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Longitudinal necrotic shafts near TCFAs—A potential novel mechanism for plaque rupture to trigger ACS?

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Abstract

It has been questioned for over 15 years why only less than 20% of TCFAs trigger ACS. We illustrate TCFA rupture into adjacent longitudinal necrotic shafts of massive amounts of thrombogenic material into the blood, leading to catastrophic clot formation. This is the potential mechanism for TCFAs triggering ACS. One case presented also illustrates the dangers of stent edges rupturing TCFAs.

It is well accepted that the rupture of thin cap fibroatheromas (TCFA), characterized by intimal cap thickness <85 μ m, is an underlying substrate for acute coronary syndromes (ACS) [1]. It is not well understood why only a minority (<20%) of TCFA progress to ACS [2–4]. OCT has shown considerable promise in imaging TCFA [5,6]. We propose, based on in vivo imaging and histopathology, that the propensity of a TCFA to trigger ACS could depend critically on the presence and size of an adjacent or contiguous longitudinal necrotic (thrombogenic) core extending up or down the artery. We term these shafts (to differentiate from dissections), long longitudinal necrotic cores up or down the artery covered by intima thicker than those of a TCFA. Current characterization of TCFA is based on cross sectional histology or imaging. We argue that assessment of TCFA is incomplete without imaging of adjacent vessel segments for these longitudinal shafts. A case is included of TCFA rupture that progressed to ACS, fortuitously OCT imaged shortly after rupture, supporting the proposed mechanism.

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Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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1. Case

A 60-year old male with multiple cardiovascular risk factors, chest pain and abnormal stress test underwent coronary angiography. Significant disease of the proximal LAD was treated with 1 drug-eluting stent (DES). The patient rapidly experienced chest pain and new onset ventricular bigeminy. Repeat angiography (within 2–3 s) showed slow flow and haziness in the mid-LAD several millimeters distal to the stent. Optical coherence tomography (OCT), performed within 2 min, demonstrated a large clot in the mid LAD, several millimeters distal to the stent. The distal stent edge was noted to have landed in and ruptured a TCFA. A large necrotic core was adjacent to the TCFA and extended distally along the length of the LAD. The stent-induced the rupture of the TCFA then extended into the adjacent shaft leading to excavation of the thrombogenic material into the distal lumen and acute vessel thrombosis occurred there millimeters from the TCFA (Figs. 1, Video 1).

In addition to this case, in Fig. 2, also included is the histopathology of a non-culprit coronary artery TCFA obtained post-mortem from another patient who succumbed to a MI. This is one of many examples, of histopathology, seen by our group of a shaft in close proximity to a TCFA.

2. Discussion

Based on the rare opportunity, we could observe events almost immediately after a TCFA ruptured (it was ruptured by the edge of a stent but the stent did not compress the TCFA completely or shaft) and ACS occurred. As it was a TCFA in close proximity to a necrotic shaft, we were able to hypothesize an ACS mechanism. We propose that rupture of a TCFA into large adjacent longitudinal shafts could be a critical mechanism for ruptures triggering ACS. This hypothesis serves as the basis for further studies to examine a significant cohort for validation. With our proposed mechanism for rupture triggering ACS, 2 distinct anatomic substrates would be obligatory: TCFA and an adjacent/contiguous large longitudinal necrotic core. Either substrate alone we postulate is not sufficient to cause a serious clinical event. In our hypothesis, the volume of the adjacent longitudinal shaft may have even more prognostic import than characteristics of the index TCFA. Rupture of TCFA into the shaft provides an avenue for blood flow to excavate the thrombogenic material into the lumen, depositing it in this case several millimeters distal to the index TCFA, and resulting in thrombosis and acute vessel closure. Prior histological and computed tomographic studies have demonstrated that the total regional lipid is one of the most important determinants of plaque instability (7). Our case provides a mechanistic explanation for these observations.

Quantification of the entire volume of necrotic core contiguous with the TCFA is essential to the better understanding of the clinical import of a TCFA. We believe that cross-sectional imaging alone is insufficient to predict which TCFA may cause catastrophic clinical events. We and other groups have previously focused on cross sectional images to further risk stratify vulnerable plaque [7,8]. But it seems unlikely that small differences in TCFA seen in cross sectional images, even spectroscopic analysis for lipid composition or intimal collagen content, would identify those plaques which progress to ACS (just likelihood of TCFA rupture) [8]. Our findings support the use of 3-dimensional imaging or at least multiple cross

sections for analysis with OCT for better characterization of vulnerable plaques. It is also conceivable that armed with the knowledge of the TCFA and adjacent longitudinal necrotic region, the operator may have placed the stent more completely over the TCFA.

