TECHNICAL REPORT
8-75
業 績 報 告 書

FOCAL CARDIAC MYOCYTOLYSIS

局所性心筋細胞崩壊

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ABCC JNIH

ATOMIC BOMB CASUALTY COMMISSION

国立予防衛生研究所－原爆傷害調査委員会

JAPANESE NATIONAL INSTITUTE OF HEALTH OF THE MINISTRY OF HEALTH AND WELFARE

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FOCAL CARDIAC MYOCYTOLYSIS

局所性心筋細胞崩壊

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SUMMARY

During the course of a clinical pathologic study of cardiac lesions observed in 375 autopsies at ABCC, focal cardiac myocytolysis (FCM) was found in 21 hearts. There was no evidence that FCM was related to prior exposure at the time of the bomb. Myocardial infarction was present in only 10 of the 21 cases but more than half of the hearts with healing infarcts had FCM. Death due to cancer and thrombo-emboli in small intramural cardiac arteries were also associated with FCM. It was concluded that FCM was a unique histologically recognizable cardiac lesion which has received relatively little attention. The hypothesis was advanced that FCM could be a mechanism for extension of myocardial infarcts after the initial ischemic episode.

INTRODUCTION

When Schlesinger and Reiner[1] coined the descriptive phrase "focal myocytolysis of the heart" to describe a unique morphologic change at the level of light microscopy, they were convinced that the lesion was not due to myocardial infarction although the two were frequently associated. Necrobiosis of myocardial fibers with inflammatory and reparative reaction was not present but instead there was microfocal disappearance of myocardial fibers with scant cellular reaction. Once recognized, this

要　約

ABCC における剖検 375例にみられた心臓病変に関する臨床病理学的研究の過程で，21例に局所性心筋細胞崩壊（FCM）が発見された．FCM が原爆被爆に関係があるという証拠はなかった．心筋梗塞症を伴っていたのは21例中10例にすぎなかったが，心臓に治癒した梗塞のある例の半数以上に FCM がみられた．癌死亡例および心臓の壁内小動脈血栓塞栓症を有する例にも FCM がみられた．結論としては，FCM は従来あまり注目されなかったが，組織学的に発見できる特異的な心臓病変である．FCM は，最初の虚血性発作が生じてから心筋梗塞が伸展するための機序の一つであるかもしれないという仮説が提示された．

緒　言

光学顕微鏡検査で認められる特異な形態的変化を記述するために Schlesinger および Reiner[1] は"局所性心筋細胞崩壊"という用語を作ったが，この病変は心筋梗塞としばしば関連はあっても心筋梗塞によるものではないことを確信していた．炎症性および修復性反応を示す心筋線維の類壊死は認められず，その代わりに細胞反応の少ない心筋線維の細局所性消失を認めた．一度見分けがつけば，この"脱落壊死"は容易に識別できる．新しい

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"falling out necrosis" was readily identified and was found in nearly two-thirds of hearts with fresh infarcts and in 16% of hearts with old infarcts or areas of fibrosis. They also found cytolytic lesions in 5 of 213 hearts which were free of myocardial infarcts or fibrosis, including the hearts from 3 persons who had died of malignant tumors.

In addition to myocardial infarction, a wide variety of conditions have been cited as causes of or associated with focal cardiac myocytolysis (FCM) including intractable congestive failure, idiopathic cardiomegaly, viral and bacterial infections, Fiedler's myocarditis, subacute bacterial endocarditis, thrombo-embolic occlusion of intramural coronary arteries, scleroderma, poliomyelitis, uremia, pregnancy, insulin shock, oxygen deprivation, hyperthyroidism, vitamin B and protein deficiencies, beer drinkers cardiomyopathy (cobalt poisoning?), electric cardiac defibrillation, open heart surgery, fatal cerebrovascular accidents, and numerous experimental manipulations.[1-9] It has been postulated that FCM is the expression of many toxic or ischemic processes adversely affecting the cardiac metabolic balance.[1,2]

FCM is frequently associated with acute myocardial infarction and in certain respects resembles the healing stage of that process. Although most pathologists who have described these lytic lesions have recognized their unusual character, they have not agreed on nomenclature. Besides focal myocytolysis of the heart, terms used have included unusual myocardial lesions, acute miliary infarction, focal necrotizing myocarditis, myocardiopathy, encephalogenic cardiomyopathy, and myocardiosis.[1-7] Cytochemical and electron microscopic studies have been conducted principally in experimental animals.

The present report describes the findings in 21 hearts with FCM recognized during a study of cardiac changes in 375 autopsies performed at ABCC in Hiroshima and Nagasaki.

