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Cyclopa: from Greek antiquity to medical genetics

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Summary

Cyclops are among the best-known monsters of Greek mythology, also mentioned in art and literature. According to the most recent scientific knowledge, the malformations caused by defective development of the anterior brain and midline mesodermal structures include cyclopa (synophthalmos), ethmocephaly, cebocephaly and arrhinencephaly. These severe forebrain lesions often are accompanied by severe systemic malformations, and affected infants rarely survive. Neither true cyclopa nor synophthalmos are compatible with life because an anomalous development of the brain is involved. Thus, it is difficult to assume that ancient Greeks drew their inspiration from an adult patient suffering from cyclopa. Cyclops appear for the first time in literature in Homer's *Odyssey* (8th-7th century BC) and one of them, Polyphemus, is blinded by the hero of the epic poem. The description of the creature is identical with patients suffering from cyclopa; eyes are fused and above the median eye there is a proboscis, which is the result of an abnormal development of the surface ectodermal structures covering the brain. The next literature appearance of Cyclops is at the end of 7th century BC in "Theogonia", written by Hesiodus. Another interesting description is made by Euripides in his satyr play entitled 'Cyclops' (5th century BC). In conclusion, though it is not certain whether Homer's description of Cyclops was based on his personal experience or the narration of his ancestors, there is no doubt that the ophthalmological disease, cyclopa, was named after this mythical creature.

Key words

Ancient Greece, Cyclopa, Embryology, Mythology, History of Art

Introduction

Cyclopa is a rare congenital malformation, which is characterized by the appearance of only one eye (Hamilton et al., 1966). This deformity attracted much attention from the earliest times (Duke-Elder, 1963). Malformed human monsters, with a single median eye, have been interpreted to represent a sign of disaster or impending adversity (Trompoukis and Kourkoutas, 2007). Cuneiform characters on Babylonian clay tablets, now in the British Museum in London, refer to a monster who had one eye in the middle of the forehead, which will bring calamity to the country. These tablets were found in a mound near the Tigris river, and may be almost 4000 years old (Warkany, 1977). In Greek mythology the cyclopic giant Polyphemus's only eye was destroyed by Ulysses with a burning stake so that the latter could escape from

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the island of the Cyclops (Murray, 1974). Many authors relate these mythological figures to human congenital malformations (Regnault, 1901; Schatz, 1901; Phalippou, 1910; Popp, 1939). However, there are also authors who are convinced that fossils of animals were the examples for these mythological figures (Mayor, 1989). According to the palaeontologist Othenio Abel (1914), prehistoric dwarf elephant skulls, about twice the size of a human skull, were found by the Greeks on Cyprus, Crete, Malta and Sicily. Their large, central nasal cavity in the skull might have been interpreted as a large single eye-socket (Abel, 1914). The finding of the skeletal remains of a pygmy elephant from the glacial period in Sicily, in Messina, Palermo and Trapani, may have given rise to the idea of the fabulous cyclopic giant (Caloi et al., 1993). There is evidence for the presence of a medial frontal eye ("third" eye) in historical literature from China and India. This could be related to the frontal eye of fossil and existing amphibians and reptiles (Wendt, 1925).

Two of the most likely theories are that the Greek writers were possibly familiar with the teratological human Cyclops and that Homer with his story about Polyphemus, and later the Arabic poet who wrote Sinbad the Sailor, influenced medieval writers. In the Middle Ages there was no doubt about the fact that Cyclops lived in the unknown parts of Asia and Africa. The place where the 'Monoculi' lived was described exactly in the *Cosmographia Universalis* of Sebastian Munster (Münster, 1540; Baljet et al., 1991).

Cyclopia in Ophthalmology

Cyclopia is characterized by the anomalous development of the ocular primordial during the first month. Most instances involve a fusion of the two optic vesicles, or synophthalmia. True cyclopia with a solitary optic anlage is extremely rare. The prevalence is about 1 in 13.000 to 20.000 live births (Apple and Rabb, 1998).

Neither true cyclopia nor synophthalmia are compatible with life because an anomalous development of the brain is involved. Typically, the division of the telencephalon in the two hemispheres fails, often leaving a median dorsal cyst lined by ependyma. In cases of synophthalmia, the eyes may exhibit varying degrees of fusion; this may involve merely the optic nerves or a portion of the medial sclera, or more extensive portions of the globes. In addition to the ectodermal aberrations affecting the brain and eyes, there is abnormal development of the mesodermal structures of the face, leading to creation of the proboscis above the medial eye or eyes. The orbital region is grossly deformed from failure of the frontonasal bony processes to develop so that the maxillary processes fuse, resulting in an absent nasal cavity and a single central cavity or pseudo-orbit (Yanoff and Fine, 1991).

