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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Risk factors and treatment approach for subarachnoid hemorrhage in a patient with nine intracranial aneurysms

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SUMMARY

Introduction In about one-third of the patients with aneurysmal subarachnoid bleeding, multiple intracranial aneurysms are confirmed. Risk factors such as female sex, smoking, hypertension, and age over 60 tend to be associated with multiple aneurysms. In this paper, we also discuss family predisposition and the treatment approach for multiple cerebral aneurysms.

Case outline Here, we present a case of a 64-year-old female patient, with spontaneous subarachnoid hemorrhage that had nine intracranial aneurysms. The patient was treated for hypertension for a long time, excessive smoker, and two of her nearest members of the family died from intracranial bleeding. The patient was fully conscious, without any neurological impairment. Subarachnoid bleeding was diffuse and neither brain-computer tomography finding or digital subtraction angiography could not suggest the source or location of bleeding among nine presented aneurisms. Magnetic resonance imaging had to be done, and the T1W fast spin-echo sequence showed a 9 mm large ruptured an aneurysm at the basilar tip, after contrast application, beside others. Three days after the insult, endovascular embolization was done and two basilar aneurysms were excluded from the circulation, including the one that bled.

Conclusion The patient had the majority of risk factors for multiple intracranial aneurysms. Knowledge of the family predisposition of multiple intracranial aneurysms allowed us to make a proper diagnostics of a patient's descendant and reveal a new patient.

Keywords: risk factors; subarachnoid hemorrhage; multiple intracranial aneurisms

INTRODUCTION

Even after a serious therapeutic breakthrough in recent decades, mortality and morbidity in patients with aneurismal spontaneous subarachnoid hemorrhage (SAH) remain unacceptably high. Overall case fatality is usually around half of the cases, although there are some novel studies that present in-hospital mortality much lower [1]. In more than one-third of the patients with SAH, multiple intracranial aneurysms are reviled [2] which usually makes their treatment difficult.

It is believed that the risk factor for the formation of multiple aneurysms is identical to a single intracranial aneurysm. It seems that both external factors and genetic are of significance with the insult. Magnetic resonance imaging (MRI) plays an important role in the diagnostic workup of SAH patients with multiple aneurysms, while endovascular embolization could be the therapeutic option in the majority of the cases. Other adverse events can complicate SAH, like electrocardiographic (ECG) changes caused by electrolyte disbalance [3]. Abnormal ECG changes in patients with acute SAH are as high as 65%, and if fluctuate from one abnormal change to another are usually associated with a poor outcome [4].

CASE REPORT

A 63-year-old woman was admitted with a severe headache, vomiting, and stiff neck. She was fully conscious, without any neurological deficit. Initial computer tomography (CT) brain scan revealed diffuse SAH, Fisher grade III (Figure 1).

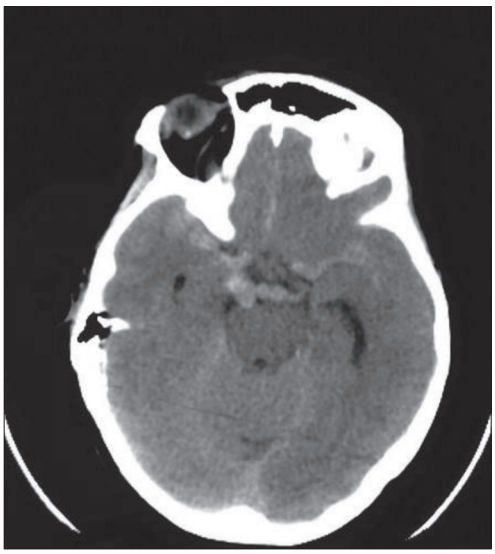

Figure 1. Initial brain computed tomography scan demonstrates diffuse subarachnoid hemorrhage and aneurism-like formation in front of the pons

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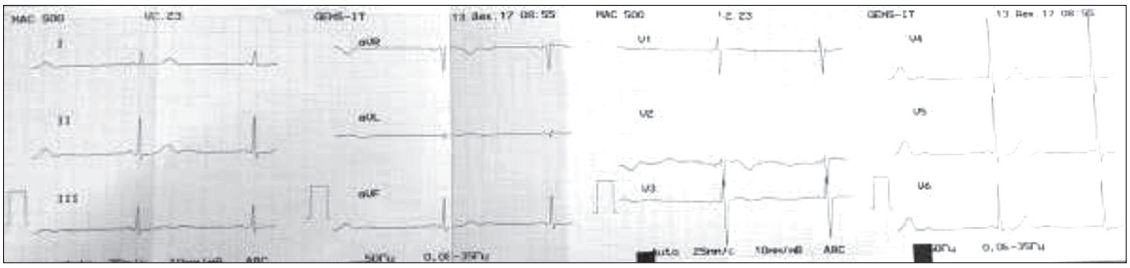

