Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Data Sharing Statement: See Supplement 2.

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OBSERVATION

Sudden Death in a Child With Ocular Lesions

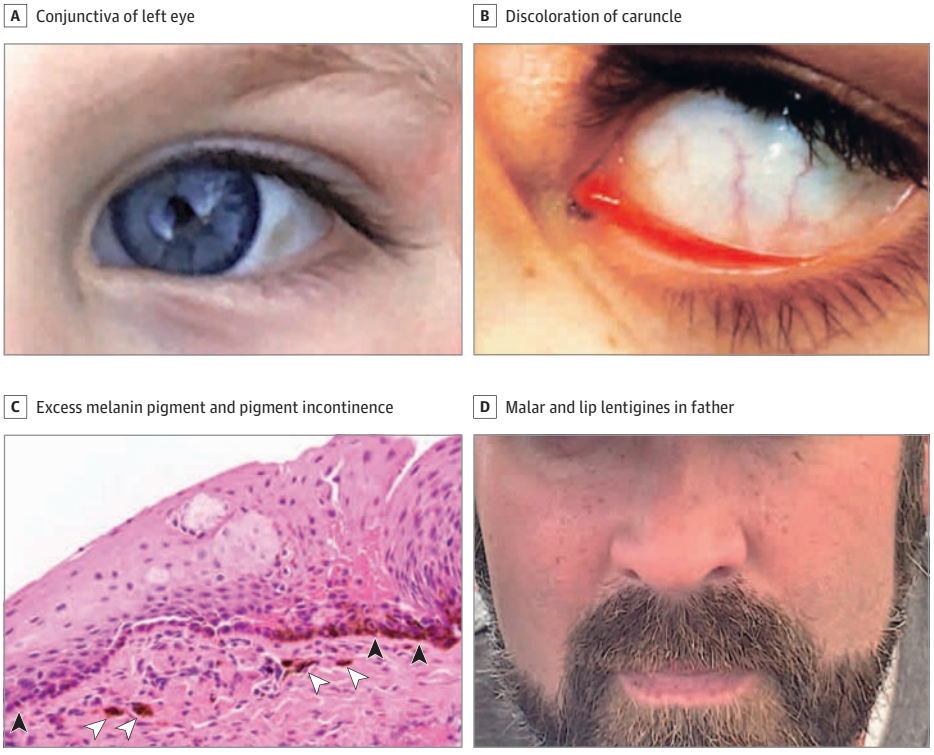
Carney complex (CNC) is a multiple endocrine neoplasia syndrome characterized by endocrine tumors, myxomas, schwannomas, and pigmentation abnormalities, commonly lentigines in the malar and perioral regions, vermilion border, conjunctiva, and canthi.[1-5] We describe a patient treated for ocular lesions who died suddenly at age 8 years and was diagnosed postmortem with CNC.

Report of a Case | An 8-year-old boy collapsed on a trampoline and could not be resuscitated. The boy was a dizygotic twin born at 36 weeks' gestational age. Medical history included a chest wall nodule, pigmented ocular lesions, anxiety, mild hypospadias, and idiopathic toe-walking. Left conjunctival biopsy at age 7 years and left caruncular biopsy at age 8 years both showed hyperpigmentation without melanocytic atypia (**Figure 1A-C**). Minor malar and perioral freckling was observed but not documented with photography; both the father (Figure 1D) and paternal relatives also had freckling of the face and mouth. There was no history of sudden unexpected death in childhood, sudden cardiac death, or any known genetic condition in relatives within 3 degrees of relation to the child.

Multifocal left ventricular fibrous scars, coronary arterial "recanalized thrombi," and borderline cardiomegaly (215 g, 89-190 g expected) were reported on the original forensic autopsy. Our secondary review identified embolic cardiac myxoma within the coronary arteries and left ventricular subendocardial replacement fibrosis consistent with healed infarcts (**Figure 2**) likely originating from the aortic valve that had been harvested by an organ procurement team before autopsy.

