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Genetic diseases and other unusual disorders presented in art paintings

Choroby genetyczne i inne rzadkie zaburzenia przedstawiane na obrazach

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Abstract

Genetic disorders are a diseases caused by abnormalities in an individual's genetic material. A good source providing purported evidence of the existence of genetic diseases in the past, before their identification by medicine, are European artists' paintings. Such paintings quite frequently depicted human anomalies and disorders. In this work we present the examples of paintings depicting people suffering from diseases such as Down Syndrome, spondyloepiphyseal dysplasia congenital, Marfan syndrome, myotonic dystrophy, Paget's disease and tetralogy of Fallot.

Key words: genetics diseases, art paintings, Down syndrome, spondyloepiphyseal dysplasia congenita, Marfan syndrome, myotonic dystrophy, Paget's disease, tetralogy of Fallot

Streszczenie

Choroby genetyczne człowieka są wynikiem zaburzeń w materiale genetycznym. Źródłem historycznym dostarczającym dowodów na istnienie tych schorzeń w przeszłości, zanim zostały one zidentyfikowane, są obrazy dawnych europejskich malarzy. Artyści często w sposób bezwiedny uwieczniali w swoich pracach ludzi obarczonych anomaliami. W prezentowanej pracy zamieszczone zostały przykłady dzieł przedstawiających ludzi dotkniętych chorobami takimi

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jak zespół Downa, dysplazja kręgosłupowo-nasadowa, zespół Marfana, dystrofia miotoniczna, choroba Pageta oraz tetralogia Fallota.
Słowa kluczowe: choroby genetyczne, malarstwo, zespół Downa, wrodzona dysplazja kręgosłupowo-nasadowa, zespół Marfana, dystrofia miotoniczna, choroba Pageta, tetralogia Fallota

Introduction

Speculations about artistic depictions of medical entities have been an ongoing pastime among physicians. Such representations have been used as the bases for hypotheses about past incidence, the place of handicapped individuals in a society, and the evolution of modern concepts of pathogenesis. Researchers notice the relationship between paintings and genetic disease. Some conditions have been seen with high frequently (such as Down syndrome), whereas others have rarely been noted [1, 2]. Paintings quite frequently depicted medical anomalies and disorders, including genetic ones whether clearly recognized as such or not by the artists concerned [3]. Certain well-defined congenital malformations and genetic disorders can be identified in paintings throughout the ages. Portraits of an artist him/herself, or of others, may intentionally or unwillingly document a congenital abnormality or genetic disorder in the subject. Such works of art provide a fascinating study for those with interests in the field as well as widening our enjoyment of paintings in general [4, 5].

Our work is focused on diseases (particularly genetic diseases) present in paintings. We have chosen and created the list of genetic diseases which were actually depicted in paintings. But we have to remember that the specific diagnosis is often not certain.

Down Syndrome

Down syndrome (DS) is the most common example of a neurogenetic aneuploid disorder leading to mental retardation. In most cases, DS results from an extra copy of human chromosome 21 producing deregulated gene expressions in the brain, that gives raise to subnormal intellectual functioning [6]. Down syndrome was the subject of a series of letters and, later, several articles discussing its depiction in various paintings of the 17th century and later. This disease carries the eponym of Langdon Down, who described the condition in 1866 in his monograph “Observations of an Ethnic Classification of Idiots” but was also described by Seguin and later by others [2, 7].

One of the earliest paintings of someone with Down’s syndrome is a Flemish painting by an unknown artist “The Adoration of the Christ Child” (oil on wood, The Metropolitan Museum of Art, New York, USA), which is dated approximately 1515. It shows an angel (next to Mary) and possibly one other figure, the shepherd in the centre of the background - with the syndrome. The diagnosis of Down’s syndrome in the angel was based on a number of features: a flattened mid-face, epicanthal folds, up slanted palpebral fissures, a small and upturned tip of the nose, and downward curving of the corners of the mouth. The hands, crossed over the breast, have short fingers, especially on the left (Fig. 1) [8]. Beyond, “The Adoration of the Christ Child”, there are a lot of paintings by European artists providing purported evidence of the existence of Down syndrome before Down's identification. Among these there are instances of children whose appearances have been suggestive or firmly indicative of Down syndrome to some observers.

For example the painting by the a Carmelite monk Filippo di Tommaso Lippi “Madonna della Humilita” (tempera on wood, 1429-1432, Ambrosiana Library & Picture Gallery, Milan, Italy) show the representations of angels with some facial characteristics of babies with Down syndrome (Fig. 2). There is a hypothesis suggesting that the Down syndrome facial appearances of these “baby angels” likely was influenced by Lippi's early years in an orphanage where he could have seen rejected babies and infants with Down syndrome [3, 9, 10].

The child in a “Madonna and Child with Seraphin and Cherubin” (tempera on wood, 1460, Metropolitan Museum of Art, New York, USA) painting, by a follower of the Italian artist Andrea Mantegna, might have cretinism, Down syndrome or both. As the evidence of Down syndrome we could list slant eyes, a small nose, an open mouth and adenoidal expression. A clearly evident additional feature is the wide space between the 1st and 2nd toes of the right foot, but, though common in Down syndrome, the feature is not limited to the syndrome [3].