Figure 2. Echocardiography of the patient presented with bradycardia 35 per minute and prolonged QT interval

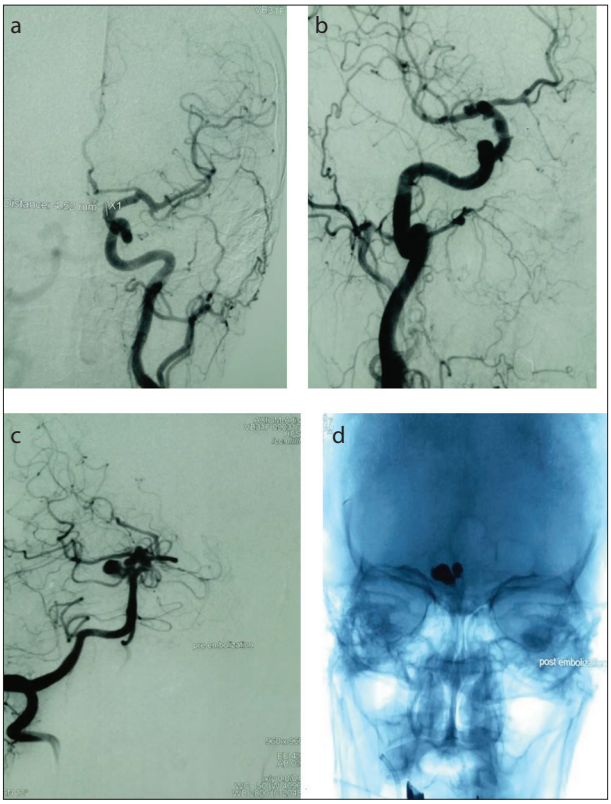

Figure 3. Digital subtraction angiography of the magistral cerebral vessels and postembolization finding; A – digital subtraction angiography of the branches of the left internal carotid artery; two aneurysms are revealed: one on supraclinoid segment of the internal carotid artery at the ostium of the anterior communicant arteria, and the second smaller at the bifurcation of the middle cerebral artery with the dimension of the 2.5 mm; B – digital subtraction angiography of the branches of the right internal carotid artery; three aneurysms are revealed: one on supraclinoid segment of the internal carotid artery, the biggest one at the bifurcation of the internal carotid artery with the dimension of the 6 mm; C – multiple aneurysms, four of them, on the tip of the basilar artery; D – postembolization finding – complete embolization of the ruptured and nearby aneurisms

The patient has been treated for arterial hypertension for 20 years, smoking 15 cigarettes a day for four decades, with intracranial bleeding in family history. The patients' father and brother died from massive intracranial bleeding. MRI of the patient's son revealed an aneurysm, also.

ECG findings revealed sinus bradycardia and prolonged QT interval (Figure 2). The serum finding showed low values of potassium throw all the periods of hospitalization ranging from 2.6 to 3.4, while serum finding showed a normal level of sodium. Therefore, getting sufficient potassium was imperative during therapy, and we managed it through Ringer lactate solution administration, 2000 ml, and an ampule of potassium chloride once a day.

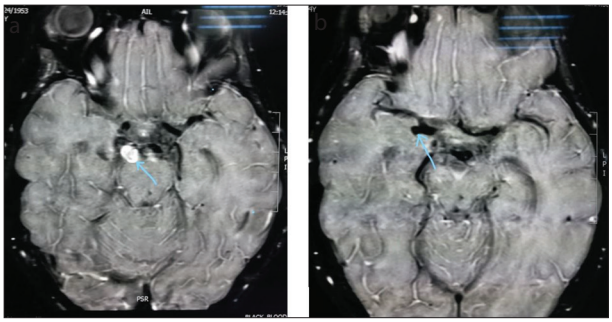

Figure 4. Magnetic resonance angiography of the brain T1W FSE sequence reveals an exact aneurysm that has ruptured (A) compared to unruptured (B)

The patient was treated with Mannitol solution 125 ml every six hours during and corticosteroids Lemod Solu 40 mg every eight hours for three days, analgesics, and antihypertensive therapy as amlodipine and ramipril in a dose of 5 mg in the morning.

