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Extensive Fibrofatty Infiltration of the Left Ventricle in Two Cases of Sudden Cardiac Death

REFERENCE: Collett, B. A., Davis, G. J., and Rohr, W. B., **"Extensive Fibrofatty Infiltration of the Left Ventricle in Two Cases of Sudden Cardiac Death,"** *Journal of Forensic Sciences,* JFSCA, Vol. 39, No. 5, September 1994, pp. 1182–1187.

ABSTRACT: Replacement of the myocardium by fibrous and adipose tissue is well documented in the right ventricle, but has been rarely described in the left ventricle. We present two cases of extensive fibrofatty infiltration of the left ventricle without significant right ventricular involvement in young men whose presenting symptom was sudden death.

KEYWORDS: pathology and biology, sudden death, fatty infiltration of myocardium

Right ventricular cardiomyopathy that results in clinical symptoms has been well documented in the literature. In 1952 Uhl reported [*1*] a case of near total congenital absence of the right ventricular myocardium, resulting in right ventricular dilatation, congestive failure and death at age 8 months. A newly recognized clinicopathologic entity is arrhythmogenic right ventricular dysplasia, or ARVD, where the right ventricle is partially or completely replaced by fibrous and adipose tissue, and results in right ventricular electrical instability [*2,3*]. Similar histologic features of fibrolipomatous change have been reported in the left ventricle, but always in the presence of significant right ventricular involvement. We report two cases of extensive left ventricle fibrofatty infiltration without a large coexisting right ventricular lesion.

Case 1

A 34-year-old white male collapsed while attending a wedding. He could not be resuscitated and was pronounced dead.

Past medical history was significant for asymptomatic mitral valve prolapse diagnosed nine years previously, and occasional epigastric discomfort in the last year of his life, which

Received for publication 14 Feb. 1994; accepted for publication 13 March, 1994.

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Case 1 was presented at the American Academy of Forensic Sciences 45th Annual Meeting, February 1993, Boston, (Abstract G17).

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was treated with ranitidine. The decedent was not diabetic, did not smoke, and had no known family history of ischemic heart disease.

At autopsy, the decedent was an atraumatic, well developed, mildly obese man, 220 pounds, and 72 inches tall (100 kg, 183 cm). Toxicologic investigation of postmortem blood revealed no ethanol, cocaine or morphine. All organ systems except the heart were grossly and histologically unremarkable.

The heart weighed 460 g. The coronary arteries arose normally, followed the usual configuration and were widely patent, without evidence of significant atherosclerosis. The mitral valve demonstrated hooded, redundant anterior and posterior leaflets with a 0.5 cm septal endocardial strike lesion under the distal extension of the anterior leaflet; the chordae tendinae were intact. A yellow-tan, subepicardial irregularly bordered area was identified in the left ventricular myocardium which extended from base to apex and penetrated from one third to one half of the left ventricular thickness (Fig. 1). The chambers and valves were otherwise unremarkable.

Histologic examination of the discolored areas of the left ventricle revealed extensive fibrofatty infiltration, with entrapment of myofibers in fibrous tissue and replacement of myofibers by fibrous and mature adipose tissue (Fig. 2). Foci of active lymphocytic myocarditis were identified in the adjacent myocardium. (Fig. 3).

Case 2

A 29-year-old white male felt ill after playing basketball for 20 minutes. He sat down and then collapsed. Bystander cardiopulmonary resuscitation was begun immediately and continued on transport to the emergency room. He could not be resuscitated and was pronounced dead.

Past medical history revealed only reactive airways disease with occasional use of an inhaler. There was no history of tobacco, alcohol or substance abuse.

At autopsy, the decedent was a well developed and well nourished man, 73 inches in height and 163.5 pounds (185 cm, 74 kg). No external or internal injuries were identified,

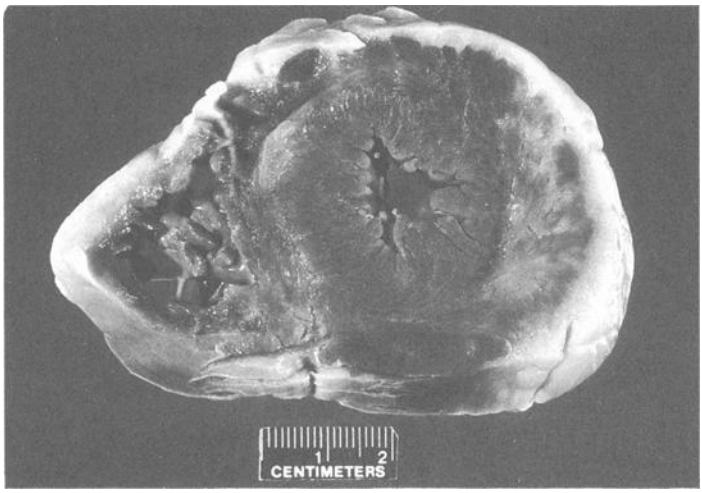

FIG. 1—*A cross section through the ventricular barrel of the heart from Case 1 shows a large mottled discoloration in the anterolateral left ventricular free wall. The right ventricle is unremarkable.*

