN is a benign condition, and no malignant transformation of ASN has been reported to date. However, given the known possibility of malignant transformation and unclear biologic behaviors over time, long-term clinical follow-up for ASN and

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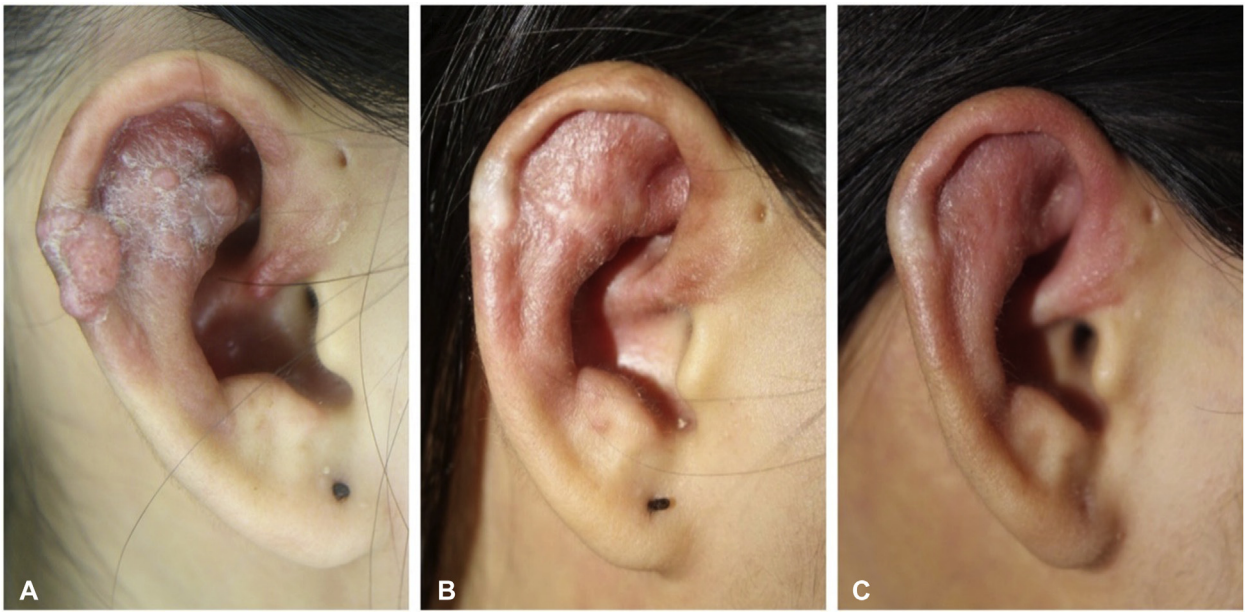

Fig 1. Clinical progression of agminated Spitz nevi with cryotherapy. **A,** At presentation, one indurated irregular erythematous plaque was observed with overlying *round* erythematous *dome-shaped* papules of variable sizes, some of which had verrucous surfaces. **B,** Four months after cryotherapy treatment, a significantly reduced number of papules was observed. **C,** At the 11-year follow-up, no clinical evidence of recurrence with mild postinflammatory hyperpigmentation and hypopigmentation was observed.

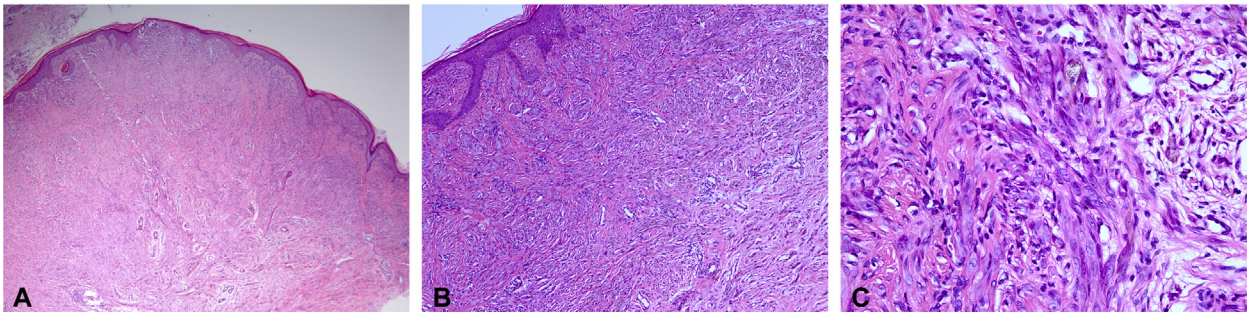

Fig 2. Hematoxylin-eosin staining of agminated Spitz nevi (ASN).Histopathology of the auricular lesions showed mild epidermal hyperplasia and numerous dermal nests composed of epithelioid and spindled cells with occasional melanin pigments (**A-C,** Hematoxylin-eosin stain; original magnification: **A,** ×4; **B,** ×10; **C,** ×40).