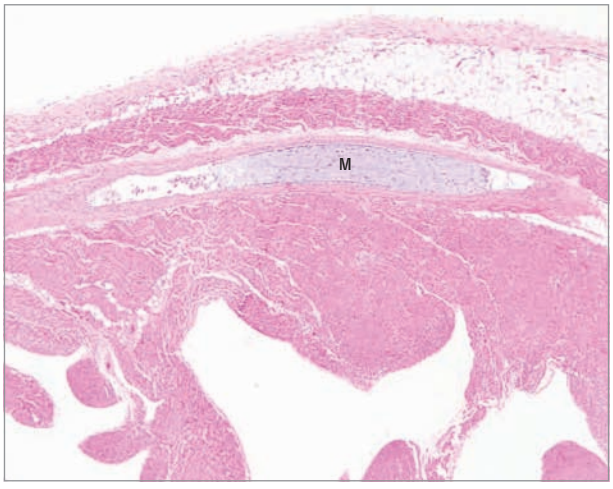
Exome sequencing on the child-parent trio identified a paternally inherited pathogenic variant in *PRKAR1A* (c.682C>T, p.R228*), confirming a diagnosis of CNC. Cascade testing was unavailable in the paternal relatives.

Figure 1. Pigmented Ocular Lesions and Lentigines



A, Light brown patch involving conjunctiva of the left eye. B and C, Dark-brown discoloration of the caruncle (B), characterized histologically by an excess of melanin pigment in the basal layer (black arrowheads) with prominent pigment incontinence (white arrowheads) (C). D, Father with malar and lip lentigines, prominent at the vermilion border.

Figure 2. Autopsy Finding



Myxoma (M) embolized to an epicardial coronary artery (hematoxylin-eosin, original magnification ×40).

Discussion | A subset of sudden unexpected pediatric deaths is caused by fatal presentations of unrecognized syndromes.[6] The 8-year-old boy in this case died of sudden cardiac death in the setting of myocardial infarction from embolic cardiac myxoma, owing to CNC caused by a pathogenic *PRKAR1A* variant. The boy died of complications of a rare disease, preceded by subtle indications that received medical attention.

While CNC is rare, penetrance is greater than 95% by age 50 years.[1-3] In CNC, myxomas can develop in mucocutaneous tissue, breast, heart, and elsewhere. Cardiac myxomas occur in up to 50% of affected individuals, including children, with 16% of affected individuals experiencing sudden death or near-death events.[1] Embolization of this boy's cardiac myxoma chronically compromised coronary arterial blood flow, leading to infarction and ultimately sudden cardiac death. In retrospect, his "anxiety" may have been referable to ongoing ischemic heart disease.

Pigmented skin lesions are the most common presenting feature in CNC, reported in 96% of affected individuals.[1-3,5] Ocular lentigines occur in 27% and are frequently brought to an ophthalmologist's attention, typically before signs or symptoms of cardiac myxoma.[5] Both ophthalmologic biopsies showed basal melanocytic proliferation and hyperpigmentation without atypia. Such lesions of the caruncle or semilunar fold are particularly suspicious for CNC, even without additional apparent stigmata.[5]

In retrospect, this boy's congenital chest wall nodule, unsampled at autopsy, was likely an osteochondromyxoma.[4] Considering this together with the lentigines in this boy and his relatives, the possibility of CNC might have been entertained,[2] prompting antemortem genetic evaluation and a cardiology referral, where the myxoma might have been identified.

This case demonstrates that sudden unexpected death in childhood may be a sentinel family event that can identify previously unrecognized familial genetic disease. It highlights the opportunity for clinical detection of pigmented conjunctival lesions to elicit antemortem concern for a syndromic disorder. Although CNC lesions may exhibit no obvious difference from flat nevi in unaffected children, the interpretation of ophthalmic findings in the context of personal and family history, and interdisciplinary care involving ophthalmologist, primary care physicians, and subspecialists like endocrine, cardiology, and genetics professionals, can offer opportunities for life-saving interventions.

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Published Online: March 7, 2024. doi:10.1001/jamaophthalmol.2024.0089

Conflict of Interest Disclosures: Dr Vargas reported advisory board fees from Millipore Sigma Pathology and consulting for Vertex and occasional work consulting as an expert witness on the subject of pathology. Dr Folberg reported being an employee of EyeCare Partners. No other disclosures were reported.

Additional Contributions: We thank the parents of the patient for granting permission to publish this information.

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Association of Conjunctival Ulceration With Pembrolizumab

Pembrolizumab and other immune checkpoint inhibitors are an effective alternative to traditional chemotherapy in sensitizing the immune system to combat cancer cells.[1] While effective against malignancies, this mechanism of action can lead to immune-related complications.[2] We present a case of conjunctival ulceration following pembrolizumab therapy for breast cancer.