MATERIALS AND METHODS

The ABCC-JNIH Adult Health Study (AHS) sample has been described elsewhere.[10,11] Members of the group receive biennial physical examinations supplemented by various laboratory, roentgenologic, and other tests at ABCC.[12] The 375 AHS cases included in this study were autopsied during the period 1965-70 (Hiroshima) and 1968-70 (Nagasaki); all but four had at least one premortem cycle

梗塞を有する心臓のほとんど⅔，および古い梗塞または線維症を有する心臓の16%にこれを認めた．また，心筋梗塞または線維症のない213例の心臓中5例に細胞崩壊性病変を認めたが，その中には悪性腫瘍で死亡した3例の心臓も含まれていた．

心筋梗塞のほか，局所性心筋細胞崩壊の原因または心筋梗塞と関連性のある疾患または状態として，次のものが挙げられている：不応性鬱血性心麻痺，特発性心肥大症，ウイルス性および細菌性感染，フィードラー心筋炎，亜急性細菌性心内膜炎，冠動脈壁内血栓塞栓性閉鎖，鞏皮症，灰白髄炎，尿毒症，妊娠，インシュリン・ショック，酸素欠乏，甲状腺機能亢進症，ビタミンBおよび蛋白欠乏，ビール常飲者の心筋症(コバルト中毒?)，電気による心臓細動除去，開放心臓手術，致命的脳卒中および多くの実験的疾患状態．[1-9] 局所性心筋細胞崩壊は心臓の新陳代謝の平衡に悪影響を及ぼす多くの中毒性または虚血性心疾患の現われであるとの仮説がなされている．[1,2]

心筋細胞崩壊は，しばしば急性心筋梗塞と関連があり，ある面ではその治癒像に似ている．これらの崩壊病変について記述を行ったほとんどの病理医は，その特異的な特徴を認めながらも，これに対する名称については意見が一致していない．使用された用語には，心臓の局所性心筋細胞崩壊のほか，異常な心筋病変，急性粟粒性梗塞，局所性壊死性心筋炎，心筋病，脳源性心筋症，および心筋症[1-7]などが含まれていた．細胞化学的調査や電子顕微鏡調査は主として動物実験をもとに行われている．

本報では，広島・長崎のABCCで行われた375剖検例にみられた心臓の変化に関する調査の過程に局所性心筋細胞崩壊が認められた21例の心臓における所見について述べた．

材料および方法

ABCC－予研成人健康調査集団については別に報告がある．[10,11] この集団の対象者は2年ごとにABCCで診察ならびに各種臨床検査，X線検査，およびその他の検査を受ける．[12] 成人健康調査集団の対象例で本調査の対象に含めた375例は，広島で1965－70年，長崎で1968－70年の間に剖検の行われたものであり，このうち4例を除く

examination. Weight loss or gain was based on the difference between the weight at the time of the last clinic visit and at autopsy. Although different scales were used, they were shown to differ by less than 3%. In each case, blocks of tissue were taken for histologic section from the following seven sites: 1) anterior septum; 2) posterior septum; 3) anterolateral wall, left ventricle; 4) posterolateral wall, left ventricle; 5) posterior wall, left ventricle; 6) apex, left ventricle; and 7) right ventricle. Additional blocks were taken from other areas if macroscopic abnormalities were present.

全例は死亡前に少なくとも1度はABCCで周期診察を受けている．体重の増減は，最後の受診時と剖検時の体重との差とした．使用体重計は異なっていたが両者間の差は3％以下であった．各例とも次の七つの部位から組織ブロックを採取して組織切片を作成した．1)中隔前部；2)中隔後部；3)左心室前側壁；4)左心室後側壁；5)左心室後壁；6)左心室心尖部：7)右心室．なお，肉眼的異常が認められた場合は，他の部位からも組織ブロックを採取した．

During gross examination of the heart, special note was made of the heart weight, coronary status, presence of myocardial infarction and valvular abnormalities. The first 5 to 7 cm of the three major coronary arteries were graded for atherosclerotic involvement using the American Heart Association panel method[13,14] modified in that vessels with any area of narrowing were rated 5 or higher and vessels with occlusion were graded as 7 regardless of the presence or absence of atherosclerosis elsewhere in the vessel.[15] The presence of thrombo-emboli in intramural arteries was recorded during the examination of histologic sections.

心臓の肉眼的検査の際は，心臓の重さ，冠動脈の状態，心筋梗塞の有無および弁の異常に特に注意を払った．米国心臓学会のパネル法の変法を用いて三つの主要な冠動脈の最初の5－7cmの部分をもとにアテローム性硬化症の分類を行った．すなわち，血管の他の部分にアテローム性硬化の有無に関係なく狭窄のある場合は5以上の評点を与え，閉鎖のある場合7とした．組織切片検査の際，壁内動脈に血栓塞栓が認められた場合は記録した．

All histologic sections were routinely stained with hematoxylin and eosin, and the following stains were used as required: lipofuscin, iron, PAS, acid fast, Alcian blue, Masson trichrome, reticulum, Weigert-van Gieson elastic stain, Aldehyde fuchsin-Masson trichrome, fat, and amyloid.

