Focal Myocytolysis Mimicking the Electrocardiographic Pattern of Transmural Anteroseptal Myocardial Infarction*

Donald R. Düren, M.D., and Anton E. Becker, M.D., F.C.C.P.

Two patients are documented, one with a cerebral infarct and one with a primary brain tumor, both of whom initially had a normal electrocardiogram but subsequently developed the classic pattern of transmural anteroseptal myocardial infarction; however, in both cases the autopsy proved the electrocardiographic pattern to be related to "focal myocytolysis" of the myocardium. Both patients also exhibited coronary arterial disease of the localized type and to a maximal luminal narrowing of 75 percent without a history of anginal complaints. It is of interest that the intensity of the lesions of focal myocytolysis was greatest in the areas supplied by the affected arteries. This peculiarity suggests that ischemia, though not primarily involved in inducing the lesions, could be of additional significance.

Intracranial disease processes can be accompanied by abnormalities in the electrocardiogram. These changes are often quite variable and nonspecific. They may consist of (1) rhythm disturbances, such as bradycardia, tachycardia, and premature beats; (2) conduction disturbances, such as a decreased or increased P-Q interval and bundle-branch block; (3) abnormalities in the configuration of the ST-T segment which induces changes in the Q-T interval; and (4) abnormal QRS complexes, which may mimic the pattern of a transmural myocardial infarction. The latter cardiographic abnormality is extremely rare. As far as we are aware, there are only five previous reports of an ECG consistent with a transmural infarction. In only two of these reports, both of which dealt with the same patient, was a morphologic substrate for the electrocardiographic abnormality found. Histologic examination of the myocardium showed a lesion classified as focal myocytolysis.

It is the purpose of this presentation to document two patients, one with a cerebral infarct and one with a primary brain tumor, both of whom initially had a normal ECG but subsequently developed the classic pattern of a transmural anteroseptal myocardial infarction; however, in both cases, autopsy proved the electrocardiographic pattern to be related to focal myocytolysis of the myocardium.

*From the Departments of Cardiology and Pathology, University of Amsterdam, Wilhelmina Gasthuis, Amsterdam, the Netherlands.

Manuscript received August 26; revision accepted November 5.

Reprint requests: Dr. Becker, Department of Pathology, Wilhelmina Gasthuis, Amsterdam, The Netherlands

506 DUREN, BECKER

CHEST, 69: 4, APRIL, 1976
narrowing of the lumen, located at the posterior aspect, close to the crux cordis. The anterior descending coronary artery had a 7-mm long segment of luminal narrowing of not more than 75 percent. This segment was located just after the artery took origin from the left coronary main stem. Nowhere in the coronary arteries was there total occlusion of the lumen or a stenosis of more than 75 percent. The myocardium was sectioned in parallel slices from the apex to the base of the heart. Grossly, there was nothing to suspect the presence of myocardial infarction. The ventricular wall had a fleshy red-brown appearance throughout its entire circumference. Microscopic sections were taken from the total circumference of the slices at three different levels, i.e., (1) near the apex, (2) near the middle of the left ventricle, and (3) near the base of the heart. The histologic studies revealed extensive alterations which involved a large part of the left ventricular myocardium (Fig 3). Foci of "necrotic" muscle fibers enwrapped by a cellular infiltrate were scattered throughout otherwise unaffected myocardium (Fig 4). The affected fibers were swollen and showed a distorted cytoplogic architecture. Contraction bands were present, and loss of myofibrils became apparent. The degenerating fibers showed encroachment by mononuclear cells, some of which contained phagocytosed lipofuchsin pigment and nuclear debris. There were no polymorphonuclear leukocytes in the cellular infiltrate. The myocardial cells surrounding the foci of degeneration were all viable, without any recognizable sign of degradation. The lesion was designated as "focal myocytolysis," in accordance with previous descriptions. Nowhere in the many sections studied was a "classical" myocardial infarction present.

Figure 3. Schematic drawing of cross sections through heart of patient 1. Stippled areas indicate presence of focal myocytolysis. Greatest intensity of lesions was found in apical area of left ventricle (LV), where it was circumferential, and in part of posterior left ventricular wall supplied by dominant right coronary artery. RV, Right ventricle; POST, posterior; and ANT, anterior.

CHEST, 69: 4, APRIL, 1976
FOCAL MYOCYTOLYSIS 507
FIGURE 4. Left ventricular myocardium from patient 1. Amidst viable myocardium, cells are recognized showing far advanced degeneration with encroachment of mononuclear cells. There are no polymorphonuclear leukocytes present. Contraction bands (CB) are visible. (hematoxylin-eosin, × 350).

