An unusual case of scrotal plexiform hypomelanotic cellular blue naevus in a child

Mohammad Haini
Neil Sebire
Eduardo Calonje
Cyril Fisher
Michael Ashworth

Abstract

Amelanotic/hypomelanotic variant of cellular blue naevus (CBN) can present a challenge for the clinician and histopathologist. We report a case of amelanotic/hypomelanotic variant of CBN that presented as a painless scrotal swelling in a child. We review the literature on amelanotic/hypomelanotic CBN, the key histological features and important differential diagnoses.

Keywords amelanotic; cellular blue naevus; hypomelanotic; skin

Case report

A 10-year old boy presented with a 2-year history of painless left-sided scrotal swelling. Ultrasound and MRI scans demonstrated a heterogeneous, hypoechoic lesion measuring 4.4 x 1.4 x 1.8 cm. The testes appeared normal, with the lesion confined to the scrotal wall. The clinical suspicion was a vascular malformation but the imaging was not typical, hence excision biopsy was performed.

Histology of the excised lesion showed a multinodular tumour in the subcutis comprizing cellular fascicles, sheets and whorls of short ovoid to spindled cells with minimal stroma (Figures 1—3).

Mohammad Haini *MBBS, Paediatric Pathology Specialty Trainee, Department of Histopathology, Great Ormond Street Hospital NHS Foundation Trust, London, UK. Conflicts of interest: none declared.*

Neil Sebire *MBBS BClinSci MD FRCPG FRCPath FFCI, Professor of Paediatric and Developmental Pathology, Department of Histopathology, Great Ormond Street Hospital NHS Foundation Trust, London, UK. Conflicts of interest: none declared.*

Eduardo Calonje *MD Dip RCPath, Director of Diagnostic Dermatopathology, St John's Institute of Dermatology, St. Thomas' Hospital, London, UK. Conflicts of interest: none declared.*

Cyril Fisher *MA MD Dsc FRCPath, Consultant Histopathologist, Department of Histopathology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK. Conflicts of interest: none declared.*

Michael Ashworth *MD FRCPath, Consultant Histopathologist, Department of Histopathology, Great Ormond Street Hospital NHS Foundation Trust, London, UK. Conflicts of interest: none declared.*

This Short Case is brought to you in association with the Pathological Society of Great Britain and Ireland. Each month we feature a Short Case written by a member of the Trainees' Subcommittee of the Pathological Society of Great Britain and Ireland. The Short Case includes a series of Test Yourself Questions at the end to check your understanding of the case. We hope you enjoy reading it.

Pathological Society
Understanding Disease — Guiding Therapy

There was no nuclear pleomorphism, necrosis or cytological maturation. Mitotic activity was 2/10 high power fields. Sparse scattered melanin pigment was seen. Immunohistochemical staining with HMB45 and Melan-A were focally positive (Figure 4). SOX10 was diffusely positive. Tumour cells also expressed BAP-1. S-100 and BRAF stains were negative. The proliferation index (Ki-67) was low. Fluorescent in-situ hybridization (FISH) for *ESWR1* rearrangement was negative.

The features were those of an unusual hypomelanotic plexiform variant of cellular blue naevus.

Discussion

Cellular blue naevus (CBN) is a benign distinct melanocytic neoplasm.[1,2] CBN usually affects patients younger than 40 years.[3,4] Histologically, CBN comprises oval, fusiform or epithelioid melanocytes with clear or finely pigmented cytoplasm and vesicular nuclei in the deep dermis. Components of a common blue naevus (BN) are usually found adjacent to a CBN. The cellular component of CBN typically extends along adnexal structures and neurovascular bundles into the subcutis. Molecular studies show that both CBN and BN have somatic mutations in the *GNAQ* gene and neither harbour mutations in *BRAF*, *NRAS* or *c-kit* genes.[4]

Amelanotic or hypomelanotic variants of CBN have been reported including a series of 20 unusual amelanotic variants of CBN.[5] In this series, the clinical demographics of the amelanotic variant showed considerable overlap with the more typical variant. There was a predilection for young individuals, with a