組織切片は通常すべてヘマトキシリンおよびエオジンで染色し，必要に応じて次の諸染色法を用いた：リポフスチン，鉄，PAS，抗酸性，アルシアン青，Masson三重染色，細網織，Weigert-van Gieson弾性stain，アルデヒド・フクシン－Masson三重染色，脂肪およびアミロイド．

By definition, myocardial infarcts were limited to lesions which extended more than 5 mm in any direction. Lesions were coded as old when composed of scar tissue with little or no cellular infiltrate or fibroblastic activity, as healing when cellular proliferation and granulation reaction were predominant, and as recent when necrosis and inflammatory reaction were present. These three stages corresponded roughly to durations of more than 3 months, 3 weeks to 3 months, and less than 3 weeks, respectively.

心筋梗塞とは，いずれの方向であれ病変が5mm以上伸びている場合に限定した．細胞浸潤または線維芽細胞活動がほとんどまたは全然ない瘢痕組織から構成された場合，その病変は“陳旧性”とコードし，細胞増殖および肉芽形成反応が多く認められる場合は“治癒”，壊死および炎症反応が認められる場合は“新鮮”とコードした．これら三つの段階は，それぞれ，3か月以上，3週間－3か月，および3週間未満の各期間にほぼ相当する．

Identification of Cytolytic Lesions

細胞崩壊性病変の確認

Cytolytic foci were characterized by the absence of necrosis and acute inflammatory reaction in areas where muscle fibers had disappeared leaving a stromal framework and sarcolemma sheaths with sparse aggregates of mononuclear cells (Figure 1). Cells containing nonferrous pigment were prominent and most appeared to be phagocytes, but some may

細胞崩壊性病巣の特徴としては，間質構造および単核細胞群がまばらに散在する筋鞘が残り，筋線維の消失した部分に壊死および急性炎症性反応が認められなかったことである（図1）．非鉄性色素を含む細胞は多く認められ，そのほとんどが食細胞のようであったが，一部は

have been muscle nuclei surrounded by a condensation of lipofuscin pigment (Figure 2). In all stains this brownish pigment reacted like the lipofuscin pigment in neighboring intact muscle fibers. Foci of FCM were not sharply demarcated, and the process appeared to involve occasional muscle fibers at the periphery of the lesions in a continuing process. However, at the margins of lysed muscle bundles, typical palisades of viable myocardial fibers often persisted (Figure 3) and in this respect resembled the distribution of necrosis as it occurs in ischemic heart disease. The lesions varied considerably in size, the larger lesions appearing to be a confluence of smaller foci. In one case they extended from epicardium to endocardium (Figure 4). FCM was found in both ventricles and in all locations: subepicardial, mural, subendocardial and in papillary muscles. The atria were not examined.

The histologic sections of myocardium from all 375 autopsies were examined for the presence of any pathologic alterations. To test reproducibility in the recognition of cytolytic lesions, identification labels of all sections with healing or cytolytic lesions (133 of 358 sections from 47 autopsies) were replaced by random numbers, and the slides were examined 3 times during a period of 6 months. A fourth reading of the 133 identified sections from the 46 autopsies was correlated with clinical records and gross autopsy findings, and a final evaluation was established. The data in the results section are all based on this final evaluation.

RESULTS

Three groups emerged from the repeated examination of the histologic sections: 1) 10 autopsies with typical FCM associated with myocardial infarction, 2) 11 autopsies with typical FCM but with no other myocardial changes, and 3) 25 autopsies without typical FCM but with ischemic healing lesions containing foci of residual necrosis and a rich cellular reaction including fibroblastic proliferation. There were 47 sections which were finally accepted as containing lytic lesions. It was not difficult to identify FCM when no other myocardial lesion was present; the diagnosis for 32 of the 47 sections remained constant from one reading to the next. Variation in diagnosis was noted for the remaining 15 sections from 7 of the 21 hearts with FCM. The problem involved distinguishing lytic foci from the healing stage of small necrotic lesions in the presence of recent and healing myocardial infarcts in 5 cases and in the recognition of very small lesions in 2 cases.

リポフスチン色素の凝集に囲まれた筋核であったかも知れない（図２）．いずれの染色法を用いても，この褐色の色素は隣接筋線維に含まれているリポフスチン色素と同じように反応した．局所性心筋細胞崩壊の病巣の境界は鮮明でなく，その状態は場合により病変の周囲の筋線維までもおかすようであった．しかし，崩壊した筋束の辺縁では，活力のある典型的な心筋線維柵がしばしば存続しており（図３），この点では虚血性心臓疾患に発生する壊死の分布に似ていた．病変の大きさにはかなりの差があり，大型の病変は小さい病巣が集合したものと思われた．１例では，病変は心外膜から心内膜まで及んでいた（図４）．局所性心筋細胞崩壊は左右両心室ならびにすべての部位，すなわち，心外膜下，壁，心内膜下，および乳頭筋内に認められた．心房は検査しなかった．

