Two Cases of Multiple Spitz Nevi

Correlating Clinical, Histologic, and Fluorescence In Situ Hybridization Findings

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Background: The occurrence of multiple Spitz nevi is rare, especially the disseminated variant. Multiple Spitz nevi may be confused with, and must be differentiated from, primary spitzoid melanoma and cutaneous melanoma metastases. Over the past decade, fluorescence in situ hybridization (FISH) has emerged as a tool for studying melanocytic neoplasms, helping to differentiate between melanoma and benign melanocytic nevi. We describe 2 cases of patients with multiple Spitz nevi and their FISH results.

Observations: One case of disseminated Spitz nevi, in a 17-year-old female, showed balanced tetraploidy using FISH, while the other case, in a 51-year-old female with multiple Spitz nevi, showed normal diploid cells without significant gains or losses in chromosomes 6 or 11.

Conclusions: Patients may present with multiple, even disseminated, Spitz nevi. This phenotype should not be confused with melanoma and/or cutaneous metastasis. The use of FISH studies in context with careful correlation of clinical features and dermoscopic and histologic findings can assist in the diagnostic workup.

Arch Dermatol. 2011;147(2):227-231

S P I T Z N E V I A R E B E N I G N M E L A N O C Y T I C P R O L I F E R A T I O N S W I T H D I S T I N C T H I S T O L O G I C F E A T U R E S . T h e y u s u a l l y p r e s e n t a s s o l i t a r y l e s i o n s , b u t s o m e p a t i e n t s d e v e l o p m u l t i p l e l e s i o n s . M u l t i p l e S p i t z n e v i m a y p r e s e n t w i t h a n a g m i n a t e d p a t t e r n o r w id e l y s c a t t e r e d o v e r d i f f e r e n t p a r t s o f t h e b o d y . I n d i v i d u a l l e s i o n s o f S p i t z n e v i t y p i c a l l y p r e s e n t a s r e d o r p i n k d o m e - s h a p e d p a p u l e s t o b r o w n o r b l a c k m a c u l e s . W h i l e m o s t c o m m o n l y f o u n d i n c h i l d r e n y o u n g e r t h a n 1 0 y e a r s o n t h e h e a d , t r u n k , o r e x t r e m i t i e s , t h e y c a n a l s o b e s e e n i n a d u l t s . M o r e t h a n 4 2 c a s e s o f t h e a g m i n a t e d t y p e h a v e b e e n d e s c r i b e d , o c c u r r i n g m o s t f r e q u e n t l y o n t h e f a c e , b a c k , a n d e x t r e m i t i e s . T h e d i s s e m i n a t e d v a r i a n t i s t h e m o s t r a r e , w i t h o n l y 1 5 c a s e s r e p o r t e d i n t h e l i t e r a t u r e . F I S H , w h i l e t h e o t h e r c a s e , i n a 5 1 - y e a r - o l d f e m a l e w i t h m u l t i p l e S p i t z n e v i , s h o w e d n o r m a l d i p l o i d c e l l s w i t h o u t s i g n i f i c a n t g a i n s o r l o s e s .

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These cases can be challenging to interpret from a clinical and histologic perspective, and distinction from melanoma or melanoma with multiple epidermotropic metastases is critical. Cutaneous metastases has a poor prognosis and is staged as either IIIB or IIIC for in-transit disease if localized to an anatomic region, or stage IV for distant cutaneous metastases according to the most current American Joint Committee on Cancer Staging system. The 5-year survival rate is less than 25%, with almost no 10-year survivors. In contrast, the disseminated variant of Spitz nevi is entirely a benign entity, with no reports of malignant transformation or disease progression. Hence, the importance of recognizing and differentiating between the 2 must be stressed to avoid unnecessary diagnostic procedures and therapeutic interventions.

Fluorescence in situ hybridization (FISH) is evolving to become a routine diagnostic tool for the evaluation of melanocytic lesions. FISH findings in malignant melanomas include frequent imbalanced clonal chromosomal alterations. While most Spitz nevi are karyotypically normal, approximately 5% to 10% may have balanced gains with tetraploidy, and approximately 20% may have an isolated gain in chromosomal locus 11p. We describe 2 cases of patients with multiple Spitz nevi, 1 of which was found to have balanced tetraploidy by FISH, the other with normal diploid cells without significant gains or losses.

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The first patient was part of an earlier study looking at incidence of polyploidy in Spitz nevi. We review how the clinical and histologic features, along with the FISH results, confirm the diagnosis of disseminated Spitz nevi in these 2 patients.

REPORT OF CASES

CASE 1

A 17-year-old female of Italian descent was referred to the Pigmented Lesions Clinic at the Department of Dermatology, Northwestern University, Chicago, Illinois, in late 2007 with multiple pink and brown dome-shaped papules. All lesions had appeared during the 1 year prior to presentation. Several lesions were first noted on her elbows and buttocks as pink to tan macules. She continued to develop more lesions over the next 10 months as many became enlarged to raised dome-shaped papules. The lesions seemed to be precipitated by sun exposure.