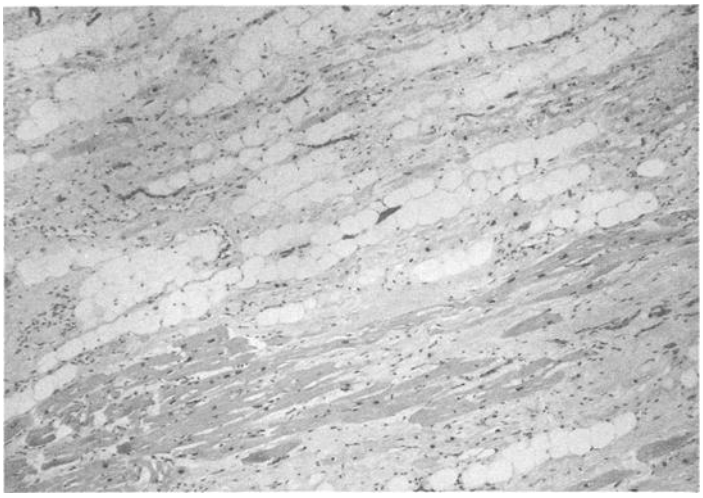

FIG. 2—*Histologic examination of the area described in Fig. 1 demonstrates replacement of the myofibers with fibrosis and adipose tissue. Similar findings were present in the affected left ventricle in Case 2.*

and postmortem blood toxicology was negative for ethanol and an acid/neutral drug screen. No significant gross or microscopic abnormalities were identified except in the heart.

The heart weighed 405 g, and the coronary arteries arose normally, followed the usual configuration and were widely patent, without evidence of significant atherosclerosis. The left ventricular myocardium demonstrated on the epicardial aspect an extensive, patchy to confluent, variegated gray-white to yellow area which was focally contiguous with the

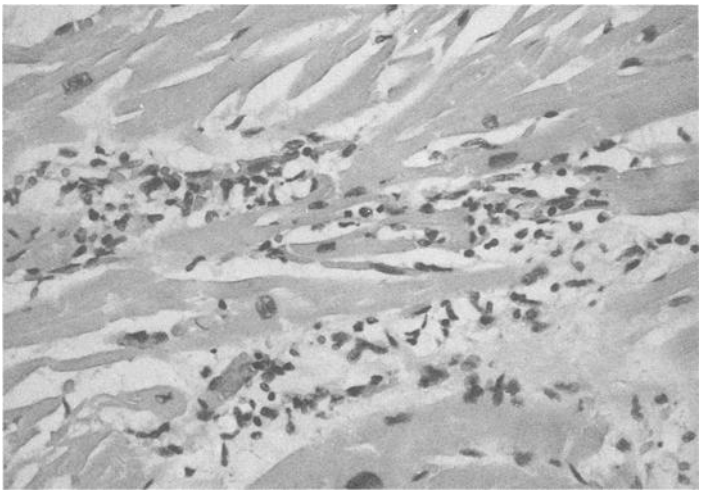

FIG. 3—*A focus of active lymphocytic myocarditis adjacent to the fibrofatty infiltration in Case 1 shows an inflammatory infiltrate of lymphocytes surrounding necrotic myofibers. 400X magnification.*

epicardial fibroadipose tissue (Fig. 4). A single area of fat infiltration, 0.5 cm in greatest dimension, was identified in the right ventricular myocardium. The valves and chambers were otherwise unremarkable.

Histologic examination of the discolored region of the left ventricle revealed extensive replacement of myofibers with mature adipose tissue and fibrosis. No inflammatory foci were identified.