375例の剖検例から得た心筋層の組織切片について，病理学的変化の有無を調べた．細胞崩壊病変を再度確認できるかどうかを調べるため，治癒した病変または細胞崩壊性の病変を有するすべての切片（47例の剖検から得た358の切片中133）の識別ラベルを無作為の番号に置き換え，６か月間に３度これらのスライドを調べ，判定を行った．これら46例の剖検から得た識別切片133についての４回目の判定結果は，臨床記録および肉眼的剖検所見と相関させ，最終的な評価がなされた．結果の項における資料は，すべてこの最終評価に基づくものである．

結　果

組織切片の反復検査により，次の三つの群に分類することができた：　a）心筋梗塞を伴う典型的な局所性心筋細胞崩壊を有するもの10剖検例，　b）心筋性変化の認められない典型的な局所性心筋細胞崩壊を有するもの11剖検例，　c）典型的な局所性心筋細胞崩壊は認められないが，残留壊死病巣および線維芽球増殖などの豊かな細胞反応を含む虚血性治癒病変を有するもの25剖検例．最終的には，崩壊性病変と認められた切片が47あった．他の心筋性病変がない場合は局所性心筋細胞崩壊を識別することは困難ではなかった．47の切片のうち，32の診断結果は判定の都度同じであった．局所性心筋細胞崩壊を示した21の心臓のうち，七つの心臓から採取した残り15の切片に診断の差違が認められた．新しい梗塞および治癒梗塞の認められた小さい壊死病変５例の識別ならびに極めて小さい病変のあった２例が発見されたことから，問題は治癒段階にある小さい壊死性病変と崩壊性病巣との識別であった．

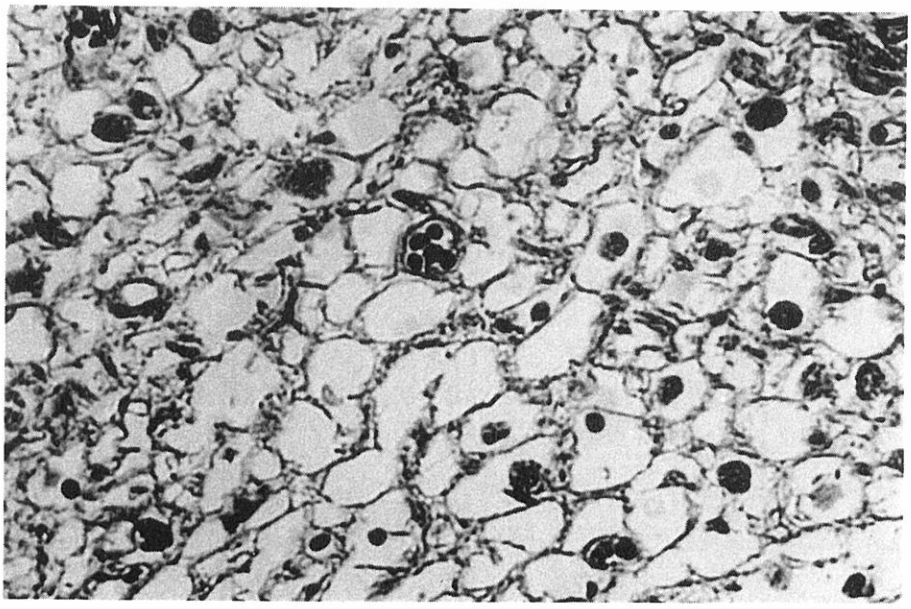


FIGURE 1. Center of an area of typical focal cardiac myocytolysis. Most of the rounded cells on the right are filled with pigment and appear to be phagocytes.

図1　典型的な局所性心筋細胞崩壊の中心部．右の円形細胞のほとんどは色素でみたされており，食細胞と思われる．

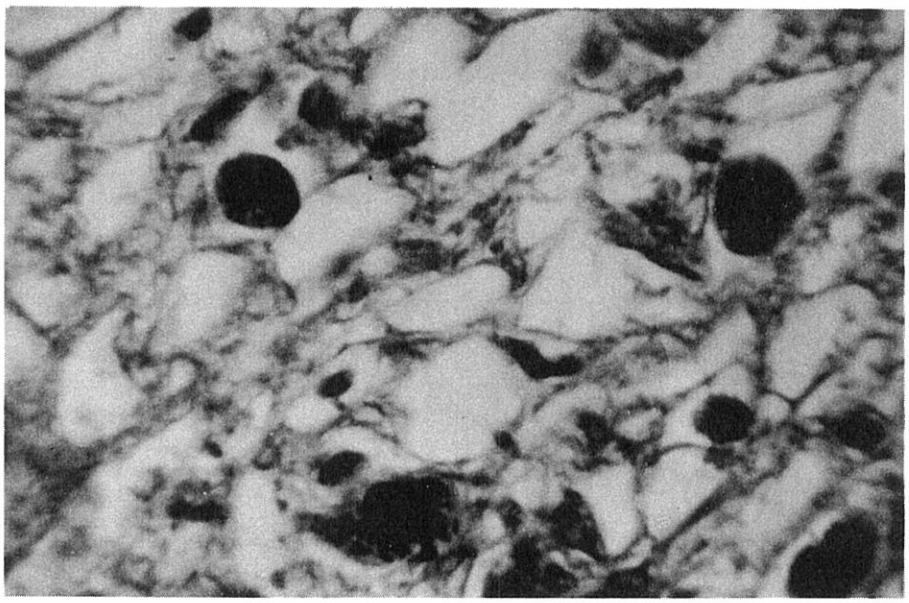


FIGURE 2. Pigment laden macrophages in an area of focal cardiac myocytolysis.

