

Cystic fibrosis – a probable cause of Frédéric Chopin’s suffering and death

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Abstract: Frédéric Chopin – a great Polish composer and pianist – suffered from a chronic disease. Both during his life and after death physicians disagreed on the subject of Chopin’s diagnosis. His contemporaries accepted the diagnosis of a disease common in the 18th century – tuberculosis. Description of new clinical entities provoked new dilemmas in the 20th century. In our opinion the most tenable seems to be the diagnosis of cystic fibrosis. In this work we present F. Chopin’s case history and discuss cons and pro for cystic fibrosis as the cause of F. Chopin’s suffering and death.

Key words: Chopin, cystic fibrosis, genetics, late diagnosis.

Introduction

Cystic fibrosis (CF) is the most common autosomal recessive disorder of the Caucasian population. It affects approx. 1: 2500 newborns. Though common, CF was first described only in the late 1930’s (ANDERSEN, HODGES 1946). It was unknown to physicians as a separate clinical entity before that time, although there are historical descriptions of possible CF cases, which date back to the Middle Ages (QUINTON 1999). It is hence probable that some patients who suffered from

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cystic fibrosis before the 20th century were underdiagnosed. Cystic fibrosis could have been a cause of death also of people who carried well-known names, like a great Polish composer and pianist – Frédéric Chopin. In this work we discuss the differential diagnosis of Frédéric Chopin's disease and the possibility that it was cystic fibrosis.

The case of Frédéric Chopin

It is beyond any doubt that Frédéric Chopin suffered from a chronic multiorgan disorder, which was possibly inherited. Beneath we present a summary of F. Chopin's case history.

Childhood

There are controversies on F. Chopin's date of birth. According to Chopin's father recollections it was either February 22 or March 1, 1810, in Żelazowa Wola, near Warsaw (KUBBA, YOUNG 1998). Both in the writings of his contemporaries and in his personal letters there are notes on his frail health and multiorgan complaints that started early in the childhood of his boyhood. Recurrent diarrhoeas gastro-intestinal ailments result in weight loss and delicate posture. This was accompanied by frequent respiratory tract infections (SIELUŻYCKI 1981). In 1826 (at the age of 16), he had an illness lasting 6 months, in which respiratory symptoms and headaches were prominent symptoms (KUBBA, YOUNG 1998), and which endangered his life. Frédéric did not compete with his peers, as he did not have enough stamina to comply with his physician's recommendations to walk in the countryside. He was always coming back from these excursions "tired and without any breath" (SIELUŻYCKI 1981). Heller described Chopin as "frail, slim, with sunken cheeks, he was said to die early as many geniuses before him did" (SIELUŻYCKI 1981)

Adulthood

Political instability in Poland and Chopin's desire to master his skills made him decide to leave Poland in 1830 (at the age of 20). His health problems continued on the way to and in France. He experienced exacerbation of nasal infection with very troublesome blockage of air passage (polyps?), pulmonary infections with productive cough, hemoptysis and recurrent fevers. He presented also symptoms of delayed puberty. At the age of 22 he wrote in despair: "I have one-side – whisker – the other won't simply grow" (KUBBA, YOUNG 1998). Chopin never fathered any children, though he had sexual relationships with a few women, and a long-lasting relationship with George Sand (a mother of two from the first marriage). This can justify the assumption of Chopin's infertility. His gastro-intestinal complaints continued, so finding a proper food for him was very dif-

ficult. According to G. Sand, Chopin had abdominal pain and diarrhea especially after eating fatty pork (O'SHEA 1998). The heatstroke that Chopin had on Majorca seemed at that time to be the least disturbing. Chopin was often so weakened by his disease that he was unable to climb up the stairs and had to be carried out after performances or was forced to call them off. Chopin's symptoms were constantly progressing, confining him to his bed for many days or even weeks. Unhappy about his ill health and awaiting improvement, Chopin was treated by many physicians, the majority of whom were not sure about his diagnosis (SIELUŻYCKI 1976).

F. Chopin was a disabled person depending on his friends' care during, last four years of life. He was carried up the stairs, teaching piano in a lying position. He had attacks of exhausting cough productive of sputum with blood streaks in the mornings, and even large doses of opium were unable to stop them (SIELUŻYCKI 1981). He suffered from illusions and confusion at night, which was probably due to the development of respiratory failure (O'SHEA 1987).

