



Atypical Histologic Features Associated with Metastasis in Blue Naevi

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Abstract

Atypical blue naevus is a controversial entity with histologic features that can be similar to both benign blue naevi and melanoma. Evaluated were 30 blue naevi for atypical histologic features that conventionally include increased lesion size, increased cellularity, polymorphous spindle and epithelioid cells, vesicular nuclei and prominent nucleoli, intense pigmentation, and infiltrative growth with 'dumbbell'-shaped nesting. It was found that when present together, atypical histologic features of fatty infiltration, polymorphous population of spindle and epithelioid cells with prominent nucleoli, perineural infiltration and deep 'dumbbell-shaped' lesional cell nesting were associated with sentinel lymph node metastasis. In select cases, these histologic features, when present together, may impart higher clinical risk and may warrant adequate complete lesional excision and sentinel lymph node sampling.

Keywords: Atypical Blue Naevus; Cellular Blue Naevus; Malignant Melanoma; Sentinel Lymph Node Metastasis

Introduction

Diagnosis and management of atypical blue nevus can be challenging and controversial [1]. Increased size and cellularity, polymorphous spindle and epithelioid cells, vesicular nuclei and prominent nucleoli, intense pigmentation, and infiltrative growth with 'dumbbell-shaped' dermal nesting are considered atypical features in blue naevus [2]. These atypical features may impart high clinical risk and can make distinction from melanoma difficult. The presence of these atypical histologic features in blue naevi may justify complete resection of these lesions [3]. Thirty blue naevi were evaluated for atypical features correlated with clinical follow-up. For clinical audit of atypical features in blue naevi, a CoPath electronic archive search using keywords blue nevus was performed. Thirty cases were identified from 2019 through 2023 and anonymized reports and hematoxylin and eosin slides were reviewed by consultant histopathologist. Clinical and histologic data were compiled in an anonymized XL file. Patients were 13 males and 17 females ranging in age from 19-88 years (m = 46). Gross lesions ranged in size from 2mm to 7mm (m = 3.5). Enlarged regional lymph node was suspected in one patient. Atypical histologic features were seen in 7 cases. Lymph node metastasis was detected in one case, the latter being the only case with the constellation of all atypical features: increased cellularity, fatty infiltration, poly-

morphous cells, prominent nucleoli, perineural infiltration, intense pigmentation and deep dumbbell shaped nests.

Materials and Methods

For clinical audit of atypical features in blue naevi, a CoPath electronic archive search using keywords blue nevus was performed. Thirty cases were identified from 2019 through 2023 and anonymized reports and hematoxylin and eosin slides from these cases were reviewed. Clinical and histologic data were compiled in an anonymized XL file and consisted of age, gender, clinical examination findings, cell morphology, cell nesting, pigmentation, mitoses, necrosis, fatty infiltration, perineural invasion and lymph node sampling results.

Results and Discussion

Patients were 13 males and 17 females ranging in age from 19-88 years (m = 46). Gross lesions ranged in size from 2mm to 7mm (m = 3.5). Enlarged anatomically sentinel lymph node was suspected in one case by clinical examination and ultrasound. Polymorphous cell population of spindle and epithelioid cells was seen in four cases with focal conspicuous nucleoli in one case. Pure spindle cells were seen in 23 cases and three cases had only epithelioid cells. Naevus cell nests were present in six cases, three with larger deep

nests with one case showing 'dumbbell shaped' nesting and three with small superficial nests. Heavy pigmentation was seen deep in the lesion in 21 cases. Perineural infiltration was seen in five cases and deep irregular fatty infiltration in one case. Mitoses were not conspicuous in any case. Only five cases had more than one and no more than two atypical features present together. Lymph node metastasis was detected in one case, with spindle cells immunoreactive with melan A and HMB-45, the latter being the only case with the constellation of all atypical features: increased cellularity, fatty infiltration, polymorphous cells, prominent nucleoli, perineural infiltration, intense pigmentation and deep 'dumbbell shaped' nests.

Diagnosis and management of atypical blue nevus can be challenging and controversial [1]. Atypical histologic features may impart high clinical risk and can make distinction from melanoma difficult. Thirty blue naevi were reviewed for atypical features correlated with clinical follow-up. The presence of atypical histologic features in blue naevi may justify complete resection of these lesions [3], and perhaps sentinel lymph node evaluation in select patients.

Blue nevi have a 2:1 predilection for female patients [4] and there are multiple variants of blue nevi, including common, cellular, amelanotic, combined, sclerosing or desmoplastic, epithelioid, and subungual. Common and cellular blue nevi are the most prevalent [5]. There is substantial disagreement among experienced histopathologists about the definitions and biologic nature of cellular blue naevi particularly those with atypical features [6]. Atypical features, as in this study, have been defined as increased lesion size and cellularity, polymorphous spindle and epithelioid cells, vesicular nuclei and prominent nucleoli, intense pigmentation, infiltrative growth with 'dumbbell-shaped' dermal nesting and necrosis [2,7]. In addition to diagnostic challenges to pathologists, their biological potential is difficult to establish [8]. Even when proliferation markers such as Ki-67 show less than 1% of tumour cells immunoreactive, lymph node metastases have been detected, up to 7cm in size [9]. Therefore, it is not possible to predict the biologic behavior or malignant potential of atypical blue naevi with certainty. In this difficult diagnostic area, it may be of greater value to utilise the term 'atypical blue nevus-like lesion of uncertain malignant potential,' than to attempt to precisely categorize all such lesions as either benign or malignant when there is a significant possibility that such categorization may be inaccurate [10].

In this study, lymph node metastasis was detected in one case, and the only case, with the constellation of all atypical histologic features that represent atypical blue naevus: increased cellularity, fatty infiltration, polymorphous cells, prominent nucleoli, perineural infiltration, intense pigmentation and deep dumbbell shaped nests. It would be useful to have sentinel lymph node sampling results on all cases; however, this is not clinically feasible. Molecular findings of atypical blue naevi compared with benign cellular blue naevi and nodular melanomas would be useful. Future work would benefit from long-term prospective study of a pure population of atypical blue naevi with close clinical follow up.

Conclusion

When present *together*, atypical histologic features of increased cellularity, fatty infiltration, polymorphous cells, prominent nucleoli, perineural infiltration, intense pigmentation and deep 'dumbbell shaped' nests were associated with sentinel lymph node metastasis. Fatty infiltration by lesional cells and 'dumbbell' nesting was present only in the case where metastatic cells were detected. Multiple atypical histologic features, when present together, and perhaps only fatty infiltration by lesional cells and 'dumbbell' nesting, may impart higher clinical risk and may warrant adequate complete lesional excision and sentinel lymph node sampling in a subset of patients.

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Conflicts of Interest

None.

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