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Sudden death due to aortic dissection

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Acronyms
AD: aortic dissection
PTE: pulmonary thromboembolism

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ABSTRACT

Introduction: Aortic dissection is one of the cardiovascular causes of sudden death; hence deepening into its morphology will help improve diagnosis.
Objective: Clinicopathologic study in cases of sudden death secondary to aortic dissection.
Method: Thirty-four cases of sudden death due to aortic dissection were studied in the histopathology laboratory of the Legal Medicine Institute (1998-2015). Forensic autopsy was performed with complementary histological and toxicological studies.
Results: 73% corresponded to men with a lower average age than women (42 vs. 49 years). The cardiac weight was increased (88%), regardless of age, with a mean of 534 g, and was higher when presenting dilated aortic root (74%) or high blood pressure (53%). Cystic medial degeneration (57%) was associated to aortic dilation ($p<0.05$) and bicuspid aortic valve, and both with younger age ($p=0.001$), but not related to high blood pressure and left ventricular hypertrophy in older ages. Horizontal line was more frequent (66%) and Type II DeBakey predominated. Most of them died suddenly at home (66%); 61% from previously known symptoms (51% of the total) was associated with chest pain (mainly precordial). 40% had sought medical attention the day before and were erroneously diagnosed.
Conclusions: Post-mortem study helps to better define the macroscopic and histological characteristics in the most severe cases of aortic dissection to achieve accurate diagnosis.
Key words: Aortic diseases, Aortic dissection, Sudden death

Muerte súbita por disección aórtica

RESUMEN

Introducción: La disección aórtica resulta una de las causas cardiovasculares de muerte súbita, por lo que profundizar en su morfología debe contribuir a mejorar su diagnóstico.
Objetivo: Estudio clínico-patológico en casos de muerte súbita secundaria a disección aórtica.
Método: Se estudiaron 34 casos de muerte súbita por disección aórtica en el laboratorio de histopatología del Instituto de Medicina Legal (1998-2015). Se realizó autopsia forense con estudios complementarios histológicos y toxicológicos.
Resultados: El 73% correspondió a hombres con edad media menor que las muje-

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res (42 vs. 49 años). El peso cardíaco estaba aumentado (88%) independientemente de la edad, con una media de 534 g, y fue mayor cuando hubo dilatación de la raíz aórtica (74%) o hipertensión arterial (53%). La degeneración quística de la media (57%) se asoció con dilatación aórtica (p<0,05) y válvula aórtica bicúspide, y ambas con la menor edad (p=0,001), mientras que no se relacionó con la hipertensión arterial y la hipertrofia ventricular izquierda en edades más avanzadas. La rotura horizontal fue más frecuente (66%) y predominó el tipo II de DeBakey. La mayoría falleció súbitamente en el domicilio (66%); el 61% de la sintomatología previa conocida (51% del total), se asoció a dolor torácico (principalmente precordial). El 40% había acudido al hospital un día antes y había recibido diagnósticos erróneos.

Conclusiones: El estudio post mortem puede definir mejor las características macroscópicas e histológicas de los casos más graves de disección aórtica para mejorar su difícil diagnóstico.

Palabras clave: Enfermedades de la aorta, Disección aórtica, Muerte súbita

INTRODUCTION

The aortic dissection (AD) is an acute process of the aortic wall in which a continuity solution occurs by a tear in the intimal layer, and it is characterized, from the anatomopathological point of view, for a separation between this and the middle layer, exposing the pulsatile blood flow, which penetrates, dissecting it, in variable longitudinal and circumferential extensions, distally and occasionally of proximal extension; this creates a false light, in addition to a reentry site into the true light. The pressure in the false light produces compression of the true light and can occlude the branches of the aorta, which can generate distal ischemic complications due to bad perfusion. It is a clinical condition in which there is an alteration at the level of the arterial intimal and the middle layer of the aorta, which leads to a risk of aortic rupture and other complications, and it has a high mortality rate in the acute phase. It is the most common within the called Acute Aortic Syndromes, including the intramural hematoma and the penetrating aortic ulcer[1,2].

