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The radiologist's tragedy, or Bland-White-Garland syndrome (BWGS). On the 80th anniversary of the first clinical description of ALCAPA (anomalous left coronary artery from the pulmonary artery)

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Abstract

In 1933, three doctors from the Massachusetts General Hospital in Boston, Paul Dudley White, William Franklin Bland, and Joseph Garland, described a case of an anomalous origin of the left coronary artery arising from the pulmonary artery (ALCAPA) in a three-month-old boy. The infant died following two weeks of hospitalization. The child's father was Dr. Aubrey Hampton, a radiologist and colleague of White, Bland, and Garland. The paper presents a perspective view on the occasion of the 80th anniversary of the first clinical description of ALCAPA.

Key words: Bland-White-Garland syndrome, ALCAPA, history of medicine.

Streszczenie

W 1933 r. trzej lekarze ze szpitala w Bostonie: William Franklin Bland, Paul Dudley White i Joseph Garland, opisali przypadek nieprawidłowego odejścia lewej tętnicy wieńcowej od tętnicy płucnej (ALCAPA) u 3-miesięcznego chłopca. Dziecko zmarło po 2 tygodniach hospitalizacji. Ojcem tego niemowlęcia był dr Aubrey Hampton, radiolog, kolega z pracy White'a, Blanda i Garlanda. Niniejsze opracowanie jest spojrzeniem z perspektywy 80. rocznicy pierwszego klinicznego opisu ALCAPA.

Słowa kluczowe: zespół Blanda-White'a-Garlanda, ALCAPA, historia medycyny.

Introduction

In 1933, three doctors from the Massachusetts General Hospital (MGH) in Boston, William Franklin Bland, Paul Dudley White, and Joseph Garland, described a case of an anomalous origin of the left coronary artery arising from the pulmonary artery (ALCAPA) in a three-month-old boy. The infant died following two weeks of hospitalization. The authors stressed the credibility of information obtained from the infant's parents, i.e. the alarming symptoms they observed at home before leaving for hospital. The infant's father, Dr. Aubrey Hampton, a radiologist, was White, Bland, and Garland's colleague at MGH [1, 2].

Anomalous origin of the coronary artery, a rare congenital cardiac defect, has been known since 1866, when John Brooks described anomalous origin of right coronary artery from the pulmonary artery (ARCAPA) in his post-mortem examination report for two patients. Brooks wrote: *During the course of the Winter Session, 1884-5, two very remarkable instances of a coronary artery of the heart, springing from the pulmonary artery, occurred in the Practical Anatomy Rooms of this University. The apparent rarity of this abnormality, and the curious effect which it has in producing a cirsoid dilatation of the vessels in connection with the anomalous arteries, have induced me to put on record the two cases in question. In the first case that was discovered, the anomalous coronary artery was a vessel which (...) sprang from the right anterior sinus of Valsalva of the pulmonary artery (...)* [3]. Brooks' conclusions included a very important observation. He stated that the flow of blood in the right coronary artery is reverse, i.e. that arterial blood flows from the normal left coronary artery arising from the aorta through anastomoses to the right coronary artery leading into the pulmonary artery. What is interesting, most contemporary authors referring to Brooks' article misquote it as a description of a case of anomalous left, rather than right, coronary artery...

The first report on anomalous left, rather than right, coronary artery from the pulmonary artery appeared in 1911. In his extensive article illustrated with photos of autopsy preparations and microscope sections, the Russian pathologist Alexei Ivanovitch Abrikosov described left ventricular aneurysm observed in the post-mortem examination of a 5-month-old girl, as well as the origin of the left coronary

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artery from the pulmonary artery. The girl, named Margarethe, was admitted to the hospital in a serious condition in January 1901, with "an unknown history". She was diagnosed with left-sided pneumonia and enlargement of the heart silhouette, suggesting exudative pericarditis. During the night, the child passed away. Six hours later, Abrikosov conducted a post-mortem examination of the infant's body. Some facts of Abrikosov's later life are very interesting: in January 1924, he spent three days embalming Lenin's corpse, the effects of which can still be viewed in the famous mausoleum on Moscow's Red Square. Abrikosov's wife was also an anatomical pathologist, while their son, Aleksei Alekseyevitch, received a Nobel Prize in physics in 2003.

