East African Medical Journal Vol. 78 No. 4 April 2001
CORONARY ARTERIAL VESSELS IN RELATION TO SUDDEN CARDIAC DEATH: A REVIEW
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CORONARY ARTERIAL VESSELS IN RELATION TO SUDDEN CARDIAC DEATH: A REVIEW

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ABSTRACT

Objective: **To review literature on the coronary vascular factors related to the syndrome of sudden cardiac death.**

Data source/synthesis: **Major published articles and case reports on the nature of sudden cardiac death were searched electronically (Medline, Internet) and through hand scanning. Comparison of the different studies with regard to common themes was undertaken and consensus opinions highlighted.**

Results: **The aetiology of sudden cardiac death is diverse. Many conditions, hitherto considered benign, including coronary arterial anomalies and muscle bridges have been shown to cause sudden cardiac death. Coronary atherosclerosis, hypoplastic coronary vessels, coronary artery dissections are the commoner causes. The role of coronary arterial thrombi is controversial. The protective role of exercise is seriously questioned by the many reports of sudden cardiac death in long distance runners.**

Conclusion: **Cases of sudden cardiac death are increasingly being reported. As a minimum, autopsy worksheets for cases of sudden death should include atherosclerosis, congenital coronary anomalies, tunneling of coronary vessels and hyposplastic vessels in addition to valvular and myocardial disorders.**

INTRODUCTION

Sudden cardiac death (SCD) usually refers to unexpected death within six hours after onset of ischaemic symptoms in normal patients. Bateman defines sudden cardiac death as instantaneous deaths and those occurring up to 24 hours of symptom onset(1). If at autopsy no other pathology other than evidence of coronary stenosis is found, the term sudden ischaemic death is coined. The importance of this phenomenon lies in its devastating psychosocial agony to both relatives and physicians. For some time it was assumed that vigorous body exercises results in absolute protection against sudden cardiac deaths(2,3). This is no longer true as cases of SCD in healthy athletes continue to be reported(4-6). Sudden cardiac death is associated with atherosclerotic and nonatherosclerotic coronary abnormalities, myocardial disorders and valvular disorders. The list includes myocardial infarction with normal coronary arteries, myocarditis and hypertrophic cardiomyopathy, arterial anomalies, coronary ectasia, coronary arterial fistulae and coronary atresia. Many of these pathologies do exist in normal people and no simple relation exists between their presence and the risk of SCD. In this regard the true prevalence of the condition and the aetiology remains a subject of great debate. No age bracket is excluded from SCD. In the United Kingdom, up to 200 sudden deaths a year are reported in young fit individuals with negative toxicology and normal myocardium(7). Local reports of this condition are scarce, although cases are encountered from time to time. This paper reviews some of the anatomical and pathological possibilities forming part of "undetermined aetiology" autopsy reports of sudden death.

ANATOMICAL CONSIDERATIONS

Sudden deaths due to anatomical abnormalities of the coronary arterial system form the aetiology of sudden deaths in many reported series. There are normally two coronary arteries, right and left that exit respectively from the right anterior and left coronary sinuses. The predominant courses of the main parts of the vessels are epicardial with the right coronary artery forming the dominant vessel in 85% of human hearts. Coronary dominance classically refers to the vessel that supplies the posterior diaphragmatic surface of the left ventricle and the interventricular septum. Some authors have considered this a misleading term as coronary artery disease is primarily the result of interruption of blood supply to the left ventricular myocardium, in which situation the non dominant left coronary artery is almost always the more important vessel than the dominant right coronary artery. Anomalies reported to cause sudden death include abnormal coronary origin from the aorta, anomalous origin of the coronaries from the pulmonary artery, accessory coronary artery from aorta, aberrant coronary artery from aorta, hypoplastic coronary arteries

and intramyocardial course of the vessels. Congenital anomalies of the coronary arteries are generally uncommon, being detected in less than one per cent of all patients undergoing coronary angiography(8) and 0.6% of all patients with congenital heart disease(9,10). The anomalies occur in 2.85 out of 1000 general autopsies(11).

