306 CD
DOI: 10.1017/S1431927606062106
Microsc Microanal 12(Supp 2), 2006

Which One Is The Culprit Lesion?

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Atherosclerosis is a disease of the intima of elastic and the larger muscular arteries. It consists of the focal accumulation of lipids, complex carbohydrates, blood and blood products, fibrous tissue and calcium deposits, associated with secondary changes in the media. It is a systemic disease, but, it is very focal in its manifestations, with the presence of lesion-prone sites, which differ structurally and functionally from non-lesion-prone sites. This is well demonstrated in the aorta, where lesions-prone sites have been demonstrated at areas of curvature, flow dividers and branching. Another postulate is that there is a region specific gene and the flow pattern determines the gene expression profile. Experimental work has suggested that atheroprotective genes are formed in lesion protected foci. It is well known that different levels within a vessel will show different degrees of severity of atherosclerosis, and, this has formed the basis of bypass procedures. However, it is distinctly unusual to find two diametrically opposite lesions within millimeters of each other, as is demonstrated by our case: Figs 1 and 2. Both sections are from the anterior descending branch of the left coronary artery (LAD).

In the pathogenesis of atherosclerosis there is an interaction between endothelial cell dysfunction, low density lipoprotein (LDL) in the blood and circulating monocytes, which become adherent to the intima. There is insudation of LDL into the intima and a transendothelial migration of the monocytes. Within the intima, the monocytes undergo activation to macrophages, which generate a spectrum of enzymes, such as metalloproteinases, as well as oxygen free radicals, which cause oxidative modification of LDL. The modified LDL is recognized by the scavenger macrophage receptor, which does not down regulate with lipid accumulation.

Platelets, activated monocytes and endothelial cells release a growth factor (mitogenic hormone) which stimulates the proliferation of smooth muscle cells in the lesion. The smooth muscle cells undergo a phenotypic change from a contractile to a synthetic state, when they take up LDL. They also secret large amounts of extra cellular matrix, which includes collagen, elastin and glycoaminoglycans.

As long as the lipid is intracellular, it is possible for this lesion to undero resolution, if the inciting factor is removed. Otherwise, there is death of the lipid laden “foam cells”, with release of the lipid in to the extra cellular matrix. There is a reaction on the part of the vasa vasosum, with the formation of new vessels within the lesion, known as the vasa plaquorum, and, the smooth muscle cells, which deposit a fibrous cap over the lesion.

The subsequent progression or regression of the lesion depends on the relative size of the lipid core, the thickness of the fibrous cap and the number of macrophages. Fig. 1 demonstrates dense fibrous cap formation with a small lipid core in the depth of the lesion. However, the lumen has been reduced to a mere slit like opening by the gross encroachment of the fibrous cap, upon it. Fig. 2 is at the extreme end of the opposite pole. The extensive lipid core has ruptured through the fibrous cap and the lumen is completely occluded by the atheromatous material. There is also evidence of calcification.

The patient was a 52-year-old man, who presented with substernal chest pain after a spicy meal. The EKG showed small Q waves, and, the cardiac enzymes were within normal limits. The patient was allowed to go home. At his request, he was given antacids to take with him. One hour later, he was brought back in a state of full cardiac arrest.

Which one of these two lesions dealt the coup de grace?

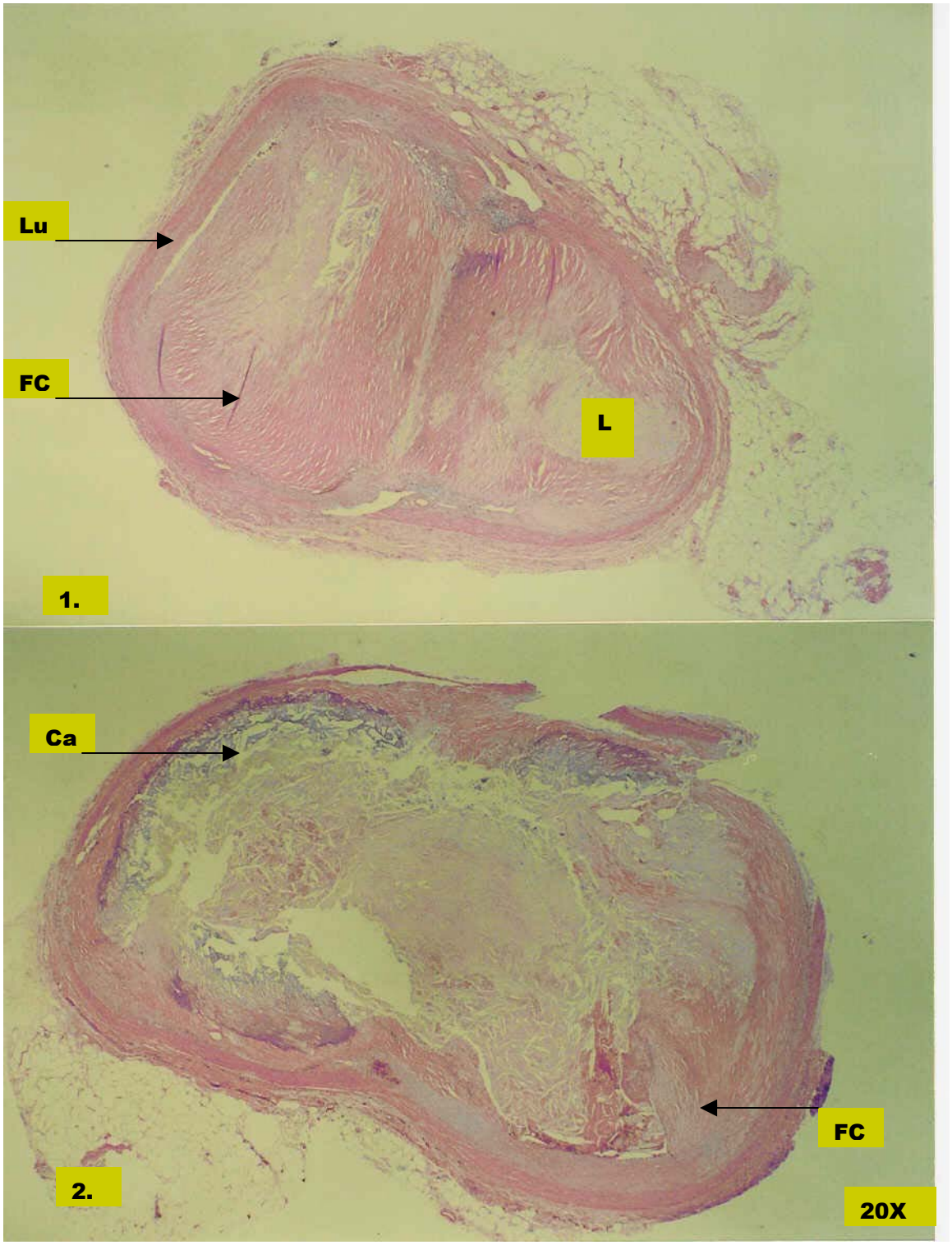

Fig. 1. Section of LAD FC Dense fibrous cap, L Small lipid core, Lu Slit-like lumen.
Fig. 2. Section of LAD Lumen completely occluded by ruptured plaque, Ca Calcification, FC Remnants of ruptured fibrous cap.

https://doi.org/10.1017/S1431927606062106 Published online by Cambridge University Press