3. Potential limitations

The potential limitations are: 1) only a single example is shown, though it represents the rare occurrence of OCT imaging almost immediately after a TCFA rupture with progress to ACS; 2) that the example shown was associated with a stent being implanted with the distal edge landing in a plaque—it is therefore not confirmed that blood will penetrate the shaft on TCFA rupture without the stent; and 3) it cannot be absolutely ruled out that the case shown might be an unusual case of dissection (though three experienced OCT readers ruled out dissection, based on the well defined boundaries of the shaft, which aided in generating the hypothesis).

But based on the observations of this unusual case, as well as theoretical considerations, we propose that rupture of a TCFA into large adjacent longitudinal shaft is a novel potential mechanism for ruptures to trigger ACS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1.

1A. The OCT images are arranged from proximal to distal, beginning with the distal stent edge. A. This angiogram demonstrates the stent (white arrow) and at least two clots distally (red arrow). B. The arrows show distal stent struts in the TCFA with a ruptured cap (TCFA more clear on next image). C. This slide shows a ruptured TCFA (yellow arrow) that broke into a deeper distal necrotic core or shaft (blue arrow). D. Shown is blood in TCFA breaking into distal plaque. The blue arrow is the necrotic core and the red arrow is the point of penetration into the distal plaque. E. Slightly more distal, the extension of the blood into the distal plaque (blue arrow) leads to the lifting of the intima (yellow arrow). F. Blood entering the core. G. The yellow arrow is blood that has entered the core, excavating necrotic contents into the lumen. H. Blood is occupying the former necrotic region of the plaque (blue arrow). The plaque is solid above and below the shaft (yellow arrows). The red arrow is the beginning of fracturing back into the lumen (see next slide). I. The yellow arrow is the shaft opening back into the lumen. J. In this frame, distal to the re-opening into the lumen and approximately 8 mm from the ruptured TCFA, is a clot (yellow arrow) attached to a

plaque surface. This is consistent with the necrotic core being forced into the blood from the distal opening and not the TCFA. K. The blue arrow is beautiful normal adventitia for illustration. A large clot fills most of the lumen from 6 o'clock clockwise to 1 o'clock. The clot extends for about 10 mm distal to the shaft. L. A distinct ruptured TCFA not in proximity to a shaft and with no evidence of thrombus. M. Intima with just minimal intimal hyperplasia distally. N. The yellow arrow shows a small ruptured TCFA in close proximity to a necrotic core. Unlike the earlier shown plaque, this plaque does not connect into the deeper shaft. No thrombus is noted in the area. 1B. In the proximal portion of the sketch, a TCFA is ruptured by stent struts. The TCFA fractures into a large nearby necrotic core or shaft. The blood drives through the shaft, evacuating the thrombogenic core, and re-enters the lumen distally. A clot forms not at the TCFA or stent, but several millimeters distally where the shaft reconnects with the lumen. Another ruptured TCFA is seen distally but it has minimal core and also has no observable clot (see attached video).

Fig. 2.

This figure shows the histopathology of a non-culprit coronary artery TCFA obtained post-mortem from a patient who succumbed to a MI (each cross section is approximately 250 μ m apart). The histopathology again illustrates the reasoning for not just examining a single cross section but also the adjacent necrotic shaft. The histopathology is stained with picrosirius to sharply differentiate the necrotic core. In Fig. 2A, a TCFA is seen with its thin cap (white arrow) and necrotic core (c). The core at risk for rupture has white dots placed at its periphery. An extension of the shaft in 2B is surrounded by red dots. In Fig. 2B, no longer at the TCFA, the intima is much thicker than 2A. But the necrotic core (c), now a shaft, is much larger (white dots) and is contiguous (or in proximity) with the core in 2A. If the cap in 2A ruptures, the large amount of thrombogenic material in the core in 2B would potentially be evacuated into the lumen now being exposed to high circulation pressures, a postulate of the paper.