Digital subtraction angiography (DSA) revealed nine aneurysms (Figure 3), four on the tip of the basilar artery (BA) (Figure 3 A), three on the right internal carotid artery(ICA) (Figure 3B), one on the left ICA and one on the bifurcation of the left middle cerebral artery (Figure 3C). Neither the deposit of blood clot in the brain CT, nor the shape or size of an aneurysm displayed on the DSA, and could not point out an exact aneurysm that had ruptured.

Therefore, we have examined the patient using the Philips Ingenia 1.5-T magnet resonance scanner (Phillips, Amsterdam, The Netherlands). Sequence Bleck blood T1-weighted 3D VWi was obtained using a flow-sensitized 3D fast spin-echo technique (T1W FSE) and it showed a 9 mm ruptured aneurysm at the basilar tip, after contrast application (Figure 4) where the intramural high signal and intimal flap were observed. Next to it, also at the basilar tip, two more unruptured aneurysms were located. Three days after the insult, endovascular embolization was done and two of the basilar aneurysms were excluded from the circulation (Figure 3D). After the intervention, the patient was fine, without any neurological deficit nor complications. An antiplatelet therapy – acetilsalil acid was administrated in a dose of 100 mg a day after the intervention.

She was released from the hospital 10 days after hemorrhage. The other six aneurysms are to be treated several months later after the patient had fully recoved.

The patient gave her informed consent about this publication.

DISCUSSION

Newly published studies present a typical patient with SAH and multiple aneurysms as a female, with a history of hypertension [5] and smoking [2].

In any of reviewed studies [6, 7], dealing with multiple aneurysms there were no more than five or six saccular cerebral aneurysms in one patient, but highly significant association between the presence of multiple aneurysms and hypertension, cigarette smoking, family history of cerebrovascular disease, female sex, and postmenopausal state in female patients was found. Nine aneurysms in one patient is a number unique for our case report. In these large studies, the authors did not consider family predisposition. We managed to link the deaths caused by intracranial bleeding of two closest relatives of the patient (father and brother) to actual hemorrhage and recommended a MRI to the patient's son that also revealed an aneurism.

Each of the factors that correlate with SAH in multiple cerebral aneurysms has either unexplained or unsatisfying explained role in the pathogenesis of the cerebral aneurysms or their rupture. Nowadays we accept the etiology of it as multifactorial, with environmental factors as a major, but also genetic one as important.

The possible role of smoking in the pathogenesis of the aneurysm formation or SAH could be explained by serum elastase/α_1-antitrypsin imbalance or increased elastase activity of cigarette smokers [8]. These can not be taken aside from the role of inflammatory and cell adhesion molecules, enzymes and hormones, and other cerebral proteins that affect cerebral vessels and damage it, which is crucial for the formation and rupture of aneurysms [9]. Smoking is connected to a transient increase of the blood pressure for a few hours and it could play an important role in the rupture of an aneurysm. A bimodal pattern of SAH occurs in the morning and the evening [10] when cigarette smoking and alcohol use usually displays its peaks.

Solid majority of the SAH patients are hypertonic [11]. One interesting hypothesis tries to find a connection between chronic arterial hypertension (HTA) and the formation of the aneurisms. Initiation of the effecting HTA is injuring the endothelium, occlusion of the vasa vasorum, and disruption of the synthesis of elastin and collagen. Subsequently, intima thickens, tunica media displays foci of necrosis and internal elastic lamina degenerates. These structural changes in the arterial wall cause a focal weakening in the arterial wall with resultant bulging. In an unselected series of 737 aneurysm patients, authors confirmed that hypertension and female sex are positive risk factors for multiple cerebral aneurysms [12].

Female sex is also of significance in multiple intracranial aneurism etiology, as the large study shows: women exhibited higher rates of bilateral (6.8% *vs.* 2.6%, respectively, $p < 0.05$) and multiple (11.5% *vs.* 5.2%, respectively, $p < 0.05$) aneurism comparing to man [13].

