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Case Report

Cardiac rhabdomyoma in a slaughtered heifer

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Abstract

During routine inspection of a slaughtered heifer from a feedlot, the veterinarian in charge condemned the heart due to a lesion on the endocardium. Histopathology and immunohistochemistry showed that the lesion was composed by cardiac tissues at different degree of differentiation, disordered and out of proportion. The most conspicuous was a dispersed population of large, vacuolated and PAS positive cells, enmeshed in excessive fibrous connective tissue. These cells, identified as spider cells, resulted markedly positive for desmin, and negative for vimentin, smooth muscle α-actin and myogenin factor 4. An extensive infiltration by fibro-fatty tissue was other abnormal component of the lesion. Furthermore, abnormal cardiomyoblasts forming tortuous bundles were also recognized. Nonetheless, these cells showed distinctive striations and even intercalated discs. Some of this abnormal cardiac myoblasts resulted markedly positive for desmin and isolated strands also were positive for smooth muscle α-actin, but negative for myogenin factor 4 and vimentin. Based on the pathognomonic spider cells and immunoreactivity, the lesion was classified as a cardiac rhabdomyoma. For some, the cardiac rhabdomyomas are not true neoplasms but congenital hamartomas in heart. However, principal component in cardiac hamartomas in animals is an abnormal vascular pattern completely different from the lesion herein presented. Based on the diverse tissue components, their immature and distorted image and, positive results for immunomarkers of early myoblast differentiation as well as terminal cardiomyocyte characteristics, dysplasia must be considered as the common denominator in development of cardiac rhabdomyomas with tissue heterogeneity.

Key words: rhabdomyoma, heart, bovine.

Introduction

Fundamental literature in veterinary pathology refers that cardiac rhabdomyomas are extremely rare in animals (10, 13) but may be seen in pigs, particularly in red wattle pigs (10, 12) and have been identified in sheep, cattle (10, 13), and dog (10, 13, 14); rare cases have also been described in guinea pigs (5) and in a fallow deer (6).

A specific survey in the database of the U.S. National Library of Medicine (MEDLINE/PubMed), recovers a sole report in cattle (16). However, no other report has been published recently. On the contrary, several cases of cardiac hamartomas have been referred in cattle recently (1, 17). Two of these cases correspond to incidental findings in slaughtered animals (17), just as happened here. The aim of this report was to demonstrate the morphologic and immunohistochemistry (IHC) characteristics of a cardiac rhabdomyoma in a slaughtered female young bovine, during inspection in a slaughterhouse in Mexico.

Case report

During inspection in a bovine slaughterhouse in Mexico the heart of a commercial crossbreed heifer from a feedlot was condemned due to a focally extensive pale area inside the right ventricular wall. Apart from a congested liver that passed inspection, other lesions were not

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recognized in the carcass. The official veterinarian supposed that the lesion could be scar tissue from a previous abscess in myocardium. The lesion was trimmed for subsequent examination and fixed by immersion in 10% buffered formalin. The samples were submitted to the pathology department of the Veterinary School, Universidad Autónoma de Nuevo León for routine process including, paraffin embedding, sectioning at 4 µm, and subsequent staining with H&E, PAS, Masson trichrome, and Giemsa.

Grossly, a whitish smooth lesion with rhomboid shape but no defined edges with 4x5 cm was more evident at endocardium. The lesion was extensible as part of myocardium and affected almost the entire wall, including papillary muscles and trabeculae in endocardium but the pericardium was not involved (Fig. 1).



Figure 1. Heart. Two sections of the right free wall ventricle. Note the distribution of the lesion within myocardium with ill defined edges. The lesion appears to extend from endocardium. Samples fixed in 10% formalin.

Microscopically, the lesion was characterized by a heterogeneous aspect, due to several tissue components. The most obvious was a marked infiltration of fibrous connective tissue along with intercalated fatty tissue, replacing myocardium (Fig. 2). The fibrous and fatty tissues were both mature in appearance. However, in some areas, the fibrous connective tissue became loose, giving a myxomatous image. Furthermore, many abnormal cells that resemble Purkinje fibers were enmeshed within fibrous connective tissue. These voluminous cells that resulted PAS positive, showed large cytoplasmic vacuoles that leave the nucleus suspended by subtle cytoplasmic fibrils (spider cells) (Fig. 3). Some of these cells appear binucleate, but mitosis and bizarre chromatin figures were not observed. A third component was poorly organized bundles of cardiac myoblasts. These highly vacuolated and elongated cells, gave an appearance of empty myofibers (Fig. 4). However, most of these cells showed defined striations and even, intercalated discs (Fig. 5). Other components of the lesion were fibroplasia and neovascularization, hypertrophy of the tunica media of large arteries, hyperplasia of mast cells subjacent to endocardium, and scarce foci of perivascular lymphocytic infiltration at the limits of the lesion.

