CASE STUDY

Case study of family with multiple incidence of aortic dissecting aneurysms

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SUMMARY

Aortic dissection belongs to a group of aortic diseases with a high mortality and varied clinical manifestation. This disease does not appear very frequently and is therefore often diagnosed late. There has been an improvement in diagnostic and therapeutic procedures recently. Classification and indication criteria of prophylactic interventions in the aorta have become more specific, leading to a gradual decrease in the mortality of this disease. There are published accounts in literature of the relatively frequent accumulation of familiar aortic dissections, which may be significant for the early identification of individuals at risk.

In our case study we describe a family with an accumulation of aortic dissection coinciding with Marfan syndrome on the maternal side, and the prevalence of this disease in the siblings of the proband's father. No evident predisposition has been demonstrated in these cases. Besides the affected individuals, we examined and started to follow up also other members of the family but did not find any evidence of a predictive factor.

We would like to emphasize the importance of good interdisciplinary and institutional cooperation in the diagnostics and treatment of this disease. Further, we want to emphasize the benefit of careful sampling of the family history of the patients stricken with the disease, focusing on sudden deaths. It is well known that gene analysis may contribute to the identification of individuals at risk in these families. So far, we do not have this possibility in our country.

Key words: aortal dissection, Marfan syndrome, familial aortic dissecting aneurysm.

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Aortic dissecting aneurysm (AD) is a serious, usually acute, life-threatening disease of the aorta. It is manifested by penetration of blood into the vascular wall, usually through a tear in the intima, and the formation of a false lumen by the splitting media. Incidence is difficult to determine, but is usually given as 2/100,000/year, with a more frequent incidence in men 2-4:1. It usually appears within the age range of 50-70 years in individuals with arterial hypertension and advanced atherosclerosis (1).

AD can however occur in younger age groups, most often in coincidence with Marfan syndrome.

MARFAN SYNDROME

Marfan syndrome (MS) is a hereditary systemic disorder of the connective tissue, with a mostly autosomal dominant manner of transmission. Incidence is given as 0.2/100,000/year and the cause, identified in 1990, is a mutation in the fibrillin-1 gene on chromosome 15q21. Since that year, more than 150 various mutations connected with this syndrome have been described. In about a quarter of the cases the mutations are sporadic, *de novo.* A typical finding is the impairment of the wall of the aorta due to mediocystic necrosis, which leads to the progression of AD and significantly shortens the life expectancy of affected individuals. The diagnosis of MS is currently based on the Ghent Criteria, published in 1996 (2).

Besides the risk factors of atherosclerosis and congenital diseases of the connective tissue, a number of other AD predictors have been identified. The most common ones include ordinary aneurysms, bicuspid aortic valve, annuloaortic ectasia and coarctation of the aorta (3).

The basis of both prophylactic therapy in risk individuals, and of prevention of relapse of AD, is a regimen adjustment excluding large physical stress and including an effort to minimize the risk of injury. Hypertension pharmacotherapy is a matter of course with the drug of first choice being beta-blockers. Meticulous instruction of the patients is necessary as well as their dispensarization with the help of imaging methods (spiral CT, TEE, NMR).

Families with an accumulation of AD and evident AD predisposing factor have been described (4). On the other hand, there are families with multiple incidence of the same type without evident predisposition – in the latter case we speak of Familial Aortic Dissecting Aneurysm (FAD) (5). In some families with FAD gene mutations have been found, connected directly with this disease and enabling early diagnosis of the individuals at risk (6).

The diverse clinical manifestations often make early diagnosis difficult. We have to bear this possibility in mind during differential diagnosis of chest pain, in the case of strokes, shock states, impairment of consciousness, sudden deaths, acute abdomen or acute limb ischemia (7). In a small number of cases, AD may be asymptomatic. The triggering factor of AD may be increased physical load, trauma, labor, or an iatrogenic etiology during arterial interventions.