Discussion

Myocardium replacement by fibrous and adipose tissue has been previously described by many authors. In Uhl's anomaly, there is a congenital absence of right ventricular myocardium, leaving only epicardial fibroadipose tissue and endocardium [*1*]. A newly recognized clinicopathologic entity is arrhythmogenic right ventricular dysplasia, or ARVD. This term is used to describe patients, usually young males, with a right ventricle replaced or near totally replaced by fibroadipose tissue, who have the clinical features of ventricular tachycardia with a right ventricular origin, and left bundle branch morphology by electrocardiography [*2,3*]. ARVD has been documented as a cause of sudden cardiac death [*4*], and may have a heriditofamilial component in some patients, as multiple family members may be affected [*2,5*].

Some authors, however, prefer to use the broader term arrhythmogenic cardiomyopathy, as both functional and histologic abnormalities have been described in the left ventricles of some patients with ARVD. Using exercise testing, Manyari and colleagues identified latent left ventricular dysfunction in ARVD patients [*6*], and Webb et al. [*7*] identified some evidence of left ventricular dilatation or wall motion abnormalities in patients with ARVD by radionuclide angiography or cardiac catheterization. Left ventricular fibrofatty infiltration has been demonstrated in several studies of ARVD patients [*8–11*], and in some cases the left ventricular involvement was extensive [*10,11*]. However, we are unaware of any reports of isolated left ventricular lesions, as in our cases.

There have also been published reports of patients who fit the clinical criteria for ARVD who on biopsy show areas of active myocarditis. Hisaoka et al. [*12*] reported two autopsied cases compatible with ARVD clinically, which demonstrated irregular fibroadiposis and focal mononuclear cell infiltration consistent with chronic myocarditis in the right ventricle. Thiene et al. [*13*] and Imakita et al. [*14*] reported foci of active lymphocytic myocarditis

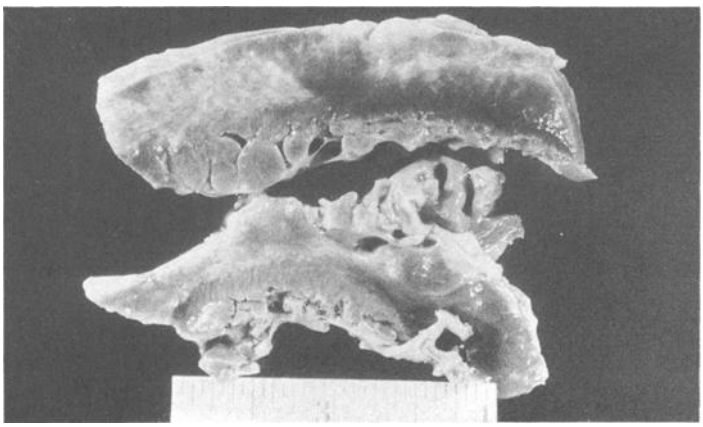

FIG. 4—*Sections of the left ventricle from Case 2, showing mottled discoloration in the epicardial aspect of the ventricle. The ruler is in inches.*

with myofiber necrosis within the area of fibrolipomatous change in the right ventricle. Our findings in Case 1 are similar to these reports. It is also possible that the year of episodic epigastric discomfort reported in Case 1 may have been cardiac rather than gastric in origin, consistent with a smoldering myocarditis.

It not clear as to the etiology of the fibrofatty change that has been reported in the myocardium of many individuals. While a select population of patients have an absent or nearly absent right ventricular musculature from birth or a familial predisposition to develop a right ventricular cardiomyopathy, there is a body of evidence that supports the role of a postinflammatory process in scarring the ventricle, resulting in an acquired cardiomyopathy. Other authors have identified abnormal mitochondria in right ventricle myofibers in a case of ARVD [*15*]. Whatever the causative factor or factors, the right ventricle appears to be a more common target for this process. However, our cases and the literature indicate that the left ventricle is not entirely spared and can be massively involved. Although our Case 1 had documented mitral valve prolapse in addition to an extensive area of affected left ventricle, the condition had been asymptomatic for years; the decedent in Case 2 had no other anatomic findings to explain his sudden death. We believe that extensive fibrofatty infiltration of the left ventricle was the most likely cause of sudden cardiac death for these two unfortunate individuals.

References

[*1*] Uhl, H. S. M., "A Previously Undescribed Congenital Malformation of the Heart: Almost Total Absence of the Myocardium of the Right Ventricle," *Bulletin of the Johns Hopkins Hospital,* Vol. 91, 1952, pp. 197–209.

[*2*] Marcus, F. I., Fontaine, G. H., Guiraudon, G., Frank, R., Laurenceau, J. L., Malergue, C., and Grosgogeat, Y., "Right Ventricular Dysplasia: A Report of 24 Adult Cases," *Circulation,* Vol. 65, No. 2, Feb. 1982, pp. 384–398.