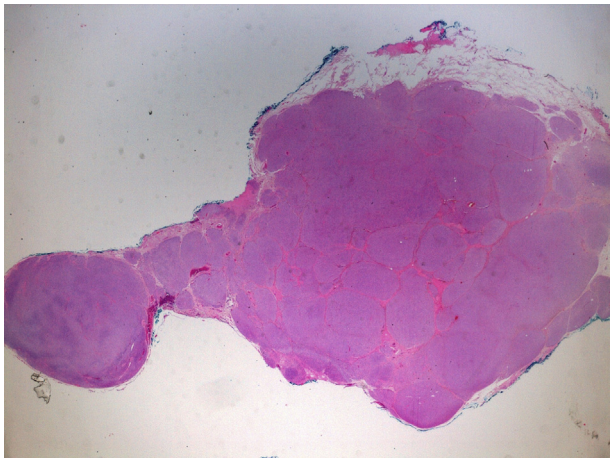

Figure 1 Low power view showing multi-nodularity (H&E, ×2 magnification).

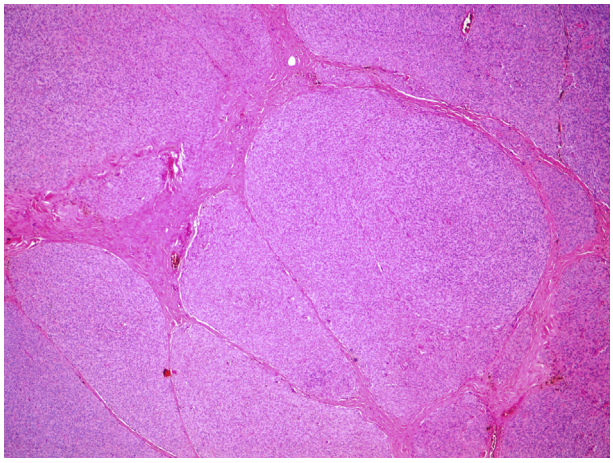

Figure 2 Medium power view showing minimal stroma between nodules (H&E, ×4 magnification).

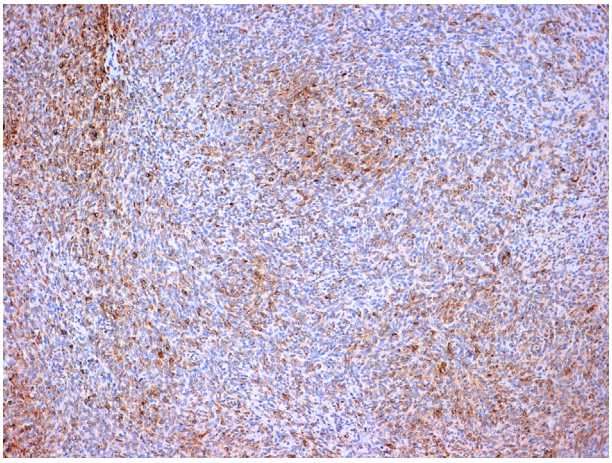

Figure 4 HMB-45 demonstrating focal cytoplasmic positivity (HMB-45, ×20 magnification).

mean age of 24 years.[5] None of their cases had a clinical diagnosis of CBN due to the atypical clinical presentation.[5] Local recurrence was not observed after complete excision.[5]

Histologically, amelanotic CBN exhibit a zonal appearance at low power. There may be foci with common blue naevus-like features. The cellular component comprises cells with round to oval nuclei and lightly eosinophilic/clear cytoplasm. Architectural patterns of the cellular component include 'biphasic', 'alveolar' and 'neural' patterns.[5] In the case series described most lesions expressed S-100 and HMB-45.[5] One was S100-negative and HMB45-positive.[5] Five showed mild cytological atypia and pleomorphism.[5] Their presence may raise the possibility of atypical or malignant CBN. Histological features indicating malignant CBN include a sheet-like growth pattern, nuclear hyperchromasia, nuclear pleomorphism, tumour necrosis, excessive mitotic activity (usually >3/mm^2) and infiltrative border.[5]