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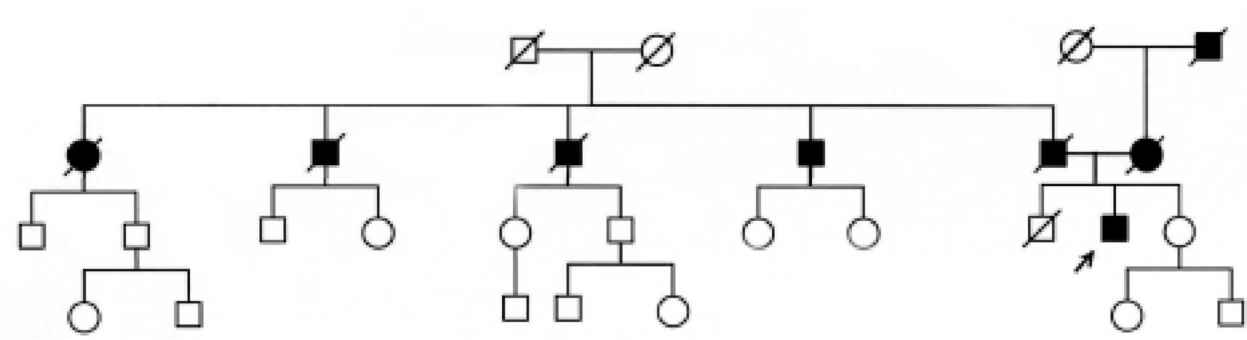

Fig. 1. Genealogic schematic diagram of a family with accumulation of aortic dissection
●́ - deceased female affected by aortic dissection, □ - healthy male, ➚■ - proband,
∅ – deceased female without aortic dissection

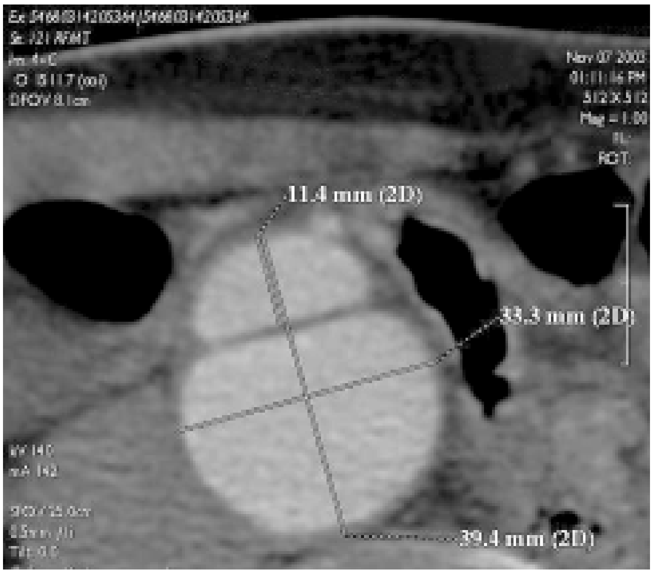

Fig. 2. Aortic dissection of the abdominal aorta, spiral CT

For practical reasons, the most commonly used Stanford classification divides AD into two types. Type A, with impairment of the ascending aorta, where, due to the risk of sudden death (SD), the intervention of choice is acute surgery. There is a danger of development of cardiac tamponade, acute myocardial infarction or severe acute aortal regurgitation with heart failure. Type B, without impairment of the ascending aorta, where the more favorable option is conservative with strict control of blood pressure and accurate staging. In the event of development of complications, the method of choice is intervention with implantation of aortic stent grafts to close the tear in the intima, or the implantation of stents into the compressed division of the branches of the aorta (8). The most commonly used type of surgical intervention into the ascending aorta is Bental's operation of aortic valve and ascending aorta replacement by a procedure with an aortic conduit. An alternative is the substitution of the ascending aorta with or without a valvoplasty. Surgical interventions on the descending aorta are becoming less common due to frequent severe complications (9).

CASE DESCRIPTION

In our case studies we describe a family with multiple incidence of AD. The genealogical schematic diagram was drafted during the collection of data for a retrospective study dealing with the analysis of individuals with AD in our region (Fig.1).

Case No. 1

The proband (i. e. the individual from whom the investigation of the family has unfolded) is a hitherto childless, single young man, in whom, at the age of 26, an annuloaortic ectasia with an ascending aorta dilated in the bulb to 52 mm was found during a laparoscopic inguinal hernia operation in 1998. He was referred to the cardiology department, where he was informed and given a beta-blocker. Genetic investigation was performed in the following years and MS was diagnosed; in August 2000 he was indicated for prophylactic surgery. However, in September 2000, before the scheduled surgery, a collapse status occurred with chest pain and shock circulation. As the predisposition was known, he was immediately transported to the cardio-surgical center with a confirmed diagnosis of AD Stanford A. The dissection extended as far as the common pelvic arteries. An operation according to Bental was performed and, since there were no complications, a conservative procedure was selected thereon. Histologically, mediocystic necrosis was described on the aorta. According to annual follow-ups on spiral CT, there is a gradual mild progression of the dilation of the aorta, with a maximum diameter of 46 x 39 mm (Fig. 2). The dissection is apparent from the distal margin of the anastomosis of the ascending aorta and ends before the bifurcation of the pelvic arteries. An unthrombotized false lumen persists and tears in the intima are visible below the division of the left subclavian artery and in the region of the abdominal aorta. The dissection extends to the division of the left subclavian artery. On TEE there is significant mitral regurgitation during the prolapse of the anterior cusp. Subjectively, the proband has had no considerable complications so far. He is employed, instead of ice hockey he now plays darts, and takes a combination of warfarin and beta-blocker for the chronic condition. An intervention on the descending aorta and mitral valve may be necessary in the future. The patient's condition has become more complicated recently due to a relapse of inguinal hernia.

