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Morphologic features of culprit lesions in sudden coronary death with family history of premature coronary artery disease

Ming Chang Zhang [a,1], Yiwen Shen [a,1], Aimin Xue [a,1], Meng He [a], Nathaniel Cresswell [c], Ling Li [a,b], Ziqin Zhao [a], Yan Jiang [a,*], Allen Burke [a,b,**]

[a] Department of Forensic Medicine, School of Basic Medical Sciences, Fudan University, Shanghai 200032, China
[b] University of Maryland Medical System, Baltimore, MD 20201, USA
[c] Department of Pathology, Georgetown University Hospital, Washington, DC 20007, USA

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ABSTRACT

The morphologic features of familial coronary artery disease (CAD) resulting in sudden coronary death (SCD) are poorly studied. The presence and type of culprit lesions may have important implications in the genetic basis for familial heart disease. Autopsies of SCD victims over a 5-year period from a statewide medical examiner's office were studied. Premature familial disease was defined as sudden death at ≤50 years in women and ≤45 years in men, with premature SCD or acute coronary syndrome in a first-degree relative. Culprit lesion was defined as acute plaque rupture, plaque erosion, and severe narrowing without thrombus (stable plaque). There were 174 acute plaque ruptures (age 49 ± 10 years, 9% women), 49 plaque erosions (age 45 ± 8 years, 37% women), and 213 stable plaques (age 53 ± 11 years, 22% women). There were 8 plaque rupture with family history. There were 9 plaque erosions with family history. There were 7 stable plaques with family history. The rate of familial history in premature coronary disease was 18.4% in erosions, 4.6% in ruptures (p = .02 vs. erosion), and 3.3% in stable plaque (p = .002 vs. erosion). We concluded that the frequency of family history of premature sudden death due to CAD may be higher in plaque erosion as compared to patients dying with acute plaque rupture or stable plaque.

1. Introduction

Atherosclerotic coronary artery disease (CAD), the leading cause of morbidity and mortality in the western world, is a chronic process that begins during adolescence and slowly progresses throughout the life. The development of CAD involves a complex interplay between environmental and genetic factors, with premature CAD having a strong genetic component [1]. The risk of premature CAD in first degree relatives is notably higher than in the general population [2–4]. There have been many pathologic descriptions of fatal coronary artery disease [5–11]. However, the morphologic characteristics of CAD in patients with family history of premature CAD, especially in sudden coronary death (SCD), are not well characterized. The purpose of this current study is to determine the presence and type of coronary thrombus in SCD with family history of premature CAD, which may have important implications in the genetic basis for familial heart disease.

2. Materials and methods

We prospectively studied coronary arteries from forensic autopsies of sudden cardiac death victims over a 5-year period from a statewide medical examiner's office. The study was approved by the institutional review board. Inclusion for study was based on referral for consultation, absence of non-coronary causes of death at complete forensic autopsy, and ≥75% area luminal narrowing of ≥1 epicardial coronary artery. The presence of thrombus was ascertained and classified as erosion or rupture as previously described (Fig. 1) [12]. Investigative reports were reviewed for family history of sudden death or heart disease prior to cardiac pathologic evaluation. Premature familial disease was defined as sudden death ≤50 years in women and ≤45 years in men, with a parent, grandparent or sibling with SCD or acute

* Corresponding author at: Yixueyuan Road 138, Shanghai 200032, China. Tel.: +86 021 54237404; fax: +86 021 64044561.
** Corresponding author at: UMMS, 21 S. Greene St., Baltimore, MD 21201, USA. Tel.: +1 410 328 5526; fax: +1 410 328 5508.
E-mail addresses: jiangyan@fudan.edu.cn (Y. Jiang), aburke@umm.edu (A. Burke).
[1] These authors contributed equally to this work and should be considered as co-first authors.

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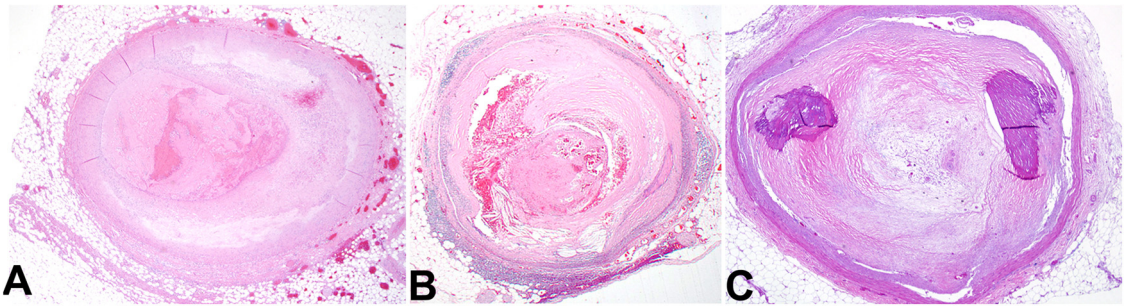

