ISSN NO: 2770-2936
April 2026

Morphological Characteristics, Histogenesis, And Differential Diagnosis Principles of Cardiac Myxoma

Rashidova Shaxlo O'rmonovna
Andijan State Medical Institute

ABSTRACT
Objective of the study: To analyze the pathomorphological and immunohistochemical characteristics, as well as modern aspects of the histogenesis of cardiac myxoma, and to systematize the criteria for differential diagnosis with other intracardiac formations.
Material and methods: A systematic analysis of local and foreign scientific literature (PubMed, Scopus, Web of Science) from the last 10 years on the subject was conducted. The recommendations of the World Health Organization (WHO) regarding the classification of heart and blood vessel tumors were studied.
Results: Although cardiac myxoma is histologically considered a benign tumor, its embolic potential and its ability to cause hemodynamic disturbances pose a serious threat to the patient's life. Immunohistochemical profiling using markers such as Calretinin, Vimentin, and CD34 is of decisive importance in distinguishing the tumor from mural thrombi, papillary fibroelastoma, and malignant sarcomas. It has been confirmed that genetic mutations related to the Carney complex (the PRKAR1A gene) play a significant role in the pathogenesis of myxomas.
Conclusion: Early and accurate pathomorphological differential diagnosis of myxoma prevents incorrect treatment tactics. The aberrant differentiation of subendocardial multipotent cells is considered the main histogenetic source of the tumor.
Keywords: cardiac myxoma, pathomorphology, immunohistochemistry, histogenesis, Carney complex, mural thrombus, differential diagnosis, cardiology.

Introduction (Relevance) Primary tumors of the heart are a very rare pathology in clinical practice, and autopsy studies note their prevalence rate to be between 0.001% and 0.3%. Approximately 75% of all primary cardiac neoplasms fall into the category of benign tumors, with cardiac myxomas accounting for 50% of these. The disease primarily occurs in individuals aged 30-60, more often in women. In 75-80% of cases, myxomas grow in the left atrium, mostly attached to the interatrial septum in the region of the fossa ovalis. Because the disease often proceeds asymptomatically or presents with an asymmetric clinical picture (a hemodynamic obstruction resembling mitral stenosis, systemic embolism, or general signs of inflammation), early diagnosis is a complex task. Today, although the formation can be visualized using echocardiography (EchoCG) and magnetic resonance imaging (MRI), a final and accurate diagnosis is made solely on the basis of pathomorphological and immunohistochemical (IHC) examinations.

Main Part 1. Macroscopic and microscopic morphology of cardiac myxoma
Macroscopic picture: Externally, a cardiac myxoma has a mucoid (gelatinous), soft, and very fragile structure. Its size can reach from 1 cm to 15 cm. Macroscopically, two main phenotypes are distinguished:

- **Polypoid (papillary) type:** Consists of numerous small, soft, and mobile outgrowths, prone to fragmentation in the blood stream. This specific type is the morphological form with the highest risk of causing embolism in the central nervous system and peripheral vessels.
- **Solid type:** A round, smooth-surfaced, massive, and firmer formation rich in fibrous tissue. Usually, this type obstructs the valve orifices, causing syncope (fainting) or sudden death.

Microscopic picture: Histologically, the tumor consists of specific "myxoma cells" (lepidic cells) located against a background of a strongly myxoid (mucoid) stroma. The stroma is rich in acidic mucopolysaccharides (glycosaminoglycans), primarily hyaluronic acid, and stains intensely with Alcian blue dye. Myxoma cells are stellate, polygonal, or spindle-shaped, with a thin eosinophilic cytoplasm. The most pathognomonic (characteristic) feature is the arrangement of tumor cells forming *perivascular rings* or chains (cords) around microvessels. Secondary changes are often identified in the stroma: hemorrhages, accumulation of

ISSN NO: 2770-2936
April 2026

hemosiderophages, mononuclear inflammatory infiltration, and foci of calcification. As a result of the encapsulation of elastin and collagen fibers, the formation of *Gamna-Gandy* bodies is observed.

2. Histogenesis and Molecular-genetic characteristics For many years, myxomas were considered merely organized mural thrombi. However, electron microscopy and IHC refuted this hypothesis. According to the modern WHO classification, a myxoma is a true neoplasm originating from pluripotent vasoformative reserve cells (subendocardial multipotent mesenchymal progenitor cells). These cells have the capacity for endothelial, smooth muscle, and fibroblastic differentiation.

