FIGURE 2. Histopathologic staining. A, Myxoma cells populating a myxoid background (hematoxylin and eosin stain). B, Lack of *PRKARIA* staining in this case. Black arrow indicates myxoma cells. C, *PRKARIA* staining of the myxoma cells (black arrow) in a nonsyndromic myxoma (for comparison).

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EDITORIAL COMMENTARY

Timely screening for Carney complex and *PRKAR1A* gene mutations

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Disclosures: Author has nothing to disclose with regard to commercial support.

Received for publication July 25, 2016; accepted for publication July 26, 2016; available ahead of print Aug 24, 2016.

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J Thorac Cardiovasc Surg 2016;152:1440-1

0022-5223/\$36.00

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<http://dx.doi.org/10.1016/j.jtcvs.2016.07.060>

“Modify, simplify, and apply.”

—Denton Cooley, MD

Carney complex (also known as “myxoma syndrome”) is a rare autosomal dominant multineoplasia syndrome, which consists of myxomas in different locations, spotty skin pigmentation, and endocrine overactivity.¹ Cardiac myxomas are the second most frequent manifestations of Carney complex. The majority of cardiac myxomas are benign; however, they may be recurrent with significant morbidity and mortality.^{1,2} Therefore, patients presenting with cardiac myxoma generally are considered to be surgical emergencies, and complete surgical resection

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Central Message

Immunohistochemistry staining of *PRKARIA* may be useful as a simple screening method for identifying patients with Carney complex.

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remains the primary therapy. More than 60% of Carney complex cases are caused by inactivating mutations in the tumor suppressor gene *PRKARIA*, which encodes the regulatory subunit type I alpha of the cAMP-dependent protein kinase A gene. *PRKARIA* is situated at the 24.2-24.3 locus of the long arm of chromosome 17 and has 11 exons, of which exons 2 to 11 are protein coding.² Currently, there are more than 125 pathogenic mutations in *PRKARIA* that have been found.²

Of note, the identification of a pathogenic variant in the *PRKARIA* gene can be used for diagnosing Carney complex. Traditionally, genetic sequencing of patient tissue samples was most commonly used for diagnosis. However, Maleszewski and colleagues³ recently reported a new method of *PRKARIA* immunohistochemical (IHC) analysis. IHC staining demonstrated that all 7 cases of Carney complex lacked *PRKARIA* antigenicity (100% sensitivity) and that 33 (32%) isolated cardiac myxomas were similarly nonreactive. *PRKARIA* gene sequencing further confirmed that the specificity of IHC staining reached 68%.³ By using the same IHC assay in the current case report, Saddoughi and colleagues⁴ observed that a patient with cardiac myxoma lacks *PRKARIA* immunoreactivity with negative staining and loss of protein expression. This is an interesting case report for screening Carney complex by using immunohistochemistry assay to quickly identify the mutation of *PRKARIA*.

This study will be most useful in bringing attention to the utility of IHC *PRKARIA* staining to screen for Carney complex. As with most IHC stains, turnaround time for this assay is 1 to 2 days. Despite the fact that there is an added charge for IHC staining in routine histopathology, the cost is less than the cost of DNA sequencing used to identify

patients who have Carney complex. However, there remain several limitations. First and foremost, this is only a single case report. Second, negative IHC staining is always complicated in its interpretation because of the potential technical limitations, such as lack of antigen retrieval and a single antibody used. Third, additional gene sequencing and mutation analysis would still be required to confirm *PRKARIA* defect in the patient. Finally, if sequencing of the *PRKARIA* gene does not demonstrate a defect, other *PRKARIA* gene deletion testing would still be needed to rule out a *PRKARIA* defect.³

Overall, IHC staining of *PRKARIA* may be useful as a simple screening method for determining which patients should undergo additional testing. The current case report has further confirmed the findings of a previous study. Despite the fact that this technique has been previously reported, it seems that many cardiac surgeons are not aware of this test or its usefulness. In this way, this case report strikes one as an ideal format for educating cardiac surgeons about this useful screening tool for this relatively rare condition.

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