After Chopin's long lasting relationship with G. Sand split up in 1847, his health deteriorated quickly. He had increasing problems with coughing up sputum, pains in the chest and lost a lot of weight. He stopped composing and developed depression. In the last year of life he was hardly leaving his bed, mainly because of strong pain in the joints. Later on, new symptoms accompanied: oedema of the ankles and legs, increasing tiredness and shortness of breath on exertion and in lying position, hoarseness and problems with sputum expectoration. He wrote a few days before the death: "As this earth will suffocate me, I implore you to have my body open so that I may not be buried alive" (KUBBA, YOUNG 1998). F. Chopin's agony lasted four days. He stayed conscious and was able to communicate but with a swollen and dark (cyanosed?) face. Last night Chopin was tormented with convulsions of unknown aetiology, severe pain and choking cough (O'SHEA 1998).

During the last four months of life, F. Chopin was treated by Dr. Jean Cruveilhier, one of the most educated physicians of that time. Dr. Cruveilhier was considered the best specialist in tuberculosis and pathology in Paris. His *Anatomie pathologique du corps humain* is still regarded as an excellent pathological atlas. It was him who confirmed Chopin's death, performed autopsy and took out his heart, which was sent back to Poland according to the great composer's last will. Chopin's death certificate gives "tuberculosis of the lungs and larynx" as the cause of death. The result of the autopsy was lost in the war or great fires of Paris. There are, however, three records preserved, which quote Dr. Cruveilhier saying that Chopin's death was caused by "a disease not previously encountered" (KUBBA, YOUNG 1998).

Family history

Both Chopin's parents died in their 70's; mother at the age of 77 (1784-1861), and father at 73 (1770-1844). His mother, Justyna, was Polish and enjoyed good

health, unlike his father, a Frenchman – Nicolas Chopin, who had recurrent pulmonary ailments his life through. Of Chopin's three sisters only one, Isabella (1811-1881), did not have any health problems.

The oldest sister, Ludwika (1807-1855), suffered from respiratory problems, which were finally a cause of her death at the age of 47. The youngest, Emilia (1813-1827), was always a weak, skinny child, devastated by recurrent pneumonias and constant shortness of breath accompanied by cough and hemoptysis. She died of a bleeding from the upper part of gastroesophageal tract, when she was only 14.

When Frederic Chopin was dying, nobody was questioning tuberculosis as a cause of his death, although all physicians – his contemporaries – found it really difficult to make a definitive diagnosis of his case. Progress in medicine and lack of *post mortem* examination have led to challenging of this diagnosis. There were many different hypotheses made and published. To name a few: pulmonary emphysema (alpha1- antitrypsin deficiency), bronchiectases, cystic fibrosis, pulmonary tuberculosis, hypogammaglobulinemia, mitral stenosis, allergic bronchopulmonary aspergillosis, tricuspid valve incompetence, Churge-Strauss syndrome, pulmonary hemosiderosis, pulmonary arteriovenous malformation. Many of them are very rare clinical entities and have, in our opinion, little in common with F. Chopin's suffering.

To our understanding two most tenable diagnoses are genetic disorders: cystic fibrosis and alpha1- antitrypsin deficiency. The first one was suggested by an Australian physician, Dr. John O'SHEA in 1987 (O'SHEA 1987), and the second by J.A. KUZEMKO in 1994 (KUZEMKO 1994).

Why genetic disease?

The arguments for genetic background of Frederic Chopin's health problems are convincing and consistent with modern knowledge. First, his family history shows that two of his three sisters had similar complaints and died prematurely. Second, those three family members (F. Chopin and his two sisters) had multiorgan and progressive symptoms that started early in life and were not initiated by any other known cause.

Why cystic fibrosis?

Balancing arguments for and against cystic fibrosis (CF) and alpha1-antitrypsin deficiency as F. Chopin's definite diagnosis, we would rather tend to support the first one. Cystic fibrosis is the only diagnosis that gives the explanation of all Chopin's complaints (Table 1). The main counter-arguments against alpha1-antitrypsin deficiency are: (1) the history of chronic diarrhoea caused by pancre-

atic insufficiency, and (2) lack of jaundice and ascites, if Chopin's and Emila's deaths were caused by variceal bleeding in a course of portal hypertension. However, none of these excludes completely the possibility of this diagnosis.

Table 1. A summary Frédéric Chopin's symptoms and signs (based on KUBBA, YOUNG 1998)

Family history	Symptoms	Signs
Two sisters with similar symptoms and premature death	Chronic pulmonary symptoms (productive cough, hemoptysis, shortness of breath) since childhood Recurrent gastrointestinal symptoms (diarrhoea, fatty food intolerance, hematemesis) General complaints (effort intolerance, fatigue, failure to gain weight) Infertility Heatstroke Artralgia (osteoarthropathy?)	Short (170 cm) and skinny (48 kg) Barrel-chested, waisted limbs (later in life peripheral oedema) Cyanosis? No finger clubbing?