図2　局所性心筋細胞崩壊の部分にみられる色素で覆われた大食細胞．

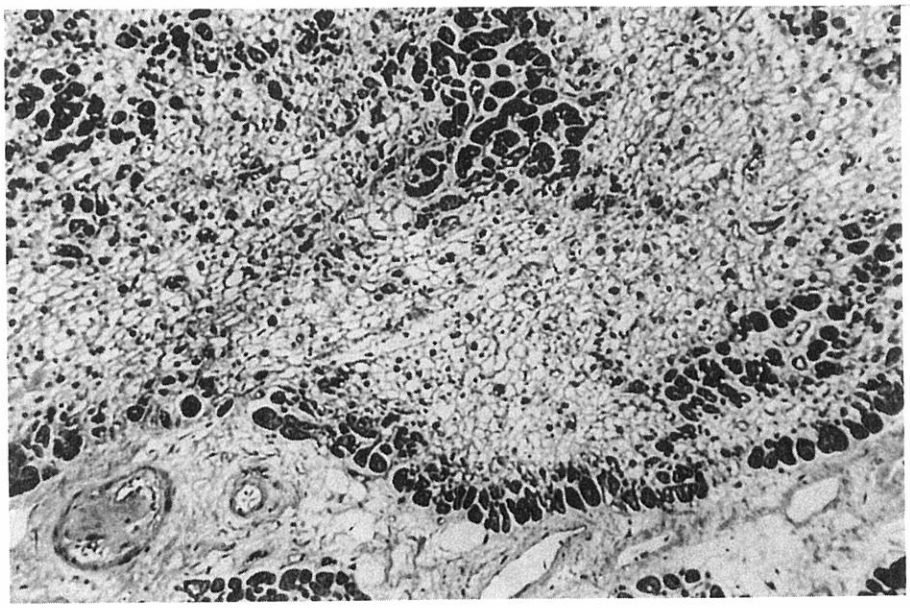


FIGURE 3. Focal cardiac myocytolysis with recanalized occluded small artery and viable peripheral palisades of muscle fibers.

図3　閉鎖された小動脈の再疎通および活力ある筋線維末梢柵の認められる局所性心筋細胞崩壊.

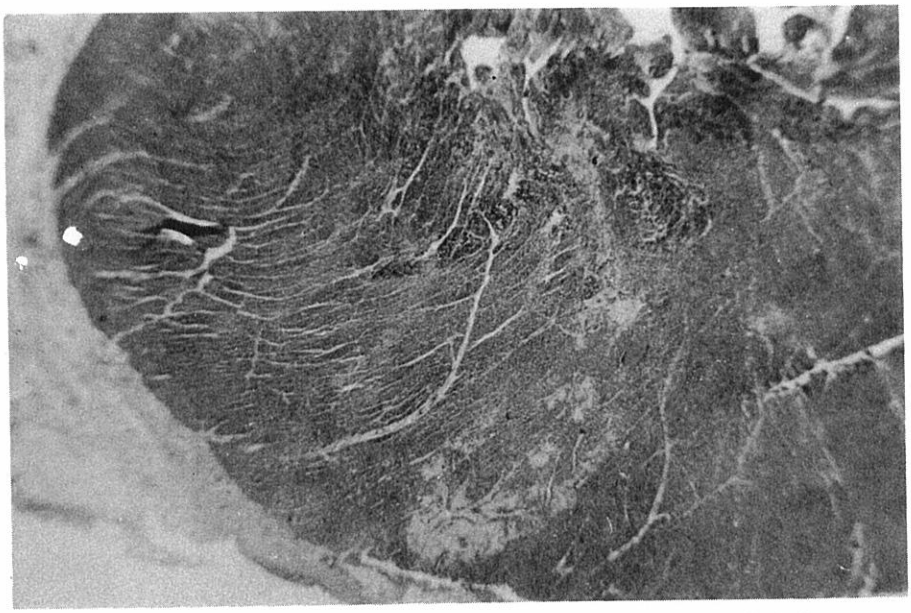


FIGURE 4. Distribution of lesions of focal cardiac myocytolysis in a section of left ventricle.

図4　左心室の組織切片における局所性心筋細胞崩壊病変の分布.