[*3*] Fontaine, G., Guiraudon, G., Frank, R., Cabrol C., and Grosgogeat, Y., "Arrhythmogenic Right Ventricular Dysplasia. A Previously Unrecognized Syndrome," Abstracts of the 52nd Scientific Session of the American Heart Association, *Circulation,* Vol. 59–60, Supplement II, 1979, Abstract 245.

[*4*] Thiene, G., Nava, A., Corrado, D., Rossi, L., and Pennelli, N., "Right Ventricular Cardiomyopathy and Sudden Death in Young People," *The New England Journal of Medicine,* Vol. 318, No. 3, Jan. 1988, pp. 129–133.

[*5*] Nava, A., Thiene, G., Canciani, B., Scognamiglio, R., Daliento, L., Buja, G., Martini, B., Stritoni, P., and Fasoli, G., "Familial Occurrence of Right Ventricular Dysplasia: A Study Involving Nine Families," *Journal of the American College of Cardiology,* Vol. 12, No. 5, Nov. 1988, pp. 1222–1228.

[*6*] Manyari, D. E., Klein, G. J., Gulamhusein, S., Boughner, D., Guiraudon, G. M., Wyse, G., Mitchell, B., and Kostuk, W. J., "Arrhythmogenic Right Ventricular Dysplasia: A Generalized Cardiomyopathy?", *Circulation,* Vol. 68, No. 2, Aug. 1983, pp. 251–257.

[*7*] Webb, J. G., Kerr, C. R., Huckell, V. F., Mizgala, H. F., and Ricci, D. R., "Left Ventricular Abnormalities in Arrhythmogenic Right Ventricular Dysplasia," *The American Journal of Cardiology,* Vol. 58, Sept. 1986, pp. 568–570.

[*8*] Sugrue, D. D., Edwards, W. D., and Olney, B. A., "Histologic Abnormalities of the Left Ventricle in a Patient with Arrhythmogenic Right Ventricular Dysplasia," *Heart and Vessels,* Vol. 1, No. 3, Aug. 1985, pp. 179–181.

[*9*] Saito, K., Kuroda, A., Arima, S., Kawataki, M., and Tanaka, H., "Arrhythmogenic Right Ventricular Dysplasia with Left Ventricular Involvement: Report of a Case," *Heart and Vessels,* 1990 Supplement, Vol. 5, pp. 62–64.

[*10*] Gallo, P., D'Amati, G., and Pelliccia, F., "Pathologic Evidence of Extensive Left Ventricular Involvement in Arrhythmogenic Right Ventricular Cardiomyopathy," *Human Pathology,* Vol. 23, No. 8, Aug. 1992, pp. 948–952.

[*11*] Shoji, T., Kaneko, M., Onodera, K., Konnno, A., Hasegawa, T., Ikeda, T., Minase, T., Uchiyama, S., and Iwamoto, M., "Arrhythmogenic Right Ventricular Dysplasia with Massive Involvement of the Left Ventricle," *Canadian Journal of Cardiology,* Vol. 7, No. 7, Sept. 1991, pp. 303–307.

[*12*] Hisaoka, T., Kawai, S., Ohi, H., Ishijima, M., Okada, R., Hayashida, N., Kaiki, S., Kabayashi, H., and Yoshimura, H., "Two Cases of Chronic Myocarditis Mimicking Arrhythmogenic Right Ventricular Dysplasia," *Heart and Vessels,* 1990 Supplement, Vol. 5, pp. 51–54.

[13] Thiene, G., Corrado, D., Nava, A., Rossi, L., Poletti, A., Boffa, G. M., Daliento, L., and Pennelli, N., "Right Ventricular Cardiomyopathy: Is There Evidence of an Inflammatory Aetiology?" *European Heart Journal,* Supplement D, Vol. 12, 1991, pp. 22–25.

[14] Imakita, M., Yutani, C., Isobe, F., and Kamiya, T., "A Patient with Ventricular Tachycardia Showing Remarkable Fatty Infiltration and Lymphocytic Myocarditis in the Right Ventricular Wall," *The American Journal of Cardiovascular Pathology,* Vol. 3, No. 4, 1990, pp. 337–340.

[15] Blankenship, D. C., Hug, G., Balko, G., van der Bel-Kann, J., Coith, R. L., and Engel, P., "Hemodynamic and Myocyte Mitochondrial Abnormalities in Arrhythmogenic Right Ventricular Dysplasia," *American Heart Journal,* Vol. 126, Number 4, Oct. 1993, pp. 989–995.

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