Case No. 2

The proband's mother died at the age of 58 (in 1997) in the neurological department. She had been admitted because of stroke with introductory syncope, dysarthria, paresthesiae of the right upper limb and left reflex dominance. SD occurred on the third day of hospitalization. AD Stanford A with cardiac tamponade was confirmed on autopsy. Histology showed mediocystic necrosis.

Case No. 3

The father of the mother was the double of the Czech actor Jindřich Plachta (Marfanoid habitus) and died of SD at the age of

44. The brother of the proband died in infancy of intracranial bleeding. His sister (now 45) has a daughter (15) and son (20). All of them have been examined by a cardiologist without finding of apparent aortal pathology and are followed up.

To our great surprise we found an accumulation of AD also in the father's family history. His mother died of SD at the age of 82.

Case No. 4

The proband's father, the eldest of five siblings, died of SD with chest pain and paresis of the upper limb at the age of 57 (in 1989). Autopsy was not performed.

Case No. 5

His sister until her admission to the neurological department where she died at the age of 61 (in 1999) had a mute history. She was admitted due to unconsciousness and right-sided hemiplegia with introductory chest pain. The hemiplegia rapidly regressed to mild and frust hemiparesis, but SD occurred on the third day of hospitalization. Autopsy confirmed AD Stanford A with cardiac tamponade and right-sided hemothorax. Histology described only signs of advanced atherosclerosis.

Case No. 6

The first of the father's brothers, thereto without regular medication, died at the age of 50 (in 1997). He was admitted to the medical department because of chest pain, hypertension crisis and the development of acute ischemic left lower limb. Acute coronary lesion was excluded; TTE and CT of the thoracic aorta were performed. There was no pathological finding on these investigations. A revision of the femoral artery using Fogarty's catheter was performed due to suspected embolism in the left lower limb. The finding was negative and the investigation was supplemented by a CT of the abdominal aorta, which showed AD. The patient was transferred to the cardio-surgical department of the teaching hospital, where the final diagnosis was made - AD Stanford A with a dissection extending to the left pelvic artery, causing compression of the right lumen and ensuing ischemia of the left lower limb. Due to the scope of the impairment and general condition of the patient, conservative treatment was indicated involving vigorous arterial hypertension therapy and palliative implantation of a stent into the left pelvic artery.

Case No. 7

Another brother died at the internal department at the age of 64 (in 2001). He was admitted because of chest pain and dyspnoea. Before then, he had been treated for chronic vertebrogenic problems and had not been taking any continuous medication. Acute coronary lesion was excluded and a pulmonary scan was taken due to positive D-dimers; the finding was negative. TTE showed mild to moderate aortal regurgitations without regional kinetic disorders and without apparent pathology on the ascending aorta. On the fourth day of hospitalization there was SD. Autopsy confirmed AD Stanford A with cardiac tamponade. Histology presents only signs of advanced atherosclerosis.

Case No. 8

The last brother had a replacement, at the age of 60, of the ascending aorta due to AD Stanford A (in 1994). After that his condition was stabilized for a long time. In 2002 he was admitted to the internal medical department due to excruciating pain between the shoulder blades and dyspnoea. Spiral CT of the thoracic aorta confirmed redissection Stanford B, and the same day the patient was transferred to a central clinic (Fig. 3). Aortography showed AD with an intimal tear of about 6 cm after the division of the left subclavian artery with a false lumen extending all the way to the divisions of