Anomalous right coronary artery: Origin of the right coronary artery from the left sinus of Valsava was once considered to be a normal anatomical variant. The current majority view is that this anomaly is a cause of both morbidity and sudden death. Symptoms such as chest pain in the absence of atherosclerosis and syncopal episodes requiring pacemaker insertion have been attributed to anomalous right coronary artery(12). Hanzlick and Slivers report sudden death due to anomalous right coronary artery in a young athletic male after a thirteen-mile marathon(5). At autopsy his right and left coronary arteries originated behind the left coronary cusp, each with its own ostium. The right artery arose tangentially from the aorta resulting in a semilunar flap occluding almost the entire ostium. The walls of the vessel itself were flattened and approximated. The vessel coursed between the aorta and the pulmonary trunk to the right atrioventricular groove and supplied both the sinoatrial node (SAN), atrioventricular node (AVN) and both ventricles. There was no evidence of gross atherosclerosis(5).

The altered haemodynamics attendant in this situation is thought to be the explanation for the morbidity and death in these patients. The vessel is compressed between the aorta and the pulmonary artery during systole. Again, the angle of origin in respect to the ostium creates a slit-like ostium, which is easily narrowed or occluded during systole. The potential for disaster is greater if the right coronary artery is the dominant vessel supplying the nodal, conducting tissue and both ventricles. In the case of strenuous activity as in the athletes, exercise enhances ventricular hypertrophy making an already bad situation worse. Analysing 21 cases of abnormal coronary origins for features that may aid in risk stratification for SCD, Taylor and his colleagues found no correlation with length of aortic intramural segments, ostial sizes, degree of displacement of the vessels and angles of take off(12).

Anomalous left coronary artery: Recorded cases of anomalous origin of the left coronary as the only postmortem finding in sudden death cases continue to be recorded. The anomalous origin may be from the pulmonary artery(8) or the right sinus of Valsava(13). Origin from the pulmonary trunk comprise the Bland-White-Garland syndrome and accounts for a major proportion of reported cases of anomalous left coronary artery origin(14,15). This condition usually present in early infancy with rapidly fatal cardiac decompensation with only twenty per cent of cases surviving to adulthood. Perper and his colleagues(8) report two cases of post-infant survival of anomalous origin of left coronary artery from the pulmonary trunk. In their case report, the right coronary artery was dominant. The ostia were enlarged with no atherosclerotic changes in both vessels(8). Analysing 33 cases of left coronary artery arising from the right coronary sinus, Cheitlin *et al.* demonstrated that 27% of the patients died suddenly(13). The death in these patients was associated with exercise. From its abnormal origin the coronary vessel passes leftward between the aorta and pulmonary artery. The mechanism of sudden death is related to acute angle of left coronary artery as it originates from the aorta and turns posteriorly thus compromising the lumen with systolic expansions of the aorta. Additionally the narrow orifice of the left circumflex artery contributes to the reduced blood flow(13,16). The 20% of patients who survive into adulthood in the Bland-White-Garland syndrome do so because of better and more efficient collateral circulation, which overcame the left to right backflow shunt to pulmonary artery(17). The enlarged coronary ostia may be another factor to the better prognosis.

Hypoplastic coronary artery disease (HCAD). This condition refers to underdevelopment of one or more coronary arteries or their branches reflected in diminutive vessels and markedly diminished and pinpoint lumina. Several isolated cases of HCAD have been reported in the medical literature spanning over more than 6 decades(11,18-22). Zugibe *et al*(26) in 1993 presented a series of seven cases representative of their cases of sudden death due to HCAD. In all the cases, the anterior descending artery was hypoplastic with luminal diameter between 1.0 and 1.8 mm. The left circumflex was diminutive in four of the cases. The right coronary artery was least affected. They contend that HCAD may be more common than is generally acknowledged. In a number of these cases, Zugibe *et al* (23) found an association between HCAD and a proximal obstructive atherosclerosis, that is, a single obstructive lesion located precisely proximal to the hypoplastic segment of the vessel and nowhere else. The authors posit that the coronary occlusion is due to the hypoplastic coronary artery disease conforming to Bernoulli's principle.