TABLE 1 FOCAL CARDIAC MYOCYTOLYSIS BY AGE AT DEATH, ESTIMATED RADIATION DOSE AT THE TIME OF THE BOMB AND BY SEX

表1　局所性心筋細胞崩壊：死亡時年齢，推定原爆時放射線量および性別

Age at Death	Total Autopsies		Focal Cardiac Myocytolysis			
	Male	Female	Male	%	Female	%
<49	14	14	0	-	1	7.1
50-59	18	16	1	5.6	1	6.3
60-69	52	65	0	-	2	3.1
70-79	67	58	2	3.0	4	6.9
80+	22	49	3	13.6	7	14.3
Total	173	202	6	3.5	15	7.4
Dose in rad						
<1	80	88	3	3.8	7	8.0
1-99	54	76	3	5.6	4	5.3
100+	39	38	0	-	4	10.5

Significance Test:

Male – <80 vs 80+ $0.01 < P < 0.05$

Female – <80 vs 80+ $.05 < P < .10$

All cases–<80 vs 80+ $P < 0.01$

All cases –100+ rads vs <1 rad *Not significant.*

Sex differences between age-specific and dose-specific percentages, all not significant.

Table 1 gives the distribution of lytic lesions by age, sex, and estimated amount of radiation received at the time of the bomb (ATB). In this series FCM was more common in older persons. There was no evidence that exposure ATB increased the likelihood of developing FCM. The occurrence of lytic lesions by principal autopsy cause of death is shown in Table 2. The association with fatal cancer and cardiovascular disease is prominent. Cardiovascular disease was the autopsy cause of death in 28 cases in four of which FCM was present. Histologic examination showed that myocardial infarction was present in the heart of 80 subjects. Most of these infarcts were old and were not the cause of death. FCM was found in 12% of the hearts with old infarcts and in 62% of those with healing infarcts.

The mean atherosclerosis scores for coronary arteries were not elevated in hearts with FCM except when myocardial infarcts were present nor was there a relation between the occurrence of FCM at autopsy and hypertension at the last clinic visit.

表1は，崩壊性病変の分布を年齢，性および原爆時の推定被曝線量別に示したものである．本調査では，局所性心筋細胞崩壊は高齢者の方に多かった．原爆被爆によって局所性心筋細胞崩壊が増大する可能性を示す徴候はなかった．表2では崩壊性病変の発生を主要な剖検死因別に示す．致命的癌および心臓血管疾患との関連は著しく高い．剖検時の死因が心臓血管疾患であった者は28例で，その中には局所性心筋細胞崩壊が認められた4例が含まれていた．組織検査では，80人に心筋梗塞があったことが認められた．これらの梗塞のほとんどは陳旧性のもので，死因ではなかった．局所性心筋細胞崩壊は，古い梗塞のある心臓の12%，および治癒梗塞のあるものの62%に認められた．

心筋梗塞がある場合を除けば，局所性心筋細胞崩壊のある心臓では，冠動脈の平均アテローム硬化評点は上昇を示さなかった．また剖検時に認められた局所性心筋細胞崩壊と当所での最終臨床検診時に高血圧症があった場合にも両者間に関係は認められなかった．

TABLE 2 FOCAL CARDIAC MYOCYTOLYSIS BY AUTOPSY CAUSE OF DEATH AND PRESENCE OF MYOCARDIAL INFARCTION

表2　局所性心筋細胞崩壊：剖検で確認された死因および心筋梗塞の有無別

	Autopsies	Focal Cardiac Myocytolysis	
Autopsy cause of death			
Cardiovascular disease	28	4	14.3%
Cancer	112	12	10.7
Cerebrovascular disease	87	1	1.2
Remainder	148	4	2.7
Total	375	21	5.6
Presence of myocardial infarcts*			
None	295	11	3.7
Old	74	9	12.2
Healing	8	5	62.5
Recent	13	2	15.4

**The following infarct duplications were present in 80 autopsies (number with FCM in parenthesis): old and healing 2(2); old and recent 5; healing and recent 2; old, healing, and recent 3(2).*

Significance Test: *FCM without MI vs FCM with recent MI – not significant*
FCM without MI vs FCM with healing MI – $P < 0.01$
FCM without MI vs FCM with old MI – $P < 0.01$

Nonbacterial thrombotic endocarditis (NBTE) was observed in 13 of the 375 autopsies, four of whom had both NBTE and FCM (Table 3). Small intramural branches of the coronary arteries were occluded by thrombo-emboli in 23 autopsies of which 9 also had FCM. In 3 cases, FCM, NBTE, and microthrombi were all present. Weight loss, body weight at autopsy, and heart weight were not related to the presence of FCM as was suggested to us by some consultants. Ten patients had a weight loss of more than 20% and 6 had no weight loss or gained weight between the time of last examination and death including one who had a weight gain of more than 20%. In 9 cases the heart weighed less than 275 g and in 8 cases more than 325 g.