Genetic aspects: Although myxomas often appear sporadically, in about 7-10% of cases they manifest within the framework of an inherited syndrome – the *Carney complex*. The Carney complex is an autosomal dominant inherited syndrome caused by an inactivating mutation of the *PRKAR1A* gene (located on chromosome 17q22-24). Myxomas against the background of the Carney complex occur in younger patients, in any chamber of the heart (often multifocal), and have a high rate of recurrence after surgery.

Immunohistochemical (IHC) profile: Immunophenotyping is a crucial step in differential diagnosis:

- **Calretinin:** The most specific marker for myxoma cells. It shows a nuclear and cytoplasmic positive reaction in almost 100% of cases.
- **Vimentin:** Confirms the mesenchymal origin of the cells (+).
- **Endothelial markers (CD31, CD34, FVIII):** Manifest moderately (+) primarily in vessel-like structures within the tumor and in some parts in the myxoma cells themselves.
- **CD68:** Indicates the histiocytic differentiation of tumor cells.

3. Differential diagnosis Clinically and morphologically, it is extremely important to distinguish a myxoma from the following formations: 3.1. Organized mural thrombus

- **Morphological difference:** A thrombus lacks the true stellate cells and perivascular rings typical of a myxoma. It generally has a layered structure (lines of Zahn) consisting of fibrin layers, erythrocytes, platelets, and ingrown granulation tissue.
- **IHC difference:** Thrombus cells (except for endothelium and fibroblasts) give an absolutely negative (-) reaction to the *Calretinin* marker.

3.2. Papillary fibroelastoma A benign tumor occurring in the endothelium of valves (most often the aortic and mitral valves).

- **Morphological difference:** Macroscopically, it resembles a sea anemone. Microscopically, it consists of avascular (blood vessel-free), thick fibrous and elastic core papillary structures covered with a single layer of hyperplastic endothelium. There is very little myxoid stroma.

3.3. Cardiac sarcomas (Angiosarcoma, Myxofibrosarcoma) Primary cardiac malignant tumors.

- **Morphological difference:** Sarcomas clearly exhibit cellular atypia, nuclear pleomorphism, pathological mitoses, massive foci of necrosis, and invasive growth into the myocardium. Angiosarcomas usually affect the right atrium.

3.4. Infective endocarditis vegetations

- **Morphological difference:** Histological examination reveals a massive inflammatory infiltrate (neutrophils), remnants of necrotic tissue, fibrin, and bacterial colonies instead of tumor cells.

Conclusion

1. Cardiac myxoma is a neoplastic proliferation of subendocardial multipotent cells with a complex histological structure, and its benign histological nature does not negate the risk of severe clinical complications (embolism, valve obstruction).
2. Pathomorphological and immunohistochemical analyses, particularly the determination of Calretinin expression, are the gold standard for differentiating myxomas from mural thrombi and malignant sarcomas.
3. Because patients with identified pathogenic mutations of the PRKAR1A gene (Carney complex) have a high risk of tumor recurrence even after cardiac surgery, it is mandatory to include their regular EchoCG monitoring in clinical protocols.

References

ISSN NO: 2770-2936
April 2026

1. Burke, A. P., & Virmani, R. (2015). Tumors of the Heart and Great Vessels. *WHO Classification of Tumours of the Heart*, 4th Edition. IARC Press.
2. Reynen, K. (1995). Cardiac myxomas. *New England Journal of Medicine*, 333(24), 1610-1617.
3. Terracciano, L. M., Mhawech, P., Suess, K., et al. (2000). Calretinin as a marker for cardiac myxoma: diagnostic and histogenetic considerations. *American Journal of Clinical Pathology*, 114(5), 754-759.
4. Pucci, A., Gagliardotto, P., Zanini, C., Pansini, S., di Summa, M., & Navino, C. (2000). Histologic and clinical characterization of cardiac myxoma: review of 53 cases from a single institution. *American Heart Journal*, 140(1), 134-138.
5. Wilkes, D., McDermott, D. A., Basson, C. T. (2005). Clinical phenotypes and molecular genetic mechanisms of Carney complex. *The Lancet Oncology*, 6(7), 501-508.
6. Amano, J., Kono, T., Wada, Y., et al. (2003). Cardiac myxoma: its origin and tumor characteristics. *Annals of Thoracic Cardiovascular Surgery*, 11(4), 215-221.