What is the presumed mechanism in death in HCAD? In coronary obstructive disease autoregulatory mechanisms are unable to meet metabolic demands and ischaemia is the result. Compensatory dilatation above and below areas of obstruction are attempted so that blood flow is increased and the heart rate increases to bring more blood to the area. In obstructive disease, increase in blood flow is not possible because the vessels are unable to dilate sufficiently because of diseased state. The increase in the heart rate is ineffective because the rapid rate allows less time for oxygen extraction because of the decreased diastolic interval(23). If the myocardium is hypertrophic as is expected in long-distance runners, this adds to the problem as the coronary blood flow is also affected by the perfusion distance from the coronary capillaries to the hypertrophied myocardium. Thus, persons with coronary hypoplasia who pursue increased athletic activity are at particular risks as the blood supply cannot adequately meet the metabolic demands due to a lack of compensatory mechanism.

PATHOLOGICAL CONSIDERATIONS

Acute coronary thrombosis: The nature of pathology in sudden cardiac death is in dispute. One of the contentious issues regarding the pathology of sudden cardiac death is the role of acute myocardial infarction. Some authors have considered the incidence of thrombi in sudden death to be low(16). Studying 500 consecutive autopsies of individual aged 20-99 years dying suddenly and unexpectedly of coronary artery disease, Di Maio and Di Maio found macroscopically visible coronary artery thrombus in only 13.4% of the cases of sudden death(24). This low incidence of thrombosis is in agreement with the studies of Roberts and Buja(25) who got eight per cent, Reichenbach *et al* (26) with 10% and Baroldi *et al* (27) with 15.3%. These postmortem reports of the frequency of occlusive coronary artery thrombosis in sudden death are at variance with the works of Davies and Thomas(28) and De Wood *et al* (29) among others. Using post-mortem angiography and histological examinations to study 100 cases of sudden ischaemic cardiac death, Davis and Thomas identified coronary thrombi in 74% of cases(28). These glaring differences may reflect methodological differences and the detail with which the coronary circulation was examined. The results from Davies and his colleague further showed preponderance of the thrombi in the right coronary artery- a finding they considered to confirm prediction that acute lesions in the artery that supplies the conduction system are life threatening(28). In the studies by Di Maio and Di Maio the left coronary artery and its branches showed slightly higher incidence of thrombosis than in the right(25).

Muscular bridges: This refers to segmental intra-myocardial coursing of an epicardial coronary artery. It has been variously referred to as intramural coronary arteries, mural coronary artery, coronary artery overbridging and myocardial loops. The condition is widespread in the animal kingdom. Its incidence in human hearts varies between 5.4% to78%(30-32). Its incidence at angiography varies between 0.51% and 12%(33). The most commonly involved vessel is the left anterior descending artery (LADA). Other involved segments include the first diagonal branch, obtuse marginal branch, posterior descending artery and the proximal right coronary artery. The significance of the presence of the muscular tunnels has remained controversial for a long time. Some authors have considered them as simple anatomical variants without any clinical importance while others consider them pathological. Their intermittent compression may lead to myocardial ischaemia. Bridges have been associated with angina, arrhythmias, acute myocardial ischaemia and even sudden death (34). Finding the presence of bridges in all ages from still born to 84 years of age, Ferreira *et al* (32) contend that the condition is congenital due to failure of incomplete exteriorisation of primitive coronary intratrabecular network during intrauterine life.