DISCUSSION

During the preliminary stages of this study the lesions of FCM were regarded with some uncertainty. The well-developed and characteristic foic, when present without other cardiac abnormality, were easily recognized and were clearly different from myocardial infarcts. Very small lesions and foci adjoining active myocardial infarcts were not as easily identified. In part this is due to the manner

非細菌性血栓性心内膜炎は375剖検例中13例に認められ，うち4例にこれと局所性心筋細胞崩壊の両者があった（表3）．23例に血栓塞栓による冠動脈の壁内小動脈閉鎖が認められ，うち9例に局所性心筋細胞崩壊があった．局所性心筋細胞崩壊，非細菌性血栓性心内膜炎および微小血栓症は3名に認められた．死亡時の体重および心臓重量の減少と局所性心筋細胞崩壊との関係は認められなかった．10例においては最終検診時の体重に比して死亡時体重に20%以上の減少があったが，6例には変化がないか，むしろ増加しており，1例では20%以上の増加があった．9例の心臓は275 g以下であり，8例では325 g以上であった．

考　察

本調査の予備的段階では，局所性心筋細胞崩壊の病変についてはいくらか不明な点があった．他に心臓異常がなく完全な特徴的病変がある場合は，容易に区別でき，しかも明らかに心筋梗塞とは異なっていた．きわめて小さい病変および活動性心筋梗塞に隣接する病巣はそれ程容易には確認できなかった．これは一部には，心筋梗塞が発

TABLE 3 FOCAL CARDIAC MYOCYTOLYSIS BY PRESENCE OF NONBACTERIAL THROMBOTIC ENDOCARDITIS AND MICROTHROMBI

表3　局所性心筋細胞崩壊：非細菌性血栓性心内膜炎および微小血栓の有無

	Autopsies	Focal Cardiac Myocytolysis	
NBTE			
Absent	362	17	4.7 %
Present	13	4	30.8
Total	375	21	5.6
Microthrombi			
Absent	352	12	3.4
Present	23	9	39.1
Total	375	21	5.6

Significance Test: NBTE absent vs present – $P < 0.01$
Microthrombi absent vs present – $P < 0.01$

in which myocardial infarcts develop and progress. The size of a myocardial infarct greatly influences the character and rate of progression of the morphologic changes. Small areas of necrosis proceed to final scar formation more rapidly than larger lesions but muscle fiber and stromal necrosis, inflammatory and granulation tissue reaction, and active fibrosis and scar formation occur and merge one with the other in orderly progression.[16] Throughout the active healing stage, cellular infiltration and proliferation are prominent. In FCM, the order of change is evidently quite different. Lysis of cardiac muscle fibers may proceed rapidly to completion without necrosis of stroma or sarcolemmal sheath as indicated by descriptions of FCM occurring in cases of acute fatal cerebrovascular accidents due to rupture of a berry aneurysm when fairly accurate timing is possible.[17] The occurrence of fully-developed typical lytic lesions adjacent to recent myocardial infarcts still in the stage of acute necrosis also supports the belief that lysis of muscle fibers progresses rapidly.

Areas that have undergone lysis apparently change very slowly. In those cases where FCM was in anatomical relation to small arteries occluded by thrombo-emboli, there was little evidence that healing of the lesion had begun although the vessel occlusion appeared to be of considerable duration as indicated by organization and recanalization of the thrombus (Figure 2). The small numbers of infiltrating and reparative cells present also indicate that the lesions were changing very slowly. Because of the indolent progression of the lesions, it was difficult to determine how long they had been

現し進行する方法によるためである．心筋梗塞の大きさは，その性質ならびに形態的変化の進行速度に大きな影響を及ぼす．小さい壊死病巣は，大きい病変よりも速く，最後の瘢痕形成へ進行するが，筋線維および間質壊死，炎症性および肉芽形成性組織反応，ならびに活動性線維症および瘢痕形成が生じ，規則的な順序に従って互いに合併する．[16] 治癒が活動的に行われている間中，細胞の浸潤および増殖は著しい．局所性心筋細胞崩壊においては，変化の起こる順序は明らかにかなり異なる．心筋線維の崩壊は，かなり正確にタイミングがつかめる脳動脈の小嚢状動脈瘤破裂によって起こる急性の致命的脳卒中の例に生じる局所性心筋細胞崩壊の記述で示されるように，間質または筋鞘の壊死がなく完全に心筋線維が崩壊するまで急速に進行するかもしれない．[17] まだ急性壊死の段階にある新しい心筋梗塞に隣接して典型的な崩壊性病変が発生している事実も，筋線維の崩壊は急速に進行するとの考えを支持するものである．

崩壊のあった部分では変化はきわめて徐々に起こるものと思われる．局所性心筋細胞崩壊と血栓塞栓による小動脈閉鎖の位置とが解剖学的に関連ある例では，血管閉鎖は，血栓の構成および再疎通があることから分かるように相当な期間経過したと思われるにもかかわらず，病変の治癒が始まった徴候はほとんどなかった（図2）．少数の浸潤および修復細胞が認められるところから，病変の変化がきわめてゆるやかに行われていることがうかがえる．病変の進行状態が非常にゆるやかであるため，それらがいつから存在していたかを決定することはむつかしかった．

present. However, it is probable that the lytic lesions in different areas of the same heart did not always occur simultaneously.