The most common primary location of the intimal tear is the ascending aorta, between 1-5 cm above the right sinus of Valsalva in 65% of cases, in the descending proximal aorta below the left subclavian artery in 20%, in the transverse aortic arch in 10%, and in the thoracabdominal distal aorta in 5% [1].

The International Registry of Acute Aortic Dissection (IRAD) has compiled a series of data that identify numerous risk factors for the development of acute AD (**Box**).

Numerous publications have sustained these risk factors and enriched them, thus, they include:

- The pregnancy, since 50% of dissections occurring in young women under 40 years old happen during pregnancy, where the rupture commonly occurs in the third trimester or the first stage of labor.
- Advanced age and sex, since the peak incidence of aortic dissection takes place in the sixth or seventh decades of life, and it affects two times more men than women.
- Endocrine disorders, through the development of high blood pressure can lead to dissection, such as Cushing's disease or the pheochromocytoma.
- A traumatism, which can result in a rupture of the intimal.

The knowledge of the AD incidence in the general population is limited; several studies indicate it between 2.6-3.5 cases per 100 thousand inhabitants per year[3]. They can be classified in different ways, but they are usually according to: 1) duration of symptoms, and 2) the presence and location of primary tears and retrograde or antegrade extension of the dissection.

According to the first, it will be acute, if the clinical symptoms have lasted 14 days or less (period of greatest morbidity and mortality); subacute, if symptoms have lasted between 2 and 6 weeks; or chronic, if the symptoms have lasted beyond 6 weeks.

Regarding the second criterion, two classifications with great importance in determining the conduct to follow are used. The Stanford Group established types A and B, as it is affected or not by the dissection of the ascending aorta; and that of DeBakey, the difference between type I when the ascending and descending aorta are affected, type II

Box. Risk factors of acute aortic dissection.

Risk factors	Comment
High blood pressure	This is the most important predisposing risk factor. In different research published by IRAD, the high blood pressure has been associated in more than 70% of patients.
Pre-existing aortic aneurysm	It is the most common cause in patients under 40 years of age.
Genetic diseases	Some with connective tissue disorder, such as Marfan syndrome or Ehlers-Danlos syndrome; others such as aortic anulectasis, bicuspid aortic valve and family AD. Common denominator of these genetic disorders is the dedifferentiation of the vascular smooth muscle cells and increased elastolysis of components of the aortic wall, leading to a weakened intimal and to aorta dissection.
Vasculitis	Inflammatory diseases that cause vasculitis like arteritis of giant cells and Takayasu's, rheumatoid arthritis or syphilitic aortitis
Turner and Noonan's syndrome, polycystic kidney disease	
Cardiac surgical interventions and their complications	
Valsalva maneuver	Results in a significant elevation of blood pressure. This factor is of great importance in those patients with risk factors or with a family history of aneurysms.
Cocaine use	With an average time of 12 hours between the last dose and the dissection.

when only the ascending aorta is concerned and type III when only the descending aorta is affected.

In recent years, advances in imaging techniques have helped establishing much more accurate medical diagnoses of this disease, which, in most cases, guide the therapeutic approach and prognosis of patients. Despite this, the diagnoses by the health staff represent a challenge because it is a disease with very different clinical presentations, which raises the need to insert this diagnosis within the diseases to discard.

The AD can produce sudden death, however, some patients can present symptoms prior to death and sometimes may even attend emergency services, thus, it is necessary to maintain a high index of suspicion by the physician to establish a rapid and accurate diagnosis. This study aims to show what are the symptoms in these patients and to contribute from the Forensic Medicine with some aspects for the Emergency Medicine when establishing differential diagnoses with other diseases.

METHOD

A descriptive observational cross-sectional and retrospective study was performed.

A total of 34 cases of sudden death due to AD were study in the histopathology laboratory of the Institute of Legal Medicine and Forensic Sciences of Valencia, Spain, between 1998 and 2015; these cases had forensic autopsy with histological and toxicological complementary studies. The symptoms presented and cases where a proper medical diagnosis was not established in life were analyzed, including other variables.

The variables analyzed were: sex, age, circumstances of death and place, heart weight, type and form of dissection, autopsy findings and histopathological examination. The latter contained the visceral generalized sampling and the specific study of the breakdown of the aorta's elastic fibers, cystic degeneration of the middle layer, the presence of intramural hematoma, among others.