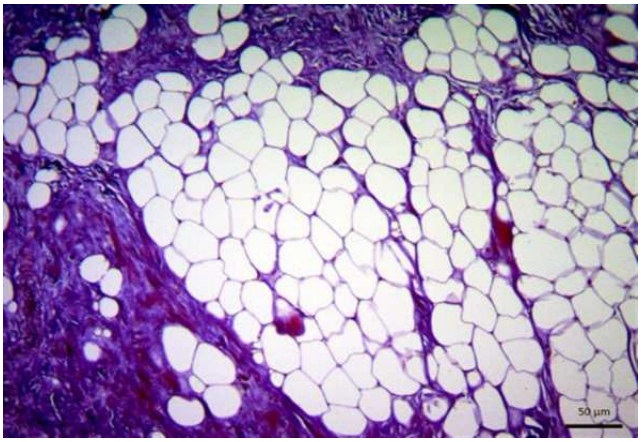


Figure 2. Extensive infiltration of fibrous connective tissue intermingled with adipose tissue. A few myocardial fibres appear atrophied. Masson trichrome, bar: 50 µm.



Figure 3. Large vacuolated cells with delicate cytoplasm fibrils, resembling Purkinje fibers were isolated and enmeshed within excessive connective fibrous tissue. These cells were identified as spider cells. PAS, bar: 10 µm.

An IHC panel was applied on xylene deparaffined sections with enzyme treatment (20 µg/mL proteinase K – Dako – at 37°C for 15 min.) for antigen retrieval. Monoclonals employed were anti-myogenin (myogenic factor 4 – clone F5D), α smooth muscle actin (clone 1A4), desmin (clone D33), and vimentin (clone V9), in accordance with manufacturer´s protocols (Dako, Mexico; Comercial Biomedico Ramirez, S.A, de C.V.). The primary complex was revealed by a streptavidin-biotin-complex with diaminobenzidine as substrate (Dako, Mexico; Comercial Biomedico Ramirez, S.A, de C.V.), slightly counterstained by hematoxylin. Positive results were obtained for desmin and actin (Fig. 4 and 5).

The lesion herein described has several abnormal tissue components, including fibro-fatty tissue (the most extensive), abnormal Purkinje fiber-like cells (the most

conspicuous), poorly arranged bundles of immature cardiomyocytes (with evidence of terminal differentiation), fibroplasia and neovascularization with hypertrophy of the wall of large arteries (probably, a myocardium physiopathological adaptation) and, a mild lymphocytic perivascular infiltration at the margins. The abnormal Purkinje fiber-like cells with large vacuolated cytoplasm, called spider cells, have been considered characteristic of cardiac rhabdomyomas in veterinary pathology (5, 14). Certainly, in medical pathology, spider cells are pathognomonic for cardiac rhabdomyoma (11, 19). The proposed term Purkinjeoma for cardiac rhabdomyomas in humans (2), and swine (4, 18) and recently in a seal (7), judge of major relevance this distinctive cellular change. This striking cellular morphology as well as the immunoprofile between myoblastic and Purkinje fiber-like cells has been interpreted as the progression from two types of cardiac fibers or a pluripotent embryonic cell origin (14). Nonetheless, the presence of these abnormal Purkinje fiber-like cells was not the sole tissue component in the present case.

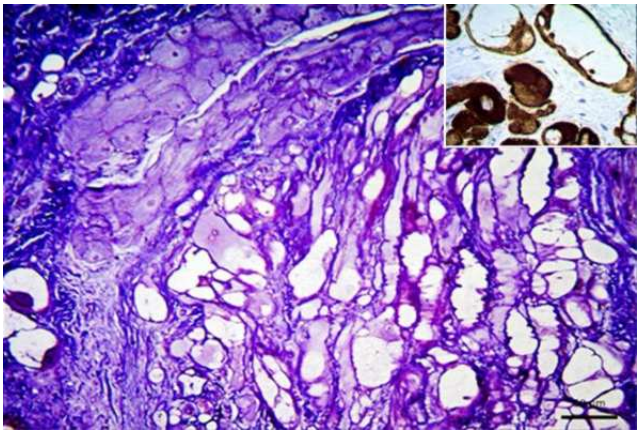


Figure 4. Disordered bundles of large vacuolated cells, some of them with a resemblance to Purkinje fibers and others resemble large myoblasts. Masson trichrome, bar: 50 µm. Inset: immunoreactivity with anti-desmin, slightly counterstained with hematoxylin.