Fig. 1. “The Adoration of the Christ Child”
(an unknown artist, oil on wood,
The Metropolitan Museum of Art, New York, USA).
Characters discussed in the text are marked in the red circle.

Fig. 2. “Madonna della Humilita”
(Filippo di Tommaso Lippi, tempera on wood, 1429-1432,
Ambrosiana Library & Picture Gallery, Milan, Italy).
Characters discussed in the text are marked in the red circle.

Fig. 3. “Achille Emperaire Peintre”
(Paul Cézanne, oil on canvas,
1867-1868,
Musée d’Orsay, Paris, France).

Spondyloepiphyseal dysplasia congenita

Achille Emperaire, an artist and a friend of Paul Cézanne, was born in Provence in 1829. Emperaire's name was saved from oblivion only by the portraits Cézanne made of him. The most notable is the full-length portrait, more than six feet high, that hangs in the Musée d'Orsay in Paris. In the painting, the "dwarf-artist" is seated in a large upholstered armchair with a flowered slipcover, his crippled body wrapped in a blue flannel robe, his outsized pensive face with fashionable moustache and goatee, and his spindly legs resting on a footstool. Above the chair, against the uniformly dark background of the canvas, a painted inscription in Bodoni-type lettering reads: "Achille Emperaire Peintre" (oil on canvas, 1867-1868, Musée d'Orsay, Paris, France) (Fig. 3). The disproportionate nature of his dwarfism is apparent, along with a large forehead and a thick-set short trunk with long and thin extremities. The differential diagnosis for short-trunk disproportionate dwarfism includes metatropic dysplasia, Kniest dysplasia, Morquio syndrome and spondylo-epiphyseal dysplasia congenita. All of these conditions are associated with normal intelligence [11].

Emperaire has a characteristic flat face with wide set eyes typical of spondyloepiphyseal dysplasia, in particular, the congenital form. The face is normal in the milder form and it is not associated with a severely short stature. Spondyloepiphyseal dysplasia congenital is suggested here by his short neck, pectus carinatum, and hands and feet of normal size comparing to the lengths of the limbs (rhizomelic and mesomelic shortening). The inheritance of this disease is by autosomal dominant transmission, but most cases are sporadic in nature and are caused by mutations in the COL2A1 locus on chromosome 12 [1, 11].

Marfan syndrome

Marfan syndrome is an autosomal dominant connective tissue disorder characterized by a combination of clinical manifestations in different organ systems. Patients with Marfan syndrome whose lifetimes are extended may be encountered as acute abdomen (*appendicitis*) cases apart from the obligatory reasons and emergencies arising naturally out of their disease [12]. Formal diagnosis of Marfan syndrome demands characteristic skeletal, ophthalmological and cardiac abnormalities, or alternatively two of these three together with a clear family history of Marfan syndrome.

"Agosta and Rasha the Flugel Mensch the Schwaze Tube" was painted in 1929 by a Bavarian artist Christian Schad. The title of this painting, which can currently be seen in the new Tate Modern gallery in London, has been incorrectly translated as the "Agosta the pigeon-chested man and Rasha the black dove", when the dominating feature is *pectus excavatum* rather than *pectus carinatum* (Fig. 4). In the picture, both Agosta and his companion are looking out at the spectator with the serene expression of those used to public scrutiny. Looking at Agosta we can see deep *pectus excavatum* with outward deformities of the lower halves of the anterior rib cage. A long and thin thorax and a relatively long left arm can be observed. In addition, there is an obvious kyphosis or kyphoscoliosis affecting his shoulder girdle. The second and third fingers of his right hand are awkwardly positioned with hyperextension of proximal and distal interphalangeal joints suggesting joint laxity. His face is straight with slant – down eyes [13].

Fig. 4. “Agosta the pigeon-chested man and Rasha the black dove” (Christian Schad, oil on canvas, 1929, Tate Gallery, London).

Myotonic dystrophy

Myotonic dystrophy type 1 (DM1), the most common form of muscular dystrophy in adults (1/8,000 individuals), is an inherited, autosomal dominant disease characterized mainly by myotonia (sustained muscle contraction), progressive muscle weakness (especially of distal limbs, the neck, and the face), muscle wasting, and variable multisystemic features. DM1 belongs to a growing group of genetic diseases caused by expansion of unstable microsatellite repeats. DM1 was shown to be caused by the expanded CTG repeat in the 3'-untranslated region (3'UTR) of the dystrophy myotonic-protein kinase (DMPK) gene in chromosome 19q [14].

In “The Adoration of The Kings” (oli on panel, 1564, National Gallery, London) painted by Pieter Bruegel the Elder, we can see Balthazar, the Moorish king, standing on the right and Casper kneeling at the lower left (Fig. 5). Melchior, tightly holding a golden pot of frankincense, shows bilateral facial drooping, partial ptosis and premature frontal balding, all the features of myotonic dystrophy [15].