There has been speculation as to the origin of cyclopia for several centuries. Ambroise Paré (1510-1590) declared that monsters, including cyclopic newborns, may have many causes including "God may punish man's wickedness or show signs of punishment at hand" (Paré, 1585).

The oldest case of cyclopia is described in a letter by F. Licetus in Italy in 1619: 'Landi conte Ippolito, Lettera al figlio Ottaviano da Vienna li 8 settembre'. However, the author did not regard cyclopia as a congenital malformation (Taruffi, 1894). In the 18th century the ideas about teratology became increasingly scientific and scientists

started to collect specimens of the congenital malformations of man and animals. It was not until the end of the 19th century that histological studies were performed on these specimens and I. Geoffroy Saint-Hilaire in 1832 classified anomalies in the face of man and animals into two categories: cyclocephaly (kyklos=circle) and otocephaly (otos=ear). In the same period Willem Vrolik (1801-1862) in the Netherlands furnished the extensive pathological collection of his father with specimens of human and animal cyclops (Baljet et al., 1991).

In the 20th century there were many attempts at trying to establish the exact aetiology of cyclopia as evident in the many case reports from this period. Exposure to drugs or to other potentially teratogenic environmental factors such as ionic radiation, contraceptives, viraemia plus corticosteroids and salicylates, rubella vaccine, antibiotics, and amidopyrine during organogenesis has been regarded as the basis of this anomaly (Rogers, 1963; Mollica et al., 1981). Genetic errors with chromosomal abnormalities such as trisomy-D (which includes chromosomes 13, 14 and 15), monosomy-G mosaicism, translocations affecting chromosome 3 and group C chromosome, and chromosome 10 short arm deletion have also been linked to cyclopia (Adelman, 1936; Barber and Muelling, 1950; Cogan and Kuwabara, 1964; Cohen, 1966; Taysi and Tinaztepe, 1972; Howard, 1977; Figure 1).

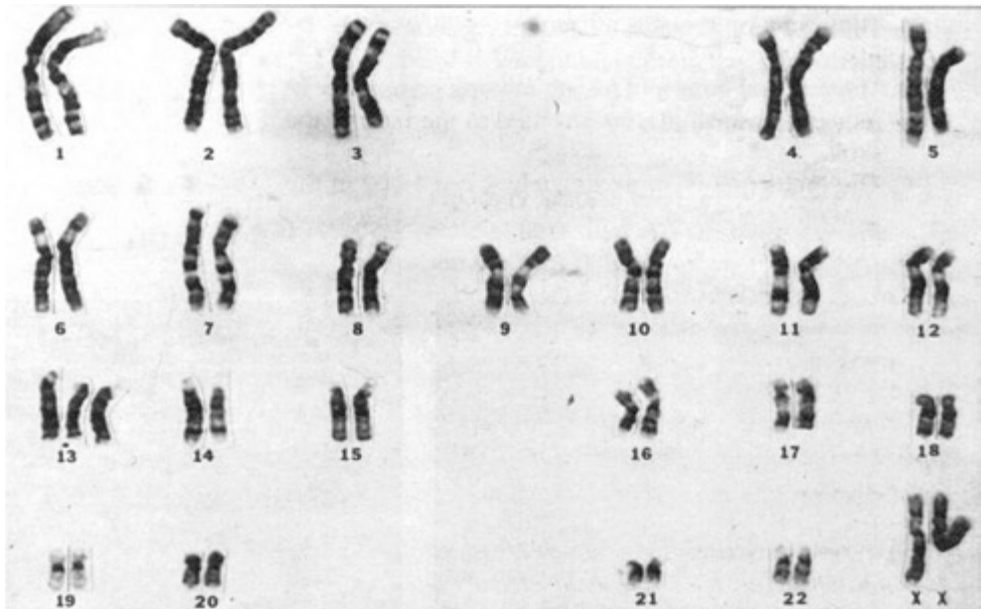


Figure 1 – Karyotype of trisomy-D (chromosome 13). Courtesy by the Laboratory of Medical Genetics, Medical School, Athens University, Athens.

Homer on cyclopa

Cyclops appears for the first time in literature in Homer's 'Odyssey' (7th century BC). It is wise to assume that the myth of Cyclops existed before Homer's epic poem. Previous narrations, which most probably vanished into the course of time, could have been the source of inspiration for his 'Odyssey'; this might as well have been the case for his other epic poem 'Iliad'.