Family predisposition for multiple intracranial aneurysms was not debated widely in the literature. Nevertheless, by reviewing the literature we managed to find a few papers dealing with this issue. In a huge study group of 8680 asymptomatic patients, results showed that aneurysms were found in the general population of 6.8% rising to 10.5% in those with a family history of SAH [14]. Multiple aneurysms were more common in the familial group than in the sporadic group, in one recent study that compared a group of patients with two first-degree relatives with SAH and a group of patients without it. Interestingly, the age at the time of rupture was similar between relatives usually in the fifth or sixth decade [15].

The specific genes involved have not yet been identified. A good trace to this breakthrough could be its certain association with some genetic disorders that exhibit some syndromes or diseases. Some of them are more often associated with multiple intracranial aneurysms like Marfan syndrome, polycystic renal disease, Rendu–Osler–Weber syndrome, pseudoxanthoma elasticum, Klippel–Trenaunay–Weber syndrome, type III collagen deficiency, and fibromuscular dysplasia.

In multiple intracranial aneurismal cases where SAH occurs, it is impossible to always determine which aneurysm has bled, a fact of essential importance in further therapy. Brain CT and DSA usually present well known radiological signs and by following them and using a simple algorithm that is based on aneurysm location it is possible to identify the site of aneurysm rupture in 97.5% of cases [16]. Also, some morphologic and hemodynamic parameters can identify the ruptured intracranial aneurysm in patients with multiple intracranial aneurysms [17, 18]. Nevertheless, new radiologic techniques have found their purpose in dealing with this particular issue. One of the MR pulse sequences, spin-echo plays a major role in determining a ruptured aneurysm. T1W images are also required for assessing the degree of contrast enhancement on postcontrast scans [19]. On the other hand, conventional postcontrast 3D T1-weighted TSE sequences are more adequate in detecting unruptured cerebral aneurism [20]. So, in our case report, the T1WFSE sequence enables us the adequate treatment of the patient.

Hyponatremia is the most common electrolyte abnormality seen in patients with aneurysmal SAH, presented in more than a half of the patients, and it is usually present owing to syndrome of inappropriate antidiuretic hormone secretion [21]. Its impact on patients outcomes remains questionable [22].

In this case levels of sodium were normal, while hypokalemia was noticed. Its cause may be complex, involving both potassium losses from the body and intracellular shifts of potassium. SAH often causes a prolongation of the corrected QT (QTc) interval during the acute phase.

Our therapy of the patient consisted, among other medications, of application of potassium chloride inside a solution of Ringer. The embolization of an aneurysm is the first treatment option for the multiple intracranial aneurysms, especially if the bleeding spot is at the posterior part of the circle of Willis. Skillful and experienced neuroradiologist, besides technical precondition, is a must.

Conflict of interest: None declared.

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Фактори ризика и терапијски приступ болеснику са субарахноидалном хеморагијом и са девет интракранијалних анеуризми

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САЖЕТАК

Увод У трећини случајева болесника са анеуризмалним субарахноидним крварењем потврђено је присуство вишеструких интракранијалних анеуризми. Код мултиплих церебралних анеуризми фактори ризика су женски пол, пушење, хипертензија и старост преко 60 година. У овом раду смо дискутовали о факторима ризика, породичној предиспозицији и приступу лечењу вишеструких церебралних анеуризми.

Приказ болесника Представљамо случај болеснице старе 64 године, са спонтаним субарахноидним крварењем, која је имала девет интракранијалних анеуризми. Она се дуже време лечила од хипертензије, прекомерно је пушила, а два најближа члана породице умрла су од интракранијалног крварења. На пријему је болесница била потпуно свесна, без икаквих неуролошких оштећења. Субарахноидно крварење је било дифузно и нити налаз компјутерске томографије мозга, нити дигитална суптракциона ангиографија нису указивали на место крварења, тј. на то која је од девет анеуризми крварећа. Дакле, требало је урадити снимање магнетном резонанцом, а *T1W* брзи спин-ехо низ показао је да је руптурирала анеуризма дијаметра 9 *mm* на врху базиларне артерије. Три дана након крварења урађена је ендоваскуларна емболизација и две базиларне анеуризме су искључене из циркулације, крварећа и некрварећа.

Закључак Овај ретки случај био је праћен већином фактора ризика за развој вишеструких интракранијалних анеуризми. Знање о породичној предиспозицији настанка вишеструких интракранијалних анеуризми усмерило нас је откривању новог пацијента – болесничиног сина.

Кључне речи: фактори ризика; субарахноидно крварење; вишеструке интракранијалне анеуризме