Amelanotic CBN must be distinguished from melanoma. The presence of bland cytological features, occasional dendritic cell component and the lack of an in-situ component can help distinguish it from melanoma in the majority of cases. Another differential diagnosis to consider is clear cell sarcoma (CCS) as the histology and immunoprofile of amelanotic CBN can be indistinguishable from a CCS.[5] In this scenario, FISH for *EWSR1* gene rearrangement – present within clear cell sarcoma – is essential.[5] Other histologic differential diagnoses to consider include cellular variant of dermatofibroma, desmoplastic naevus, intra-dermal Spitz naevus and schwannoma.[5]

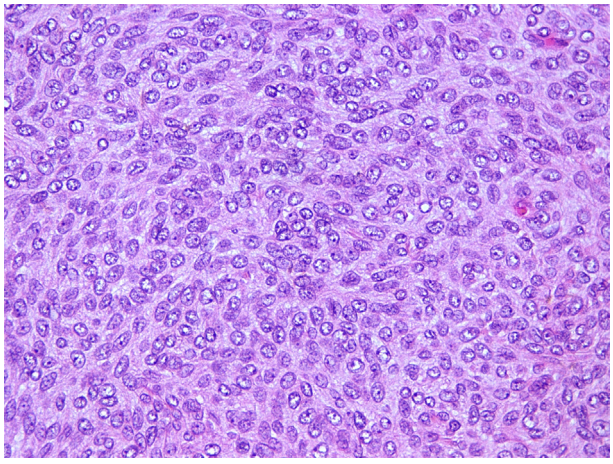

Figure 3 The tumour comprises cellular sheets and whorls of spindled to ovoid cells (H&E, ×40 magnification).

Conclusion

Amelanotic or hypomelanotic variant of CBN presents a challenge for the pathologist and careful assessment is required to avoid diagnostic pitfalls and to distinguish amelanotic/hypomelanotic CBN from atypical CBN or melanoma. ◆

Practice points

- Amelanotic or hypomelanotic CBN have an atypical clinical presentation.
- Hypomelanotic or amelanotic CBN may be negative for S-100 and other melanocytic immunohistochemical stains are required to confirm a melanocytic neoplasm.
- Molecular techniques such as FISH for *EWSR1* rearrangement are required to definitively distinguish amelanotic or hypomelanotic CBN from clear cell sarcoma.

Self-assessment questions

1. A 19-year-old female presents to clinic with a firm painless nodule in the left buttock. The nodule was biopsied and histology showed a dermal biphasic tumour extending into the subcutis. The tumour comprises bland pigmented spindled cells alternating with clear oval cells. There is no necrosis. There is inconspicuous mitotic activity. What is the most likely diagnosis?

a. Common blue naevus
b. Cellular blue naevus
c. Intradermal melanocytic naevus
d. Atypical blue naevus

e. Melanoma

Correct answer: A, Cellular blue naevus

2. Cellular blue naevus is typically associated with somatic mutation in which of the following genes?

a. *BRAF*
b. *GNAQ*
c. *c-kit*
d. *NRAS*

Correct answer: B, *GNAQ*

3. Molecular studies investigating *EWSR1* rearrangements are used to distinguish amelanotic/hypomelanotic cellular blue naevus from which of the following entities?

a. Dermatofibroma
b. Cellular neurothekoma
c. Clear cell sarcoma
d. Scwhannoma

Correct answer: C, Clear cell sarcoma

REFERENCES

1 Allen AC, Spitz S. Malignant melanoma: a clinicopathological analysis of criteria for diagnosis and prognosis. *Cancer* 1953; **6:** 1–45.
2 Rodriguez HA, Ackerman LV. Cellular blue naevus: clinicopathological study of forty-five cases. *Cancer* 1968; **21:** 393–405.
3 Zembowicz A, Phadke P. Blue naevi and Variants: an update. *Arch Pathol Lab Med* 2011; **135:** 327–36.
4 Yang C, Gru A, Dehner L. Common and not so common melanocytic lesions in children and adolescents. *Pediatr Dev Pathol* 2018; **21:** 252–70.
5 Zembowicz A, Granter S, McKee P, Mihm M. Amelanotic cellular blue naevus. A hypopigmented variant of the cellular blue naevus: clinicopathologic analysis of 20 cases. *Am J Surg Pathol* 2002; **26:** 1493–500.