CASE 2

The patient is a 51-year-old man admitted to the Department of Neurosurgery of the University of Amsterdam, Wilhelmina Gasthuis, Amsterdam, because of severe headaches, nausea, and vomiting. Physical examination revealed no abnormalities. An ECG taken at the time of admission was normal (Fig 5). Findings from routine laboratory studies were unremarkable. A chest x-ray film was normal. Echoencephalography, brain scintigraphy, and cerebral angiography demonstrated a tumor in the region of the right tempo-occipital lobe. The patient underwent surgery, and the tumor was excised. Microscopic examinations showed an astrocytoma of grade 3. Following the operation, the patient gradually developed signs of an elevated intracranial pressure, which was ultimately treated with a Spitz-Holzer drainage. The ECG 7 days after the operation showed a normal sinus rhythm with signs of an acute transmural anteroseptal infarction, with extension towards the lateral wall of the left ventricle (Fig 6). The patient had no anginal complaints and no signs of left ventricular failure. The results of enzyme studies (SCOT, SCPT, LDH, and CPK) were within normal limits. Laboratory studies revealed no electrolytic disturbances. Subsequent ECGs showed subendocardial extension of the infarction towards the inferior wall, whereas just prior to death, R waves reappeared in the right precordial leads. The patient gradually deteriorated and died from elevated intracranial pressures four months after the operation.

Autopsy. The autopsy revealed no relevant gross abnor-

FIGURE 5. Electrocardiogram of patient 2, showing sinus rhythm and nonspecific ST-T segment changes.

FIGURE 6. Electrocardiogram of patient 2, obtained seven days after operation. It now shows sinus rhythm and changes compatible with acute transmural anteroseptal and lateral wall infarction.
malities apart from those in the brain. There was extensive growth of tumor, with destruction of both left and right frontal lobes and arachnoidal extension around the brain stem. Grossly, the heart showed no signs of an acute or healed myocardial infarction. Again, the cut surface of the slices was indistinctive. The total cardiac weight was 360 gm.

A postmortem coronary angiogram showed a right dominant coronary arterial pattern with mild atherosclerosis, restricted to the left anterior descending coronary artery. The artery showed a localized narrowing of approximately 75 percent of the luminal diameter, 9 mm after its origin from the main stem. There was no thrombosis and no total occlusion in any part of the coronary arterial stem.

Microscopic sections were taken from the total circumference of the left ventricle at three different levels, as indicated for case 1. The sections revealed lesions with a predominance for the anteroseptal, apical, and inferior wall regions of the left ventricle (Fig 7). The myocardium at these sites showed multiple lesions, which, in effect, were quite variable in aspect. Occasionally, minute foci existed, where cells exhibited swollen cytoplasm, slightly granular with loss of myofibrils and encroachment of mononuclear cells (Fig 8); however, the majority of the lesions consisted of small foci characterized by the disappearance of myofibrils, while the sarcolemmal sheets remained intact. A scant mononuclear cellular infiltrate was present. Macrophages occasionally contained some lipofuchsin pigment. There were no polymorphonuclear leukocytes. Other foci showed a fine fibrillar meshwork of connective tissue fibers, which apparently had replaced lost myocardial cells. In these foci, lymphocytes and macrophages could occasionally be seen. Definite signs of a classic myocardial infarction were not seen in any of the sections studied.

**DISCUSSION**

This report has documented the development of an electrocardiographic pattern of a transmural anteroseptal myocardial infarction in two patients, one with a cerebral infarct and one with a cerebral tumor. Surprisingly, however, the gross aspect of the myocardium did not show the alterations expected to be present in myocardial infarction. In fact, only the microscopic studies revealed pathologic changes. The discrepancy between massive transmural myocardial infarction clinically and complete lack of confirmtative data from gross inspection of the cut myocardium already suggests an underlying disease process different from classic myocardial infarction. Indeed, the changes encountered were those of focal myocytolysis. 15-18
As far as we are aware, such a clinicopathologic correlation has previously been reported in only one patient.\textsuperscript{11,12} This patient was a 49-year-old white woman with a subarachnoidal hemorrhage. During her hospitalization, that patient initially had non-specific ST-T segment changes on the ECG; however, five days after surgery, the ECG had changed into a pattern with a transmural infarction of the inferior and anterior walls of the left ventricle. Levels of serum enzymes, such as SGOT and LDH, and serum electrolytes were all within normal limits. The autopsy revealed multiple foci of myocytolysis throughout the left ventricular myocardium.