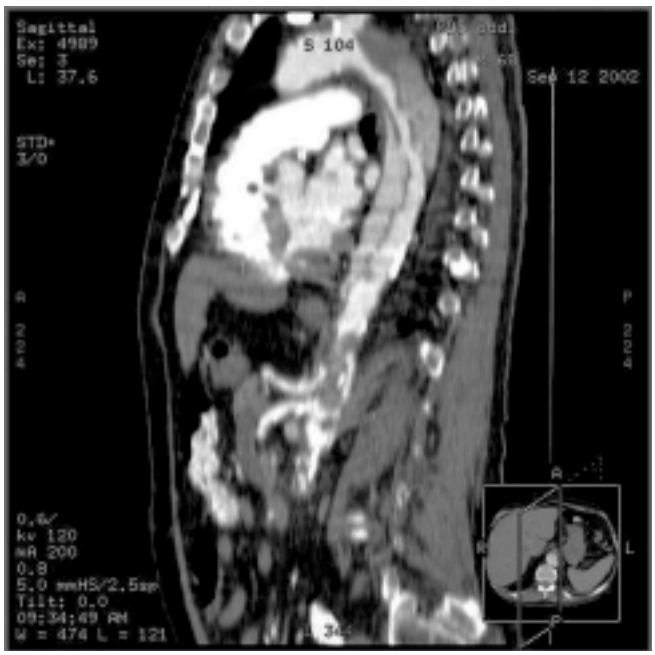

Fig. 3. Aortic dissection of the thoracic aorta, spiral CT (2D reconstruction)

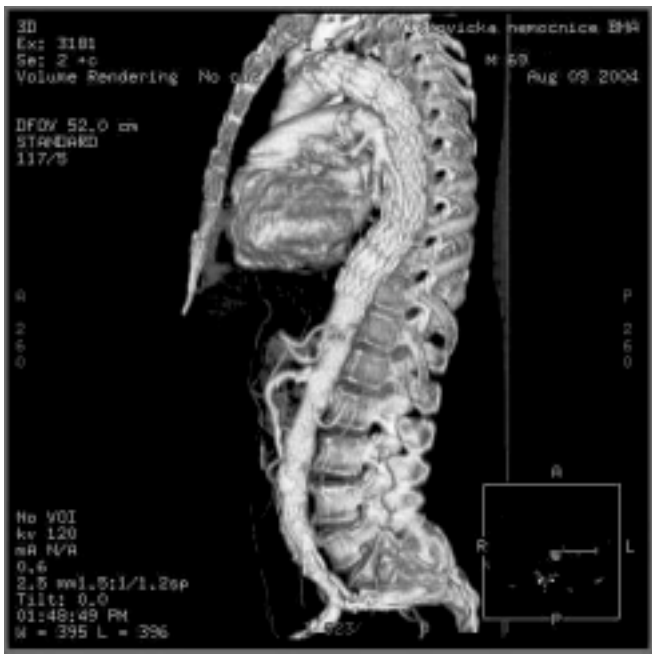

Fig. 4. Stent graft in the region of the descending thoracic aorta, spiral CT (3D reconstruction)

the renal arteries. Also significant stenoses of the pelvic arteries and multiple significant stenoses of the coronary arteries were found. Severe exulcerating atherosclerosis was described on the aorta. First, left pelvic arteroplasty and implantation of two stents was performed. This was followed by the implantation of a thoracic Zenith stent graft into the descending aorta. The left subclavian artery was covered by a stent graft with collateral filling through the left vertebral artery (steal syndrome). The patient's condition was complicated in the following days by acute bleeding into the digestive system during a stress gastric ulcer and subsequent hemorrhage into the left pleural cavity during a partial rupture of the adventitia of the thoracic artery. The presence of an endoleak under the distal end of the stent graft necessitated the implantation of two further

extensions, which was followed by the gradual thrombotization of the false lumen (Fig. 4). Later, a palliative right pelvic and common left femoral arteroplasty was performed and stents were implanted. The clinical condition of the patient is currently stabilized. Collateral circulation led to an improvement of the local finding on the left upper limb. Due to the absence of angina, there were no further surgical interventions into the coronary arteries and the last of the siblings was able to celebrate his 70th birthday recently "in good health".

Other members of this family were examined and dispensarized. No evidence of predictors has been found.

CONCLUSION

This case study is evidence of the significant progress made in the diagnosis and therapy of AD in our region over the last ten years. We see a development in the indications for surgical intervention. Unlike 1997, today a patient with unstable circulation and AD Stanford A extending to the pelvic artery would probably be indicated for surgery (Case No. 6). The reduction of mortality of individuals suffering from this disease is unequivocally influenced by the rapid advance and improved availability of intervention procedures (Case No. 8). There is the evident effect of high quality imaging methods, which is very important for early diagnosis and staging of this disease. These methods also minimize the risk of initial false negative findings (Cases No. 6 and 7). AD is a disease with diverse clinical manifestations, it may, for example, manifest as a stroke and it is therefore necessary to bear this possibility in mind during medical consultations (Cases No. 2, 5, and 6). It is necessary to realize that this is a disease with high early mortality; imaging methods (CT, TEE) must therefore be indicated immediately whenever there is suspicion of this disease. Finally, we would like to underline the contribution of the meticulous collection of family history data of individuals with AD. Reports on families with an accumulation of this disease are becoming increasingly frequent and early start of prophylactic measures in predisposed families may help prevent the development of AD. In cases where multiple AD risk factors are combined in one individual, prophylactic intervention should be considered earlier to reduce the enhanced risk of development of AD as much as possible (Case No.1). As mentioned above, DNA analysis may help us in our identification of risk individuals in such families – so far, however, this option is not available in the Czech Republic.