Fig. 1. Histologic features of culprit plaques. (A) Plaque erosion is characterized by smooth muscle cell rich plaque with luminal thrombus, in the absence of plaque rupture or thin cap. (B) Plaque rupture demonstrates a large necrotic core, rupture of the cap, and luminal thrombosis. (C) Stable plaque, in this case shows total occlusion without presence of thrombus (H&E staining).

coronary symptom with onset likewise ≤50 years in women and ≤45 years in men. The deaths were divided on morphologic examination and final full autopsy results including toxicological analysis, into three groups: sudden coronary death with plaque rupture; sudden coronary death with plaque erosion; sudden coronary death with stable plaque (≥1 epicardial artery with ≥75% cross sectional area luminal narrowing, without thrombosis).

Statistics were performed using JMP software, SAS Institute, Cory, NC. Comparison of two means was performed using Student's *t*-test, and of multiple categories was performed using ANOVA means table with Fisher's post hoc testing.

3. Results

There were a total of 436 hearts with SCD. Culprit plaque was acute plaque rupture in 174, acute plaque erosions in 49 and stable plaque in the absence of coronary thrombi in 213. Patients with plaque erosions were younger (45 ± 8 years) compared to patients with plaque ruptures (49 ± 10 years) and stable plaques (53 ± 11 years). The frequency of women was higher in plaque erosions (37%) than plaque ruptures (9%) and stable plaques (22%). The frequency of blacks was similar among patients with plaque erosion (35%) and stable plaque (31%), and lower in plaque rupture (23%). These differences were all statistically significant (Table 1).

There were 8 men with premature coronary thrombosis due to acute plaque rupture with family history, 7 Whites and 1 Black, aged 39 ± 6 years. There were 9 plaque erosions with family history, 6 men and 3 women, 7 Whites and 2 Blacks, aged 35 ± 10 years. There were 7 stable plaques with family history, 6 men and one woman, 5 Whites and 1 Black aged 35 ± 5 years (Table 2). The proportion of cases with an elicited family history was also higher when compared with the total number of premature deaths.

The related family member in plaque ruptures was the father in 6 cases, brother in 1 case, and both parents in 1; in plaque erosions, the father in 5 cases, mother in 3 cases, and grandfather in 1 case; in stable plaque, the father in 4 cases, brother in 2 cases, and mother in 1 case. One man dying with acute plaque rupture had a history of familial hypercholesterolemia, with total cholesterol of 253 and triglycerides of 688. The rate of familial history of premature coronary disease was 18.4% in plaque erosions, significantly higher than in plaque ruptures (4.6%, $p = .02$), and also higher than in stable plaque (3%, $p = .006$) (Table 2, Fig. 2).

4. Discussion

Coronary atherosclerosis represents the most important cause of sudden cardiac death [13]. Risk factors for CAD are well known,

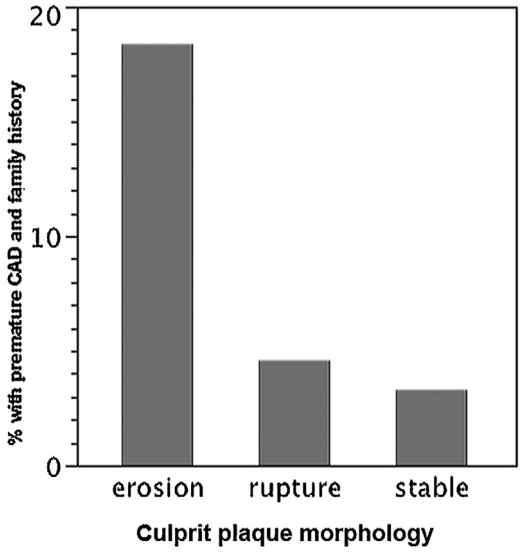

Fig. 2. Incidence of premature familial thrombi, by culprit plaque morphology. The rate in plaque erosion was significantly greater than ruptured plaques and stable plaques ($p = .006$).

Table 1
All coronary deaths during study period, by culprit plaque morphology.

	Plaque erosion	Plaque rupture	Stable plaque	*p* value
n	49	174	213	–
Age (years ± S.D.)	45 ± 8	49 ± 10	53 ± 11	<.0001
Women (%)	18 (37)	16 (9)	47 (22)	<.0001
African Americans (%)	17 (35)	40 (23)	66 (31)	.006

Table 2
Characteristics of premature coronary disease deaths with familial disease.

Culprit plaque morphology (*n*)	Premature deaths (*n*)	Premature deaths (of each group) (%)	Premature deaths with family history (*n*)	Premature deaths with family history (of each group) (%)	Premature deaths with family history (of premature deaths) (%)
Erosion (49)	31	63%	9	18.4%	29%
Rupture (174)	70	40%	8	4.6%	11%
Stable (213)	60	28%	7	3.3%	12%
p value	–	<.0001	–	.006	.05