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 × 1.4 × 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 comprising cellular fascicles, sheets and whorls of short ovoid to spindled cells with minimal stroma (Figures 1–3). 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 ESR1 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.

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
mean age of 24 years. None of their cases had a clinical diagnosis of CBN due to the atypical clinical presentation. Local recurrence was not observed after complete excision. 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. In the case series described most lesions expressed S-100 and HMB-45. One was S100-negative and HMB45-positive. Five showed mild cytological atypia and pleomorphism. 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/mm²) and infiltrative border.

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. In this scenario, FISH for EWSR1 gene rearrangement — present within clear cell sarcoma — is essential. Other histologic differential diagnoses to consider include cellular variant of dermatofibroma, desmoplastic naevus, intra-dermal Spitz naevus and schwannoma.

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
REFERENCES


SHORT CASE

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. Schwannoma
Correct answer: C, Clear cell sarcoma