Abrikosov's work met with almost no response, and it was not until the article by Bland, White, and Garland was published in 1933, containing a description of the ECG, chest X-ray, and a clinical picture, that serious interest was generated in this issue. The number of case descriptions grew in subsequent years. Bland, White, and Garland wrote that on the day the infant was admitted to the hospital, he was pale, groaning, and – according to the parents – he was sweating while eating. The physical examination of the lungs indicated dullness of the percussion sound. No cyanosis was observed and there was no cardiac murmur. The chest X-ray image showed enlargement of the heart silhouette, while the ECG registered reverse T waves with a low voltage of the QRS complex in leads I, II, and III. The infant's condition was stable at first. On the 14th day after admission to the hospital, the baby developed respiratory disorders and cyanosis, and soon the patient died. The earlier diagnosis of idiopathic cardiac hypertrophy. The heart was significantly enlarged, with a large right ventricle and relatively small left ventricle. Atrioventricular and aortic valves had a proper structure and size. The examination of coronary arteries revealed a surprise: the right artery was normal, while the left one originated from the pulmonary artery, providing vascularization of the left ventricle. The microscopic examination indicated fibrosis, particularly of the left ventricle, with no sign of infarction. The authors of the quoted article, Bland, White, and Garland, analyzed the existing literature on anomalous coronary arteries and concluded that such anomalies are associated with poor prognosis [1, 2].

Preface

Anomalous left coronary artery from the pulmonary artery is a rare cardiac defect which occurs in 1 per 300,000 live births and, untreated, leads to death within one year in 90% of cases. It is most often an isolated defect and rarely co-occurs with other cardiac defects, e.g. ventricular septal defect or patent ductus arteriosus (PDA). The occurrence of the first symptoms is associated with the arising collateral circulation, and so clinically we often distinguish between the children's and adult form. Infants rarely show any symptoms, because the relatively high pulmonary resistance imposes blood inflow from the pulmonary artery to the anomalous coronary artery. Around the second month of life the resistance in the pulmonary bed decreases, which lowers the inflow of blood into the left ventricular artery and results in the myocardial perfusion disorder in the area supplied by this artery. If the inflow of blood from the collaterals originating from the right coronary artery is insufficient, the patient shows the symptoms described by Bland, White, and Garland: pallor of skin integuments, feeding difficulties, and anxiety resembling baby colic. Chronic ischemia results in endocardial fibroelastosis (EFE) and papillary muscle damage, which leads to mitral valve incompetence and progressing left ventricular dilation. In an acute form, it is manifested as myocardial infarction. If collateral circulation is sufficient, the symptoms may be absent or weak, which makes it possible to reach the adult age without any medical intervention. Adults may also show no symptoms, although they more often suffer from collapses or syncopes, chest pains, arrhythmia, or sudden death. The predominant symptoms observed in the echocardiographic picture include left ventricular dilation with myocardial contractility disorders and mitral valve incompetence [2].

Diagnostics

Aubrey Hampton's son diagnosis was not a survival diagnosis, but a post-mortem one. Eighty years after that case, we have a number of diagnostic (both invasive and non-invasive) examinations, which make it possible to establish a correct diagnosis. In the majority of cases, an echocardiographic examination proves sufficient to recognize the defect. It shows an expanded right coronary artery and a lack of origin of the left coronary artery from the aorta sinus and its origin from the pulmonary artery. The use of the Doppler method marked with color enables visualization of the reverse flow of blood from the left coronary artery to the pulmonary artery (a permanent inflow). Echocardiography also makes it possible to evaluate the degree of dilatation and dysfunction of the left ventricle. Mitral valve incompetence is, besides left ventricular dilation, another important symptom of ALCAPA. The underlying cause of that incompetence is the dysfunction of papillary muscles and left ventricle dyskinesia accompanied by left ventricular dilation and the expansion of the mitral valve ring. Ischemia can be manifested through hyperechogenicity of papillary muscles and left ventricular endocardial fibroelastosis (EFE). Until recently, patients with a dubious diagnosis of ALCAPA were subjected to cardiac catheterization and angiocardiography. This allows one to obtain an image of coexisting cardiac anomalies and ultimately confirm or exclude the diagnosis of ALCAPA (and at the same time confirm dilated cardiomyopathy). It is also possible to use CT scanning with a vascular option (angio-CT scan, particularly the flash version). Changes in the ECG recording include characteristics of anterolateral myocardial infarction, indicated by the presence of Q waves in V4-V6, I and aVL leads, although a slightly different ECG recording was presented by Bland, White, and Garland in their article regarding the case of Dr. Hampton's son, published in 1933. The assessment of the cardiac muscle lifespan in the pediatric population is carried out using

stress echocardiography, single-photon emission computed tomography (SPECT), positron emission tomography (PET), and nuclear magnetic resonance (NMR). Perfusion disorders concern mostly the anterior and inferior wall, which allows scintigraphic imaging to distinguish between ALCAPA and dilated cardiomyopathy, the latter being characterized by perfusion disorders in a significantly expanded left ventricle, accompanied by severe contractility disorders.