In order to analyze them, there were taken into account: the corpse's information, the service report of the emergency medical attention, (In those cases where there was that kind of performance) reports from hospital admissions and laboratory tests, egress reports (in cases where there was medical attention days before death), as well as judicial autopsy reports, histopathology and toxicology. In

addition, data weight, height and body mass idex were obtained.

The information obtained was extracted from the file of manuscript documents and computer systems (Risk Assessment Unit of the Family Sudden Death Risk of the Histopathology and Melva Section). Its analysis was carried out through the statistical program SPSS v17.0.

RESULTS

In this study, a total of 34 cases were analyzed, 73.5% were men, the most affected age group was between 41 to 50 years of (38.2%) with an average age of 42 years in men and 49 in women (**Table 1**).

Circumstances of the facts

The information collected during the removal of the corpse allowed to determine that 19 cases (55.9%) took place at the residence and 9 (26.5%) at the hospital. In some of the deaths at the residence, information of prior consultation in a medical center is confirmed.

Hospital care

In 51% of cases, known previous symptoms were manifested; of them, 61% presented chest pain, 17% lumbar pain and 11% headache. Concerning the thoracic pain, it was confirmed that it was predominant at the precordial region (77%), while the remaining 23% was referred to in the interscapular region. Furthermore, in cases that had previous symptoms, the 40% had come to the hospital before death and diagnoses were established: back pain, abdominal pain, renal colic, pulmonary thromboembolism (PTE) or musculoskeletal pain.

The case diagnosed with PTE draws attention because the patient went three times to the emergency room, initially with interscapular pain radiating to left hemibody, later with chest pain associated with dyspnea and vagal symptoms, and the established diagnoses were: mechanical thoracic pain, asthmatic crisis and PTE. However, despite this latest diagnosis, the patient is discharged and goes to the hospital again, due to persistence of dyspnea and chest pain, where she eventually dies.

The most prominent risk factors were: high blood pressure (26.5%), family history of sudden death (17.6%), type II diabetes mellitus (8.8%), the exposure to tobacco (20.6%) and dyslipidemia (5.9%).

Table 1. Distribution of cases according to age, sex and place of death (n=34).

Variable	Nº	%
Age		
Younger than 20	0	0,0
Between 21 and 30	5	14,7
Between 31 and 40	7	20,6
Between 41 and 50	13	38,2
Older than 51	8	23,5
No data	1	2,9
Sex		
Man	25	73,5
Woman	9	26,5
Place of death		
Residence	19	55,9
Hospital	9	26,5
Street	2	5,9
Work	1	2,9
No data	3	8,8

Autopsy and histopathology findings

In the autopsy procedure was found that the heart weight was increased in 28 cases (82.4%), regardless of age, with a mean of 534 grams, and it was bigger if there was a dilation of the aortic root or high blood pressure (**Table 2**).

The horizontal rupture of the aorta was the most frequent (67.6%), with an average length of 4.15cm and the type II DeBakey (73, 5%) predominated, without finding significant differences concerning the anatomical location. No case was found where a type III dissection was described.

In determining the statistical associations among the variables evaluated, there was found that the cystic medial degeneration (470%) was associated with the aortic dilatation ($p < 0.05$) and bicuspid aortic valve, and both, with a younger age ($p=0.001$). No

association with high blood pressure or ventricular hypertrophy was found.

Table 2. Findings in the autopsy procedure and in the histological study (n=34).

Parameter	Nº	%
Cardiac findings		
Cardiomegaly	28	82,4
Coronary atherosclerosis	13	38,2
Aortic arteriosclerosis	13	38,2
Left ventricular hypertrophy	15	44,1
Dilation of the aortic root	20	58,8
Bicuspid aortic valve	10	29,4
Form of dissection		
Horizontal	23	61,8
T-shaped	5	14,7
Vertical	3	8,8
Circumferential	2	5,9
Double	1	2,9
Classification of DeBakey		
Type I	9	26,5
Type II	25	73,5
Histopathological findings		
Cystic degeneration	16	47,0

DISCUSSION

The acute AD is the most common cause of sudden death in the aorta's diseases and it is associated with high mortality; despite the advances in diagnosis and treatment techniques, the mortality rate is high with increase of 1-2% per hour[2]; it also represents a diagnostic challenge because of the variability in clinical presentations that, sometimes, causes delays or errors in diagnosis, with fatal results.