The IHC results herein presented are also compatible with rhabdomyoma, particularly in those cells that resemble Purkinje fibers, which were strongly positive for desmin, but resulted negative for myogenic factor 4, vimentin and, α-smooth muscle actin. This immunoreactive pattern has been referred by others in cardiac rhabdomyomas (5, 6, 14). However, in the present case, apart from strong positivity for desmin, some isolated bundles of cardiomyoblasts also resulted positive for α-smooth muscle actin.

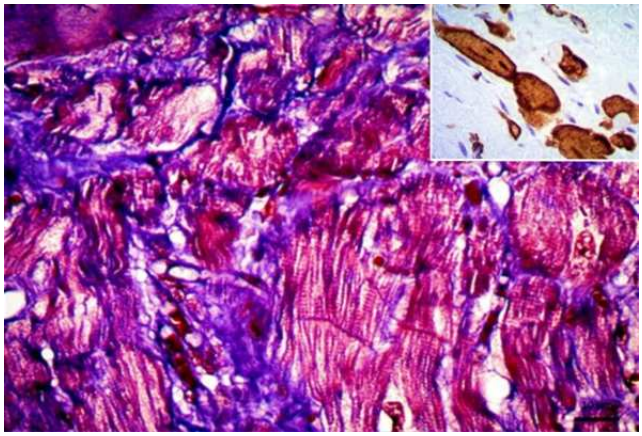


Figure 5. A closer view of the myoblast clearly showed striations and intercalated discs. Masson trichrome, bar: 10 µm. Inset: Immunoreactivity with anti- α-smooth muscle actin, slightly counterstained with hematoxylin.

Cardiac rhabdomyomas are considered in both veterinary and medical pathology, not as true neoplasms but as congenital hamartomas in the heart (10, 15, 20). Indeed, cardiac hamartomas have a pattern of immunorectivity similar to rhabdomyomas (3, 8, 19). Therefore, diagnosis of hamartoma was also feasible in this case. Nonetheless, most of the hamartomas described in veterinary medicine have a vascular component as main alteration (8, 17). Conversely, in the case herein described, the vascular component was just one among the other tissue components and probably a result of physiopathological compensation.

For the World Health Organization classification of cardiac tumours, cardiac rhabdomyomas are different from cardiac hamartomas, being the former rare neoplasms occurring mostly in ventricles in newborns, whereas cardiac hamartoma is a cardiac tumour composed by mature cardiac myocytes in adults that may occur either in ventricles or auricles but lack the conspicuous spider cell which is pathognomonic for cardiac (congenital) rhabdomyomas (19). Nonetheless, as mentioned, the immunoprofile in cardiac rhabdomyoma and cardiac hamartoma is similar (11, 19). Conversely, cardiac rhabdomyomas in adults may instead share some of the characteristics of cardiac rhabdomyomas but also occur in extracardiac locations and the principal components correspond to tightly packed striated myocytes with scant or absent vacuolated cells (19). Conversely, expression of myogenin factor antigen is a characteristic of rhabdomyosarcoma which is absent in rhabdomyoma (19), as in the case presented here.

For some authors that have diagnosed hamartomas in the heart, the absence of spider cells justifies the diagnosis of hamartomas instead of rhabdomyomas (3, 8). Noteworthy, all of the hamartomas reported in animals, including three cases in cattle (1, 17), a single case in a dog (8), and another in a squirrel monkey (3), were found in heart atria, particularly in right atrium,

which has been considered a peculiarity for diagnosis (1, 17). Conversely, the lesion reported in this case was recognized in the free wall of the right ventricle.

In the case presented here the presence of IHC markers of early myocardial differentiation as well as evidence of final differentiation in cardiomyoblasts, such as striations and intercalated discs is remarkable. These changes reflect an asynchronous differentiation, within a disordered myocardium. Therefore, a dysplastic change remains obvious. This consideration was already noticed and argued to call dysplasia to the cardiac rhabdomyoma in pigs and humans, species in which cardiac rhabdomyoma is more frequently seen (2, 18). In infants rhabdomyoma is the most common primary cardiac tumor occurring since fetal life (9, 19, 20).

The lesion herein results different from hamartoma but includes changes supporting the previous opinions that imply dysplasia in the cardiac rhabdomyoma.

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