Surgical treatment

Diagnosing the defect is almost always an indication for a surgical treatment. Its outcome depends on the technique used, the condition of the cardiac muscle before the operation, the extent of ischemia/infarction, the degree of mitral valve incompetence, and a possible necessity to replace it.

Over the past decades, a number of surgical treatments of ALCAPA have been developed. Gasul and Loeffler were the first to suggest forming an aortal-pulmonary fistula in order to increase the pressure and saturation in the pulmonary artery. This procedure has been carried out twice by Potts, both times unsuccessfully. In 1955, Kittle suggested making a distal stenosis of the pulmonary artery from the orifice of the coronary artery in order to increase the pressure within the latter, but unfortunately the child died immediately after cutting through the artery. A similar attempt was undertaken by Case and Morrow in 1958; although they were able to place a tourniquet lowering the diameter of the pulmonary trunk by about 60%, the child died as a result of ventricular fibrillation. During the postmortem examination, the authors proved that the flow in the anomalous coronary artery was towards the pulmonary artery and not the other way. For that reason, they suggested ligation of the left coronary artery at the point of its origin from the pulmonary artery in order to prevent the steal syndrome before irreversible changes in the myocardium take place. [5] The use of this technique depends on well-developed collateral circulation originating at the right coronary artery. The first two patients treated with this technique died (in Toronto and Washington, D.C.), but the third attempt, undertaken by Edgar Davies in Washington, D.C. in 1957, was successful. In 1960, the journal *Circulation* published an article by three doctors from the Johns Hopkins hospital in Baltimore, M.D. Sabiston, Neill, and Taussig described a typical case of ALCAPA in a 2.5-month-old male infant, admitted to the hospital on 3 June, 1959. The baby was initially healthy, but in the 6th week of life it started suffering from feeding difficulties, breathing disorders, and groaning. The chest X-ray revealed an enlarged heart silhouette, while the ECG examination showed symptoms of a fresh infarction of the cardiac muscle. There was a systolic murmur along the left edge of the sternum and at the apex of the heart. Angiocardiography indicated a significantly enlarged thin-walled left ventricle with impaired function, but did not show the left coronary artery in the normal place. There was no sign of an intracardiac leak. A decision was made to operate and the surgery was carried out three days after admitting the patient to the hospital. The left coronary artery was ligated proximally to the division into the anterior descending branch and the circumflex branch. The patient survived and his condition improved quickly. After six months, his body mass grew properly, ischemic changes disappeared from the ECG image, and the enlargement of the heart silhouette diminished in the chest X-ray image. The authors of the quoted work mention two other patients subjected to this procedure, with additional phenol administered for de-epicardialization, i.e. promoting collateral circulation and left ventricle revascularization. The authors concluded that in the case of ALCAPA the ligation of an improper coronary artery accompanied by de-epicardialization is both a rational and an effective method [6].

Currently, the recommended treatment for ALCAPA is to preserve both coronary arteries by transplanting the left coronary artery to the aortic sinus or making a bypass in connection with a ligature of the abnormally originating artery, or creating an aorto-pulmonary window or tunnel with the use of a patch inside the pulmonary artery (the Takeuchi method). The latter technique was introduced in 1979 [7] and is preferred in the case of a significant distance between the orifice of the abnormal coronary artery and the aorta, a massive collateral circulation around the left coronary artery, or difficult LCA mobilization. The Takeuchi method may result in supravalvular pulmonary stenosis, a leak on the patch, or a stenosis of the created tunnel [8].

The concepts postulating the transplantation of the abnormal coronary artery to the aorta were carried into practice for the first time in 1953, when a Canadian cardiac surgeon, William Mustard, performed an operation of an end-to-end anastomosis of the common carotid artery to the abnormally originating coronary artery. The operation was unsuccessful and the baby died [9]. In 1965 Denton Cooley *et al*. operated on a 5-year-old boy suffering from ALCAPA; they created a 2-coronary system by connecting a Dacron interposition graft from the aorta to the proximal LCA. There were no complications in the postoperative period, and angiography carried out 10 years later revealed a wide patent bypass. The patient led an active life and suffered no complaints. He died suddenly at the age of 24 while playing football [10, 11]. A coronary artery graft associated with the idea of anatomical correction of transposition of the great arteries was performed successfully for the first time by Neches *et al*. in 1974 [12]. In our times, patients are operated on soon after diagnosing the defect, which is most frequent among infants several months old. Early and late results are determined by the degree and extent of myocardial damage. Transplanting the left artery to the aorta results in improving the heart function, usually within several months. ALCAPA, which sometimes leads to serious and irreversible heart damage (ischemic cardiomyopathy), is often an indication for heart transplantation.