As the clinical manifestations are too diverse and the presentation can be varied, it is important to have a high index of suspicion by the physician to establish a rapid and accurate diagnosis. Thus, the objective of these studies in *post mortem* autopsies is that they reduce the mortality of this devastating disease, especially when patients have no classical symptoms and signs, or present with a rapid deterioration[3].

In the data of IRAD[4] (International Registry of Acute Aortic Dissection), the proportion of men suffering from AD is 66.7%, with an average age of 63; in the group of 31 cases of Li *et al.*[5] it was 87.1%, in the study by Moreira *et al.*[6], at the north of Portugal was 70.3% and, in our group, of 73%, which is the second largest portion of all of this studies.

The AD affects patients between the fifth and seventh decades of life. In younger than 40 years, it has a similar frequency in both sexes, because it is most frequent in women during the third trimester of pregnancy. The average age of Li *et al.*[5] and Moreira *et al.*[6] was 44 and 65.19 ± 14.35 years, respectively, with no significant differences in the type A and B of Stanford.

The most common risk factor was high blood pressure, which coincides with the 77% of cases of the study of IRAD[4]. Chronic exposure of the aorta to high tensions results in intimal thickening, fibrosis, calcification and extracellular deposition of fatty acids; the extracellular matrix can suffer accelerated apoptosis and elastolysis degradation, with intimal disruption end generally at the edges of the atheromatous plaques [7-9]. Our results coincide with those of Moreira *et al.*[6], since 54.1% of their cases presented a history of high blood pressure. This modifiable risk factor requires adequate medical control[11].

Other risk factors, such as arteriosclerosis, genetic diseases like the Marfan syndrome, the type IV Ehlers-Danlos (heritable disorders of connective tissue with cystic medial degeneration), of Loeys-Dietz and Turner, the aortic annulectasia, bicuspid aortic valve and family AD may also cause acute aortic syndromes[10]. In our study, 12% of the cases presented Marfan's phenotype and 29% bicuspid aortic valve, therefore, the forensic autopsy represented the only possibility to determine genetic implications in the deceased's family.

Increased heart weight may be evidenced of high blood pressure, left ventricular hypertrophy, valvular disease, atherosclerosis, among other conditions[12]. Our results coincide with those of other authors which found[5,6] left ventricular cardiomegaly and hypertrophy in 74.2% and 54.1% of their cases, respectively; this fact could be compatible with a history of high blood pressure.

In a high percentage of cases, death occurs at home, while performing life daily activities. The

number of deaths at the hospital are lesser. The early diagnosis of AD is essential to improve prognosis, since the mortality in the first 24 hours is 20% and reaches 62% at 7 days[13]. To achieve this, the early clinical suspicion is important, as well as identifying symptoms and signs of the disease, because it has several forms of presentation and constitutes a relevant medical problem. The clinical factors most often associated with AD are: high blood pressure, sudden onset of sustained chest pain (typical symptom, up to 75% of patients)[14] and its irradiation. It may present with syncope or neurological symptoms[5,12].

Our data show that of the cases that died due to AD, 40% had gone to the hospital a day earlier, and received erroneous medical diagnoses that have been described in the results. The bibliography also registers diagnostic errors, as acute coronary syndrome, pericarditis or even cholecystitis[4].

Limitations of the study

The main limitation was having performed the analysis only in cases where the histopathological study was available. However, this research has allowed an integrative work with families of some of the cases and results in other studies associated with genetic analysis and the development of a protocol of sudden death due to AD in the Institute of Legal Medicine and Forensic Sciences of Valencia.

CONCLUSIONS

The *post mortem* study of sudden deaths from aortic dissection can define better macroscopic and histological features of the most serious cases, which improves its difficult diagnosis before the fatal outcome. Thus, necropsy data allow better understanding of the clinical forms of presentation of this disease, complementing clinical studies and existing diagnostic guides, and allow a family study if required. All this reveals that the forensic branch is very useful in the clinical practice of medicine.

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