Abbreviations

AD – aortic dissection
CT – computer tomography
DNA – deoxyribonucleic acid
FAD – familial aortic dissection
MS – Marfan syndrome
NMR – nuclear magnetic resonance
SD – sudden death
TEE – transesophageal echocardiography
TTE – transthoracic echocardiography

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Translation: Nađa Abdallaová

COMMENTARY

Comment upon the Article by K. Zeman, V. Mrózek, R. Brát and D. Kučera : "Case Study of Family with Multiple Incidence of Aortic Dissecting Aneurysms"

Aortic dissection is one of the most serious diseases of the thoracic aorta. Diagnosis is not always simple.

As has been demonstrated, the clinical picture can be varied. This is due to the scope and localization of the dissection and its complications. Pain (absent in 10% of the cases) occurs suddenly, it is localized behind the sternum or between the shoulder blades, and it can shoot into the head or spread caudally. The state of shock is usually caused by cardiac tamponade during bleeding into the pericardium, and hypovolemia during bleeding into the pleural cavity. Myocardial ischemia - if the arterial division is affected – can also be involved. Involvement of the branches of the aortic arch or of other branches of the thoracic and abdominal aorta leads to diverse symptoms.

As the authors point out, there are several classifications of dissection. Classification according to DeBakey et al. is useful for the description of different manifestations of the disease, but it is not suitable from the surgical point of view. The most commonly used classification, as the authors mention, is the Stanford classification (Types A and B). Surgical interventions are thus sometimes described as proximal aorta surgery (ascending aorta and aortic arch) or distal surgery (operation on the descending thoracic and thoracoabdominal aorta). The classification proposed by Crawford for thoracoabdominal aneurysms is suitable for the distinction of chronic dissection affecting this region.

Initial treatment must be started immediately on suspicion of dissection. Untreated, it leads in the first 24-48 hours to death, every hour, of 1-2% of patients affected by Type A dissection. Unless there are counter-indications, surgery is performed immediately on establishment of diagnosis. In some cases, ECHO and TEE taken in the operating theatre are sufficient; in other cases the diagnosis and extent of disease must be established using additional methods as described by the authors. DeBakey performed the first successful operation of aortic dissection. Besides clinical examination, ECHO and TEE are sufficient in most cases. During surgical interventions in Type A dissections it is often possible to preserve the aortic valve and avoid its replacement by a valve conduit (usually by Bentall's operation) or supracoronary aorta replacement. Particularly in aortic dissection this offers the advantage of being able to avoid administering Warfarin. On the other hand, however, the finding on surgery often requires an intervention not only in the ascending aorta but also in the aortic arch. This, indeed, is more complex surgery, during which it is necessary to ensure good protection of the brain in particular. Nonetheless, this type of surgery is currently performed at all the cardiosurgical centers in the Czech Republic. Surgery of the descending thoracic aorta due to dissection is currently indicated only in very exceptional cases. A more common option is stentgraft implantation or conservative treatment.

Aortic dilatation is a predisposing risk factor of aortic dissection. For preventive reasons, in patients with aortic dilatation surgical intervention is recommended if the diameter of the aorta reaches 5.5 cm at the ascending aorta and 6.5 cm at the descending aorta. Smaller diameters – by 0.5 cm – apply to patients with MS; some authors adopt an even more radical approach (Tab. 1).

Tab. 1. Indication to effective surgery

	NonMarfan	Marfan
asc. aorta	≤5.5 cm	≤5.0 cm
desc. aorta	≤6.5 cm	≤6.0 cm

The authors are right when they point out the large benefit of meticulously recorded family history of individuals with aortic dissection. Investigation of family members and early introduction of prophylactic measures or early surgery in the case of aortic dilatation may prevent the development of AD. As far as I am informed, gene mutation analysis for fibrillin is currently performed in the Czech Republic, for example at the Faculty of Natural Sciences of Charles University in Prague.

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