Epilogue

Dr Aubrey Hampton was born in 1900, graduated from a medical school in Dallas, and at the age of 26 started to

work at the Radiology Department of the General Hospital in Boston, Massachusetts. In 1933, he had a son, who was born with ALCAPA, and it was the case of this three-month-old baby and its post-mortem examination that was described by Hampton's colleagues, Bland, White, and Garland. The personal tragedy that affected Aubrey Hampton significantly influenced his professional career. Chest radiology became his main area of interest. In 1941, Hampton became Head of Radiology at the Boston General Hospital. *He was one of the fastest thinking radiologists I have ever known* – wrote his successor. *The weekly radiological consultations he conducted were among the most valuable didactic sessions, not only for radiologists*. He was admired for his immense clinical intuition in his daily practice of medicine. Aubrey Hampton died suddenly of a heart attack at the age of 54 [2].

Who were the men whose names were forever combined into an eponym: Bland-White-Garland syndrome?

Edward Franklin Bland was born in 1901. Having graduated from the University of Virginia, he started his residency in a university hospital in Boston. It was at that time that – together with White and Garland – he described the case of a son of their hospital colleague. Later Bland became interested in rheumatic fever and researched it working with Duckett Jones. The outcome of his observations was an analysis of a huge number of more than 1,000 cases of rheumatic fever in patients in whom it was diagnosed after 10 or 20 years. During World War II, he served in the army in Northern Africa and in Italy. In 1949 he became Head of the Clinic of Cardiology at the Massachusetts General Hospital in Boston, the clinic established more than three decades earlier by Paul White. Bland was personally responsible for opening a heart catheterization lab. He headed the Clinic for 15 years and lived to an old age. He died of a heart attack on the day after returning from his holidays in Europe at the age of 91 [2, 13].

Joseph Garland was born in 1893 as a grandson and son of a doctor. He graduated from Harvard in 1919 and took up pediatrics. He worked at the Massachusetts General Hospital in Boston for over 30 years (1923-1954). In 1938 he became a member of the editorial board of The New England Journal of Medicine (NEJM). He published the journal for 20 years and thanks to him, the journal became one of the most important medical periodicals in the world. Joseph Garland died in 1973 [2, 14, 15].

Paul Dudley White – the oldest of the eponymous men – was born in 1886 as a son of a country doctor. He graduated from the Medical School at Harvard University in 1911. Together with Roger I. Lee he devised the technique of measuring the time of blood coagulation (Lee-White method). In 1930, Louis Wolff, Sir John Parkinson, and Paul Dudley White published an article which immortalized their names by giving the name of Wolff-Parkinson-White Syndrome to what is commonly referred to as a pre-excitation syndrome. Paul White's father died of a heart attack at the age of 71 and was known to have eaten a bowl of cream a day, recommended to him for his tuberculosis. White's mother lived to be 88, while his younger sister died of a rheumatic disease. Family experiences made White an exceptionally active exponent of cardiac diseases prevention. He is remembered for saying that *heart disease before 80 is our fault, not God's or nature's will*. Dr. Paul Dudley White served as a personal doctor to several US presidents (including Eisenhower, after his heart attack). In 2011, *The American Journal of Cardiology* published a commentary by Prof. Harvey Feingenbaum, often called the "father of echocardiography": *I enjoyed reading Dr. Blackburn's brief report about Paul Dudley White in the October 15, 2010, issue of* The American Journal of Cardiology. *Another possible subtitle could be 'Nobody Is Perfect'*. Feigenbaum justifies his claims by recalling the following story: *In the early 1950s, Drs. Inge Edler (a cardiologist) and Helmuth Hertz (a physicist) used an ultrasound device borrowed from Siemens (Dr. Hertz's father's employer) to examine his heart. After only a few years, Dr. Hertz lost interest and left the field. He advised Siemens that there was no future in cardiac ultrasound (Sven Effert, personal communication). Siemens apparently wanted a second opinion. They asked Drs. Paul Dudley White and Andre Cournand to visit Dr. Edler and review his work. They too agreed that there was no future in cardiac ultrasound. Siemens then lost whatever interest it had in the field, and Edler soon thereafter also left the field. (...) Thus, Dr. White helped temporarily bury cardiac ultrasound, at least for a few years* (H. Feigenbaum).