We did not recognize cellular alterations that indicated that myocardial fibers were in the process of or about to undergo lysis. However, the lack of well-defined margins in established FCM and the presence there of muscle fibers which only partly filled the sarcolemmal space suggested that perhaps lysis of cardiac muscle fibers was still in progress. If so, it was without cellular reaction and, by inference, due to intracellular enzymatic activity. Recent investigation of post-infarction extension of areas of necrosis in ischemic heart disease indicate that the extension is related to oxygen demand and utilization. FCM may well be the pathogenetic expression of post-infarction extension which so far has not been described in morphologic terms. Five of the 8 autopsies with healing myocardial infarcts also had FCM. The conditions of this retrospective study did not permit adequate histochemical or ultramicroscopic examination of the lesions of FCM but early changes and disappearance of cellular enzymes, myofilaments, and organelles have been described by others.[5,7,9,18,19]

The association of FCM with so great a variety of pathologic, physiologic, chemical, and mechanical processes indicates in how many different ways myocardial oxygen-dependent enzyme systems can be inhibited with resulting lysis of muscle fibers without structural damage to the supporting connective tissue framework. It also accounts for the fact that prevalence at autopsy is largely determined by the characteristics of the autopsy sample. In this study, there appeared to be an association between FCM and the previously reported association of cancer, NBTE, and occlusion of small vessels by microthrombo-emboli.[20] Weight loss and emaciation, hypertension, disseminated intravascular coagulation, radiation exposure ATB, and immunologic suppression have all been suggested to us as playing a role in the pathogenesis of FCM. There is no evidence to support any of these suggestions.

FCM is a unique and recognizable pathologic entity which surely warrants further study. In myocardial infarction, cardiac surgery, cerebrovascular accidents, cancer, and other conditions, FCM could constitute an additional burden which would be of grave consequence. There is a need to clarify its clinical significance in the many diseases in which it plays a major or minor role.

しかし，おそらく同一心臓内の別々の部分で生じた崩壊性病変は常に同時に起こったのではないと思われる．

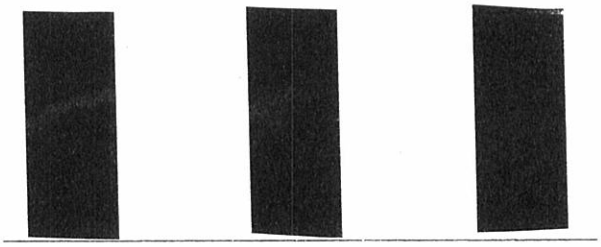
心筋線維が崩壊中である所見または今から崩壊しようとしていたことを示す細胞の変化は認められなかった．しかし，確認された局所性心筋細胞崩壊の辺縁が明確でないことや，筋線維が筋鞘腔の一部を満たしていたのみであることから心筋崩壊がまだ進行中であることを示唆するものであった．もしそれが事実であるとすれば，それは細胞の反応を伴うものでなく，細胞内の酵素活動によるものであると推測される．虚血性心臓疾患における梗塞後の壊死部分の伸展について最近行われた調査では，この伸展は酸素の欠乏および利用と関連のあることが認められた．局所性心筋細胞崩壊は，これまで形態学的に記述されたことのない梗塞後の伸展の原因の現れであるかも知れない．心筋梗塞が治癒していた剖検８例中の５例にも局所性心筋細胞崩壊が認められた．今回のretrospectiveな調査では，局所性心筋細胞崩壊の病変についての組織化学的あるいは限外顕微鏡的調査は十分に実施できなかったが，細胞酵素の早期変化および消失，筋糸状体および小器官については他の研究者[5,7,9,18,19]も報告している．

このように非常に多様な病理学的，生理学的，化学的および機械的な過程と局所性心筋細胞崩壊との関連は，心筋性酸素依存の酵素系が支持結合織の構造に損害を与えることなく，結果として起こる筋線維の崩壊によって，いかに多くの異なるパターンで抑制されるかを示す．また，剖検時における有病率は剖検対象の特性によって決まることもこれによって説明できる．本調査では，以前に報告された癌，非細菌性血栓性心内膜炎および微小血栓塞栓による小血管の閉鎖との間の関係と，局所性心筋細胞崩壊との間に関連があるようである．[20] 体重減少および痩衰，高血圧，播種性血管内凝血，原爆放射線被曝および免疫学的抑制はすべて局所性心筋細胞崩壊の成因に関係しているものと示唆されている．しかし，これを支持する証拠はない．

局所性心筋細胞崩壊は特異的な病理学的病変であり，さらに研究する必要があると考える．心筋梗塞，心臓外科手術，脳卒中，癌およびその他の疾患において，局所性心筋細胞崩壊はさらに負担を多くするものであり，重大な結果を招く危険がある．大なり小なり関係している多くの疾患におけるその臨床的意義を解明する必要がある．

APPENDIX
付　録

MASTER FILE NUMBER OF THE 21 AUTOPSIES WITH FOCAL CARDIAC MYOCYTOLYSIS
局所性心筋細胞崩壊をもった剖検21例の基本名簿番号



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