In Ulysses' myth, the hero has to confront the Cyclops called Polyphemus, who is the son of the god Poseidon and the aquatic Nymph Thoosa. Despite Ulysses' entreaties to Polyphemus in order to respect the laws of hospitality, the Cyclops devoured two men who were accompanying Ulysses. However, Ulysses, who was famous for his craftiness, as he was the one who created the Trojan Horse, managed to intoxicate Polyphemus with alcohol and then with the help of his men they 'thrust the sharp point of a glowing white-hot timber into the sleeping monster's eye – and turned it round and round, as the blood bubbled up its hot point...'. The injury was so extensive and deep, that even Poseidon could not cure it (Homer, *Odyssey IX*, 152-479; Figure 2).

At this point it is very important to discuss the connection of the myth with art. There is an impressive diversity in form and thematic material in ancient Greek earthen pots. Therefore, the myths have a distinguished position in the themes depicted in these pots. The blinding of the Cyclops is represented in several ancient pots discovered during excavations in several ancient Greek cities and dating back to the 7th, 6th and 5th centuries BC. Moreover, it is worth making a comment on the anatomical exactitude of the scene of Polyphemus' blinding which is described in 'Odyssey'. This fact, in combination with the detailed descriptions of war injuries in 'Iliad', raised the suspicion that Homer was either a physician or had extensive knowledge of medicine (Grmek, 1991).

Other literature descriptions of cyclopa

Another description of Cyclops in literature is noted at the end of 7th century BC in Hesiod's 'Theogonia' (Hesiod, *Theogony* 139). Hesiod belongs to the posterity writers and is considered as the most important representative of the didactic epic poets. In 'Theogonia', Hesiod also describes Cyclops as one-eyed cannibal giants, and according to him they were the sons of Heaven and Earth who forge the thunderbolts for Zeus (Evelyn-White, 1914). Those creatures were similar to the mortals, but they had in the middle of their forehead only one eye: 'that is the reason why they were named Cyclops, in other words men with one eye in their forehead'. The Cyclops, like all of Earth's descendants, were monstrous. According to Hesiod, these monsters were very strong and sly, inciting hatred even in their own father (Uranus). It is assumed that these verses represent the general social attitude of Hesiod's era regarding children suffering from congenital deformities.

The next interesting literature appearance takes place in the 5th century BC when Euripides presented his satyr play entitled 'Cyclops' (Euripidis, 1983). Euripides had obviously inspired the plot of 'Cyclops' from Homer's 'Odyssey'. In this drama the Cyclops is characterized as a more pleasant and less brutal creature. In addition the



Figure 2 – The blinding of the Cyclops Polyphemus by Ulysses. Funerary Proto-Attic Amphora (670-660 BC). Archaeological Museum of Eleusis. Courtesy by the 3rd Ephorate of Prehistoric and Classical Antiquities, General Directorate of Antiquities and Cultural Heritage, Athens.

Cyclops, though he is naive, is aware of the Trojan War and becomes sarcastic at Ulysses when discussing the war with him. Euripides, more precisely than Homer, believes that the island where Cyclops was found by Ulysses was Sicily and mentions that the cave where he lived was in the famous volcano of Etna. In general, the Greek tragedian does not alter the plot of the myth, but the cause for Polyphemus's blinding. The moral of his satirical drama is the triumph of human intelligence, as represented by Ulysses, over savagery and illiteracy.

The same myth was a continuous source of inspiration for numerous artists during the Hellenistic period. A typical example is the imprint of a third orbital cavity in the forehead, as depicted in a terra-cotta head found in Asia Minor. This archaeological find created among the medical historians the impression that the face depicted

suffered from leprosy, as this disease can sometimes give rise to the easily identifiable 'leonine facies'. (Grmek, 1991) However, more recently it is assumed that this find represents a case of cyclopia because of the presence of a prominent pseudo-orbit in the forehead.

Representations of creatures identical to Cyclops exist in other countries with similar culture. Cyclopes are depicted in the mosaic of Piazza Armerina in Sicily and in black-figure pots found in South Italy. Additionally, the Greek thematic material influenced the French-Roman civilisation. In the French city of Genainville there is a grave that dates from the 1st century BC, which is decorated with a fresco representing hirsute creatures with enucleated orbits and a remaining one eye in the centre of their forehead (Bonis et al., 1992). This is a very interesting archaeological find since it combines the ancient Greek myth with the tradition of Gaul's ritual.

Conclusion

The myth of Cyclops survived for several centuries following on from the initial description by Homer. Poetry, literature, ceramics, sculpture and painting have all undeniably played an important role in the preservation of this myth as well as forming a basis for our current understanding of this developmental abnormality in the 21st century. Thus, although it is not certain whether Homer's description of Cyclops was based on his personal experience or the narration of his ancestors, there is no doubt that the myth of this creature gave his name to the ophthalmological disease of cyclopia.

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