On the contrary, recent discoveries, to our mind, easily ward off the arguments against cystic fibrosis as a cause of Chopin's suffering and death. The main and the only argument given by those in favour of other diagnoses was that in the pre-antibiotic era, the survival of patients with CF was very low, as the majority of patients died in the first decade of life from pulmonary infection and right ventricular heart failure. Nowadays we know that a spectrum of clinical presentations of cystic fibrosis vary from death due to respiratory or hepatic complications early in the first decade of life to the development of "real" problems in the sixth decade. We also understand that the severity of CF symptoms is mainly defined by the genetic background.

What causes the diversity of CF symptoms? – Modern understanding of genotype-phenotype relationship in CF

Genotype-phenotype relationship in cystic fibrosis is very complex, although it is a monogenic disorder. Cystic fibrosis phenotype is caused by abnormal function of a chloride channel (CFTR Cystic Fibrosis Transmembrane Conductor Regulator) localised on apical membrane of epithelia. Hence the disease manifests itself in the respiratory tract, gastrointestinal system (mainly pancreas), sweat glands and in males' vas deferens. The CF gene, encoding CFTR protein, was identified on the long arm of chromosome 7 in 1989 (RIORDAN 1989). This discovery confirmed also the autosomal recessive pattern of inheritance in CF, which was suggested ever since it was first described as a separate clinical entity (ANDERSEN, HODGE 1946). Since then over 1,000 of its mutations have been described. Their carrier rate is estimated at the level of 5% in the white population. Despite extensive molecular studies a number of CF chromosomes in various populations

remain uncharacterised. Those characterised have been divided into 5 classes on the basis of molecular mechanisms by which they disrupt CFTR protein production or function (WELSH, SMITH 1993). Genotype-phenotype studies indicate that decreasing levels of CFTR function are associated with progressive involvement of other systems (CUTTING 2000). It was found that mutations that allow partial function of CFTR consistently ameliorate the severity of pancreatic disease. A subset of these mutations permit enough of CFTR function to modulate the degree of sweat-gland dysfunction, and selected few produce less severe lung disease. Most of the mutations affect the development of the male reproductive tract, suggesting that this process has the highest requirement for CFTR function (CUTTING 2000). The variability of phenotypic presentations in CF are greatly contributed by CFTR mutations, but also modulated by (1) genes other than CFTR and (2) environmental influences.

Understanding of CF genetics and availability of molecular diagnosis of CF, widened the spectrum of CF to mild and atypical presentations. With increasing knowledge of CF, an increase is observed in the number of CF patients diagnosed in adulthood (HUBERT et al. 2000, WIDERMAN et al. 2000, GAN et al. 1995). According to the U.S. Cystic Fibrosis Foundation Patient Registry data, the percentage of patients with the CF diagnosis made in adulthood doubled between the years 1994 and 1997 from 5.8% to 11.5% (WIDERMAN et al. 2000). Comparative cohort studies of patients depending on their age at diagnosis showed that those diagnosed late differ significantly from the group of patients diagnosed early. Patients diagnosed after the age of 16(18) years display a higher percentage of mild mutations (WIDERMAN et al. 2000, GAN et al. 1995, MAJKA et al. 2001a). This is reflected in their phenotype: they are commonly pancreatic sufficient (GAN et al. 1995) with less advanced pulmonary changes. Though they typically seek medical advice because of pulmonary symptoms (or nasal polyps) or infertility (WIDERMAN et al. 2000). In comparison to other Caucasian CF population, the Polish CF population is characterised by profound genetic heterogeneity (WITT et al. 1997, 1999). 3849 + 10kbC T and some other mild mutations are more prevalent than elsewhere (WITT et al. 1999, MAJKA et al. 2001b). There are not many data on Polish CF patients diagnosed in adulthood (MAJKA et al. 2001c), but it seems that patients with mild CF presentations should be attentively looked for in the Polish adult population. Many of CF adults with a mild course of disease were often not treated with antibiotics in their childhood and it was due to their genetics and not intensive treatment that they live long.

Conclusions

There are no final conclusions in this enunciation. There is no easy way of finding out F. Chopin's final diagnosis. Even genetic analysis of DNA from Chopin's tissue could lead us into deceptive assumptions, unless two CFTR mutations were

found. Is it not the right time to make this step now? Is it justifiable to deepen our knowledge about the great Polish composer, but foremost to give hope and meaning to those who nowadays suffer from genetically inherited disorders? Is it not right to make an attempt to prove to many suffering people that many things count in life much more than a weak physical body, and that they are not predestined to vanish without leaving something that will influence, inspire and enrich the generations to come?

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