Typical lesions from the first patient showed epithelial hyperplasia surmounting a symmetric proliferation of epithelioid and spindled-shaped melanocytes arranged in nests and vertically oriented fascicles with occasional Kamino bodies and good maturation (Figure 2A). Occasional nuclear atypia was noted (Figure 2B). All the biopsy specimens were reviewed by 2 dermatopathologists (J.G. and P.G.), and none of these lesions showed features concerning for malignant disease.

Four of these lesions were tested by FISH targeting 4 distinct loci and specific genes: 6p25 (RREB1), 6q23 (MYB), 11q13 (cyclin D1), and Cep6 (the centromeric portion of chromosome 6). Detailed methods have been reported in previous manuscripts. FISH analysis showed a significant population of tetraploid cells in 3 of 4 cases, while the fourth case showed typical diploid cells. The tetraploid cells showed balanced gains in 6p25 (RREB1), 6q23 (MYB), 11q13 (cyclin D1), and Cep6, with all cells having 3 or 4 identifiable copies of each chromosomal segment (Figure 2C-F). In each of these cases, tetraploidy was confirmed with a probe targeting the X chromosome, showing 4 copies (female) in the same regions in which copy number gains were identified with the original probe set. A diagnosis of disseminated Spitz nevi was rendered, and follow-up of the patient over the subsequent 2.5 years has been uneventful.

CASE 2

A 51-year-old white woman was referred to Memorial Sloan-Kettering Cancer Center (MSKCC), New York, New York, with a history of “atypical Spitz nevi/tumors.” Her first such lesion was removed from the groin at age 35 years. There was no associated preceding event prior to the development of that lesion. She had no family history of melanoma and was otherwise in good health.

Prior to her visit to MSKCC, the patient had a spitzoid melanocytic proliferation excised from the left buttock that had been reported as a “borderline Spitz tumor.” She then subsequently developed several additional pink papules on the left buttock, the right hip, and upper thigh (Figure 3A and B). Dermoscopic evaluation of these pink papules revealed the presence of irregular linear and serpentine blood vessels, both of which can be seen in melanoma (Figure 3, inset). Based on the medical history and clinical and dermoscopic examination, the clinical concern for a spitzoid melanoma with cutaneous metastases was raised. There was no lymphadenopathy or hepatosplenomegaly.

Four outside biopsy specimens were rereviewed, and 2 additional biopsy specimens were taken and examined histopathologically. All biopsy specimens were interpreted as being variants of Spitz nevus. The histologic appearance ranged from densely cellular compound melanocytic nevus with a predominant nested growth pattern at the dermoepidermal junction with Kamino bodies to sclerosing Spitz nevi, showing epithelioid melanocytes in a fibrotic dermal stroma, with lack of evidence...
of proliferation (a mitotic index of 0, a Ki-67 labeling index of <1%). Given the previously stated concerns by an outside pathologist about a “borderline” tumor and keeping in mind the diagnostic difficulty and controversy regarding the accurate diagnosis of spitzoid melanocytic tumors, FISH analysis was performed on 1 of the biopsy samples performed at MSKCC. The results of the analysis revealed normal diploid cells without significant gains or losses in chromosomes 6 or 11, a frequent site of genomic alteration in melanomas.

As with patient 1, the constellation of clinical and histologic findings was felt to fit best with an eruption of multiple Spitz nevi. To date, follow-up over the subsequent 1 year has been uneventful.

COMMENT

In the cases of Spitz nevi presenting with an agminated, eruptive, or disseminated pattern, it is important to ex-
Cutaneous metastases occur most frequently with primary tumors on the extremities, whereas the average age of patients with disseminated Spitz nevi is 23 years without clear lesion site predilections. Cutaneous pigmented metastases may clinically appear to be very similar to disseminated Spitz nevi, as small-to-medium dome-shaped papules or nodules that may be skin-colored, pink, brown, or black. The average age of patients with in-transit or cutaneous metastases is older than 50 years, and metastases occur most frequently with primary tumors on the lower extremity, whereas the average age of patients with disseminated Spitz nevi is 23 years without clear lesion site predilections. Cutaneous pigmented metastases dermoscopically lack the classic features of pigmented Spitz nevi, such as a starburst pattern. Frequently, history of sunburn, intravenous drug use, pregnancy, and other types of cutaneous stimulation, including trauma and radiotherapy have been reported as triggers to disseminated Spitz nevi. The eruptive presentation of clinically typical lesions following acute sun exposure favored a diagnosis of disseminated Spitz nevi in patient 1.

Histologically, in-transit melanoma metastases tend to lie within the reticular dermis or subcutis, often with an intralymphatic component. Epidermotropic cutaneous metastases may occur. Typical features of Spitz nevi, including Kamino bodies, and prominent maturational junction with the clinical and histologic features, we believe this strongly supports a final diagnosis of disseminated Spitz nevi in both cases and shows that molecular techniques maybe used to help confirm the diagnosis in such novel and challenging cases.
REFERENCES


Dermatologic Photography Tips: Take Great Publishable Images

Tip: Set your camera to 3 megapixels or greater. If you plan to crop extensively, an even higher resolution is desirable. If using JPEG file type, use the highest quality JPEG setting.1

Have a great tip? Send it by e-mail to ashish@derm.md.