biopsies of changing or atypical lesions are recommended. Although clinical observation without treatment is considered safe for ASN, treatment may be desired in certain cases, especially for cosmetically sensitive areas. Our literature review identified several procedural and pharmacologic interventions for ASN, including surgical excision with or without a skin graft, electrodesiccation, cryotherapy, and the use of crizotinib, a multi-targeted tyrosine kinase inhibitor.[3,4] The undertaking of nonsurgical techniques such as cryotherapy of Spitzoid melanocytic neoplasms rests on accurate diagnosis and exclusion of similar neoplasms that have uncertain or malignant biologic behavior, such as Spitz tumors and Spitzoid melanomas.

Surgical excision is often curative and has been utilized for ASN on the extremities, trunk, and cosmetically sensitive areas, such as the face. However, complete excision is not always feasible,[5] and recurrence after excision has been reported.[3,6] Clinical presentation and histopathologic features should be considered when determining the follow-up duration and frequency of postoperative monitoring. One case of temporary clearance with electrodesiccation was reported for a 9-year-old girl with over 20 lesions of ASN on her upper portion of

the right arm since birth, but all lesions returned 8 years after treatment.[4] This suggests that electrodesiccation may be considered but does not result in long-term clinical remission. The use of crizotinib-targeted therapy (280 mg/m^2 twice daily) was reported in a 30-month-old girl with unresectable ASN and known *GOPC-ROS1* kinase fusion.[3] Complete flattening of the periocular, scalp, and auricular lesions to faintly pigmented macules was achieved after 20 weeks of treatment. Crizotinib was well tolerated, apart from mild nausea and vomiting, but a nasogastric tube was required for drug administration, and lesions reappeared gradually following treatment.

Cryotherapy has been used for a variety of dermatologic and nondermatologic benign tumors.[7] The main antitumor effects of cryotherapy are based on direct cellular injury, tissue ischemia from vascular damage, and the subsequent release of antigenic materials leading to immunologic activation.[7] Based on our literature review, only one case of a 21-year-old woman with 50 disseminated Spitz nevi was treated with cryotherapy to achieve excellent cosmetic results in 1979.[4] However, the frequency, duration, and long-term outcomes of the treatment were not reported. Given the cosmetically sensitive location of the auricle and the relatively large area of involvement of our patient's ASN, 8 cryotherapy treatments every 2 weeks were prescribed. The treatment was well tolerated, with no clinical recurrence 11 years after treatment.

There is evidence suggesting that spontaneous involution appears to be the most common biologic behavior in Spitz nevi.[8,9] It warrants consideration that our patient's lesions may have undergone spontaneous involution with possible provocation by cryotherapy. However, the patient presented with lesions that were still gradually growing both in size and number, which most likely represents the growth phase of her disease. In addition, all lesions exhibited significant improvement 4 months after the initial treatment, demonstrating the active role of cryotherapy. As the patient did not report visible blistering or skin necrosis following cryotherapy, we suspect that the antitumor effects from the sublethal thermal injury in benign melanocytic neoplasms might be because melanocytes are more sensitive to cryodamage in comparison with other skin cells.[10]

ASNs can be difficult to treat because of the number, size, and distribution of the lesions. We recommend that treatment interventions should be individualized, considering the number of lesions, anatomic locations, histopathologic findings, and the patient's age and preference. Based on the success of our case, we suggest that cryotherapy can be used as a reasonable and affordable treatment for ASN to achieve long-term clinical remission, especially in cosmetically sensitive areas, where large excisions are not desired. The efficacy and safety of this intervention should be further investigated in large-scale studies. A limitation of our case is that genome sequencing was not performed, and the clinical phenotype, along with the excellent response to cryotherapy, remains unexplained from a genetic perspective.

Conflicts of interest

None disclosed.

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