Paul White was an ardent cyclist. A 17-mile bicycle path in Boston has been named after him. He died in 1973, the same year as Joseph Garland, of complications after a heart attack and a stroke [2, 16, 17]. It is worth mentioning that a pioneering patent in the use of ultrasound for examining heart structures was authored by Dr. Tomasz Cieszyński (the subsequent professor of the 2nd Chair and Clinic of General Surgery at the Medical Academy in Wrocław). In 1956, Tomasz Cieszyński (the son of a world renowned dentist, Prof. Antoni Cieszyński, who was executed by the Nazis at Wzgórza Wuleckie in Lviv in 1941) patented an original idea of using a device allowing for an assessment of heart structures, i.e. an echosounder placed inside the heart (ICE = intracardiac echocardiography; patent PRL no. 40332 Kl. 30 a, 4/02: "Ultrasonic echosounder for examining the heart" [18].

It is extraordinary that three of the four main characters in the story of the first clinical description of ALCAPA died of a heart attack. No biographical source on Joseph Garland available to the present authors, including four special articles in NEJM in 1973 entitled *"Four Tributes"*, which appeared soon after his death, gives the cause of Garland's death [14, 15].

References

1. Bland EF, White PD, Garland J. Congenital anomalies of coronary arteries. Report of unusual case associated with cardiac hypertrophy. Am Heart J 1932-1933; 8: 787-801.
2. Cowles RA, Berdon WE. Bland-White-Garland syndrome of anomalous left coronary artery arising from the pulmonary artery (ALCAPA): a historical review Pediatr Radiol 2007; 37: 890-895.

3. Brooks HS Jr. Two cases of an abnormal coronary artery of the heart arising from the pulmonary artery. J Anat Physiol 1885; 20: 26-29.
4. Abrikossoff AI. Aneurysma des linken Herzventrikels mit abnormer Abgangsstelle der linken Koronararterie von der Pulmonalis bei einem funsonatlichen Kinde. Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin, Berlin, 1911, 203: 413-420.
5. Case RB, Morrow AG, Stainsby W, Nestor JO. Anomalous origin of the left coronary artery; the physiologic defect and suggested surgical treatment. Circulation 1958; 17: 1062-1068.
6. Sabiston DC, Neill CA, Taussig HB. The direction of blood flow in anomalous left coronary artery arising from the pulmonary artery. Circulation 1960; 22: 591-597.
7. Takeuchi S, Imamura H, Katsumoto K, Hayashi I, Katohgi T, Yozu R, Ohkura M, Inoue T. New surgical method for repair of anomalous left coronary artery from pulmonary artery. J Thorac Cardiovasc Surg 1979; 78: 7-11.
8. Ginde S, Earing MG, Bartz PJ, Cava JR, Tweddell JS. Late complications after Takeuchi repair of anomalous left coronary artery from the pulmonary artery: case series and review of literature. Pediatr Cardiol 2012; 33: 1115-1123.
9. Reul RM, Cooley DA, Hallman GL, Reul GJ. Surgical Treatment of Coronary Arteries Anomalies Tex Heart Inst J 2002; 29: 299-307.
10. Cooley DA, Hallman GL, Bloodwell RD. Definitive surgical treatment of anomalous origin of left coronary artery from pulmonary artery: indications and results. J Thorac Cardiovasc Surg 1966; 52: 798-808.
11. Leachman RD, Zamalloa O, Tapia F, Hallman GL, Cooley DA. Reconstruction with a Dacron tube graft of an anomalous left main coronary artery arising from the pulmonary trunk with 19-year asymptomatic period thereafter. Am J Cardiol 1988; 61: 195.
12. Neches WH, Mathews RA, Park SC, Lenox CC, Zuberbuhler JR, Siewers RD, Bahnson HT. Anomalous origin of the left coronary artery from the pulmonary artery. A new method of surgical repair. Circulation 1974; 50: 582-587.
13. Friedlich AL. Edward Franklin Bland. Trans Am Clin Climatol Assoc 1993; 104: xxxix-xli.
14. Ingelfinger FJ. Dr. Joseph Garland, 1893–1973. N Engl J Med 1973; 289: 480.
15. Burgin LB. Joseph Garland: Four Tributes. The Pediatrician. N Engl J Med 1973; 289: 639-640.
16. Feigenbaum H. Paul Dudley White on Echocardiography. "Nobody Is Perfect" http://www.sciencedirect.com/science/article/pii/S0002914910024951.
17. Hurst JW. Paul Dudley White: the father of American cardiology. Clin Cardiol 1999; 14: 622-626.
18. Cieszyński T. Opis patentowy: Echosonda ultradźwiękowa do badania serca. http://pubserv.uprp.pl/publicationserver/Temp/mv5iqj0i0m7mtsfuplbi4ts7f5/PL40322B1.pdf.