The two patients presently reported show similar features. In both cases a normal ECG was obtained prior to the development of a pattern of transmural myocardial infarction. In the first patient the active stage of focal myocytolysis was present. The aspect of the foci of degenerating myocardial cells with encroachment of a mononuclear infiltrate was highly characteristic for this condition.\textsuperscript{15-18} The second patient posed a problem in this respect. His electrocardiographic changes originated approximately four months prior to death. The "follow-up" suggested that at the time of death, a healing stage of the cardiac abnormality had been reached. Indeed, the microscopic studies of the myocardium revealed "healed lesions." These were mainly characterized by a fine meshwork of connective tissue fibers replacing lost myocardial cells. Of course, such foci had to be differentiated from miliary infarcts, a phenomenon known to make the myocardial cell towards the extracellular space, in keeping with the observed depletion of mitochondria\textsuperscript{16} and the polymorphonuclear leukocytic infiltration so characteristic of primary ischemic myocardial necrosis.\textsuperscript{15,17} This type of myocardial necrosis, which Schlesinger and Reiner\textsuperscript{18} have named "focal myocytolysis" and which Baroldi\textsuperscript{17} recently termed "coagulative myocytolysis," is particularly seen in the hearts of patients with intracranial disease processes, but is also seen with phaeochromocytoma,\textsuperscript{19,20} following cardiovascular surgery,\textsuperscript{21} and in experimental catecholamine-induced myocardial necrosis.\textsuperscript{22} Focal myocytolysis can also be identified in the border zone between a classic myocardial infarct and the normal myocardium;\textsuperscript{17} however, its pathogenesis remains a matter of speculation. All workers in the field feel certain that sympathetic overstimulation is of prime importance;\textsuperscript{23-25} however, additional circumstances are probably necessary to fulfill the setting that may lead to focal myocytolysis. It has recently been postulated that a complex mechanism is operative.\textsuperscript{25} The process is probably triggered by a hypothalamic mechanism which leads to sympathetic overstimulation and adrenocortical stimulation. The latter could lead to a shift of potassium ions from within the myocardial cell towards the extracellular space, a phenomenon known to make the myocardial cell extra sensitive to norepinephrine stimulation.\textsuperscript{26,27} Experimental studies have also shown that subarachnoid hemorrhage may lead to an increased cellular metabolism.\textsuperscript{18} Such studies further indicated a significant shift of calcium ions from the extracellular space to the cell cytoplasm, in keeping with the observed depletion of mitochondrial calcium stores and indicative of a hypercontractive stage.\textsuperscript{18,28} Under these conditions the effects of norepinephrine seem to be of primary significance, while ischemia is of secondary importance only; however, the latter could play a role, in particular, in creating irreversible myocardial damage. In view of these findings, the observations made in the two patients under discussion are of great interest. In fact, both patients had localized coronary atherosclerosis, albeit neither of these patients previously had any anginal complaints. Nevertheless, the first patient had two-vessel disease, whereas the second patient had one-vessel disease, restricted to the anterior descending artery. These observations are of interest in view of the aforementioned experimentally deduced concepts and since the myocardial lesions, indeed, show preference for the areas supplied...
by the arteries shown to be involved by atherosclerosis. It, therefore, seems that the luminal narrowing is of some significance, although not primary, in inducing the myocardial necrosis. It is of interest, indeed, that one encounters such an extremely rare phenomenon of a transmural infarction on the ECG arterial disease of the vessels supplying the regions affected. These findings reemphasize the fact that focal myocytolysis, in the given circumstances of sclerosis. It, therefore, seems that the luminal narrowing is of some significance, although not primary, in inducing the myocardial necrosis. It is of interest, indeed, that one encounters such an extremely rare phenomenon of a transmural infarction on the ECG arterial disease of the vessels supplying the regions affected. These findings reemphasize the fact that focal myocytolysis, in the given circumstances of intracranial disease processes, is a result of a complex mechanism which at present is not fully understood.

REFERENCES
6 Hersch C: Electrocardiographic changes in subarachnoid haemorrhage, meningitis, and intracranial space occupying lesions. Br Heart J 26:785-793, 1964
12 Hammermeister KE, Reichenbach DD: QRS changes, pulmonary edema, and myocardial necrosis associated with subarachnoid hemorrhage. Am Heart J 78:94-100, 1969