Fig. 5. “The Adoration of The Kings” (Pieter Bruegel the Elder, oil on panel, 1564, National Gallery, London). Melchior’s face taken in the red circle.

Paget’s disease

Paget’s disease, also called osteitis deformans, is a disease of unknown etiology, but researchers have identified a gene that could possibly predispose to the disease. The familial clustering of Paget’s disease is well recognized, about one third of the patients report having a first-degree relative with the disorder, with an autosomal dominant pattern of inheritance. Familial Paget’s disease tends to occur earlier in life and be more extensive than

the sporadic form. Two independent positional cloning studies demonstrated that mutations in the SQSTM1 gene are present in 40–50% of cases of familial Paget's disease [16, 17].

The initial lesion is one of the destructions by resorption, later the excessive amount of bone is deposited in a haphazard fashion with the diminution of the vascularity of the lesion. The new bone is of poor quality and may result in increased bone fragility and a tendency to fracture. The disease may be monostotic or polyostotic. When it is polyostotic, the bones most prominently affected are those of the axial skeleton which include the skull, the vertebral column, extremities and the maxilla. There is the progressive enlargement of the skull, bowing deformity of long bones and dorsal kyphosis (spinal curvature) [18]. There are studies on pagetoid lesions of the skull and clavicles in a painting "A Grotesque Old Woman" (oil on wood, 1513, National Gallery, London) attributed to Quentin Matsys (1465–1530) (Fig. 6).

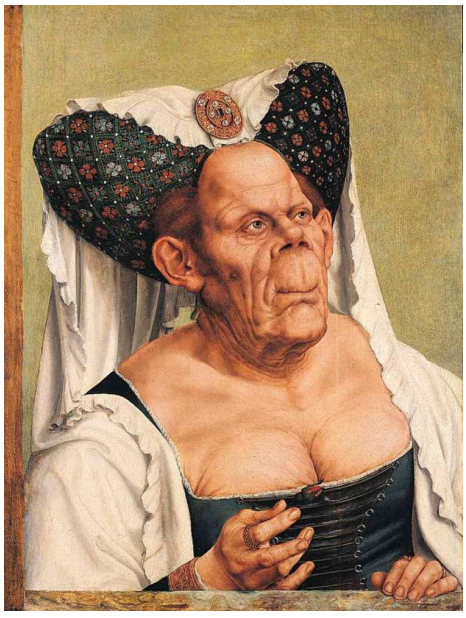

Fig. 6. "A Grotesque Old Woman" (Quentin Matsys, oil on wood, 1513, National Gallery, London).

The painting presents an old woman holding a rosebud. She is dressed in a costume with a large decolletage and a head dress of Italian fashion. The realism of each detail and the caricature-like face are most striking. The face is ugly, painfully accurate, neatly and smoothly executed with deformations, disfigurement, and distortions. The nostrils, for example, are odd, somehow more open, more flaring, and excessively arched. The broadness of the cheeks is accentuated by the ears, which stand out sharply from the head, and there is a bulging of the area beneath the nose. This broad and high cheeked face, with a wide coarse nose, gives the whole face an open, snorting look that has something of the wild animal about it-the lion. This typical face has been called by clinicians facies leontina, as seen infrequently in patients with Paget's disease and those with leprosy.

Fig. 7. Self-portrait
(Dick Ket, oil on canvas, 1932,
Museum Boijmans Van Beuningen
in Rotterdam, Netherlands).

There is a theory that Matsys based his work on Leonardo da Vinci's drawings for his grotesque heads. This grotesque figure resembles odd and grotesque personalities like those seen in the margins of society and, therefore, it is most likely a portrait made from life. Several characteristic pathological features can be seen in these faces: in the upper and lower row rhinophyma, macroglossia, facies leontina, hawk's nose, and elongated skull. The heads of the middle row resemble old fashioned Florentine respectability and caesarean personalities [19].

Tetralogy of Fallot

Tetralogy of Fallot (ToF) occurs in 3 of every 10,000 live births and constitutes approximately 7%–10% of all congenital defects. It is one of the most common causes of cyanotic heart disease beyond the neonatal age. The etiology is multifactorial and has been associated with maternal intake of retinoic acid, untreated maternal diabetes, and phenylketonuria. Chromosomal anomalies including trisomies 21, 18, and 13 have also been associated with ToF. More frequent, however, are the microdeletions of chromosome 22 [20].

Physical defects of this disease may be seen in a number of self-portraits, though sometimes the artist has taken great pains to conceal them. Dick Ket, who in series of self- portraits, clearly illustrated many of the clinical features associated with what is likely to have been Fallot's tetralogy with dextrocardia, finger clubbing, cyanosis and plethora. For example his self-portrait from 1932 (oil on canvas, Museum Boijmans Van Beuningen in Rotterdam, Netherlands) (Fig. 7). This painter eventually died of cardiac failure at the age of 38 [21].

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