The bridged segment generally shows thinner intimae, less medial hypertrophy and less atheroma. Lee and Wu(35) have demonstrated a high incidence of intramyocardial coronary tunneling among Chinese population, a finding that explains the ethnic sparing of the Chinese from coronary atherosclerosis. The partial tourniquet effect of the muscular bridge protects the artery from atheroma. In their systematic study of 39 hearts with intramural LADA, Morales *et al*(34) found 17 hearts had no myocardial lesions. However, 22 had evidence of gross myocardial alterations in the myocardial territory supplied by the intramural LADA. These alterations included interstitial fibrosis, replacement fibrosis, contraction band necrosis or vascular density. Comparing the anatomy of the coronary systems of the 22 hearts with those of the seventeen, they found that each intramural LADA was deeply placed within the ventricular walls and there was attenuation of collateral flow because of coexisting intramural posterior descending artery, other epicardial arteries and/or diminutive right coronary arteries(34). On the association of the intramural vessels with sudden death, they were able to demonstrate that thirteen of the twenty two persons died suddenly during vigorous exercise. The significance of the muscular bridges must lie in the fact that the intramural LADA is compressed during systole. The systolic compression accounts for more than 90% of stenosis of the vessel lumen. During diastole, there is associated lag in the luminal opening accounting for 50% of the stenosis. Coronary flow is thus compromised during both phases of the cardiac cycle - possible mechanism for myocardial infarction. It is possible that the prognosis in such situations will depend on the length and depth of the intramyocardial segment and the amount of collateral circulation dictated by the associated intramyocardial portions of other coronary arteries. Further, association with hypoplasia of the other vessels is detrimental(36). Shortening of the diastolic filling time as may occur in tachycardia critically impairs coronary flow and increases the likelihood of precipitating myocardial ischaemia(32,34). Occurrence of such deaths during strenuous exercise is therefore not surprising.

Dissecting aneurysms of the coronary arteries: Isolated aneurysms outside the aorta are rare. Common sites of extra aortic aneurysms include the coronary, renal and carotid arterial systems. Coronary aneurysms can be spontaneous or iatrogenic. The first case of naturally occurring dissection of the coronary arteries was described by Pretty in 1931(37). Since then over 50 other cases have appeared in the literature(38). Majority of these lesions occur in females (female: male 3:1) and especially in the post- partum period(39). The left descending coronary artery is the most commonly affected vessel with the dissection 2-4 cm in lengths and within 2 cm of the aortic ostium . Histologically, the split is commonly in the outer portion of the tunica media(38) with the lumen compressed so that the channel is reduced to less than half of the expected diameter. The adventitia is usually infiltrated with neutrophils, eosinophils and histiocytes - features generally considered to reflect a reactive response to the sudden haemorrhage. This is however not a universal

feature(38). Rare pathological phenomena related to the dissection are intimal tears connecting the lumen to the haematoma, atherosclerosis and thrombi.

The overwhelming clinical presentation of dissecting aneurysms is sudden death in a young and previously well woman who is in her post-partum period(40). Theories advanced to explain the aetiology of coronary dissections include cystic medial necrosis, increased blood volume, cardiac output and hormonal influences associated with pregnancy(41), congenital defects and even trauma. That trauma may be a primary cause is evidenced by iatrogenic cases in which surgical manipulation of vessel wall appears to initiate the pathologic process(42) . Brody and his colleagues(43) consider it secondary to the Valsava maneuver causing intimal tears during pregnancy while Manallo-Estra and Backer(44) consider it due to degeneration of ground substance of the tunica media during pregnancy. Attempts to find generalised arterial changes in post partum cases of coronary dissections to account for increased frequency of dissection have been unsuccessful. Thus, coronary dissections remain a focal process.

In conclusion, both anatomical and pathological considerations are essential in the assessment of the agonising experience of sudden death. The victims are often young and middle aged although no age is excluded. The central role of strenuous exercise as the precipitating factor is important to realise because it is what tips the balance in a significant number of otherwise benign situations. As a minimum, an autopsy worksheet for cases of sudden death should include coronary arterial anomalies, atherosclerosis, intramural vascular courses, diminutive vessels in addition to the usual myocardial, valvular and rhythm disorders. Although these factors are associated with sudden cardiac death, individual patient outcomes are highly variable. More work needs to be undertaken in the risk stratification of these individuals.

ACKNOWLEDGEMENTS

We wish to thank Ahmed Kalebi for his assitance in preparation of manuscript. We appreciate the useful suggestions by Professor Joseph Mungai of the Department of Human Anatomy, University of Nairobi.

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