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A Comprehensive and Clinical Review of Chromosome 9 Ring Syndrome

Maryam Montazeri, Shahin Asadi*

Medical Genetics-Harvard University. Director of the Division of Medical Genetics and Molecular Optogenetic Research. Division of Medical Genetics and Molecular Pathology Research, Harvard University, Boston Children's Hospital, USA

ABSTRACT

Ring chromosome 9 syndrome is a rare chromosomal disorder in which the two ends of chromosome number 9 are lost and the two ends connect to each other and form a ring. Associated symptoms and findings may vary depending on the amount and location of missing chromosomal material and other factors. As mentioned above, ring chromosome 9 syndrome may be characterized by various craniofacial abnormalities. However, in some cases, such features may not be obvious. Cranial and facial defects associated with ring chromosome 9 syndrome may include abnormally small head size (microcephaly) or premature fusion of the fibrous joint (suture) between the bones that make up the forehead (metopic suture), resulting in a narrow forehead. Ring chromosome 9 syndrome is caused by the removal of chromosomal material from the end (distal) regions of the short arm (p) and long arm (q) of chromosome number 9 and connecting its ends to form a ring. Chromosomes are found in the nucleus of all cells in the body. They have the genetic characteristics of each person.

Keywords: Ring chromosome 9 syndrome, Chromosome Abnormality, Genetics Disorders

OVERVIEW OF CIRCULAR CHROMOSOME 9 SYNDROME

Ring chromosome 9 syndrome is a rare chromosomal disorder in which the two ends of chromosome number 9 are lost and the two ends connect to each other and form a ring. Associated symptoms and findings may vary depending on the amount and location of missing chromosomal material and other factors. Some affected people may have variable abnormalities in the skull and facial area (skull and face). However, in others with a chromosomal abnormality, such features may not be evident. Cytochromosome 9 syndrome may also be characterized in some cases by additional physical features such as growth retardation, heart defects, genital tract abnormalities, or other findings. In addition, many affected individuals have moderate to severe intellectual disability. However, in some cases, intelligence may be in the lower normal range. Circular chromosome 9 syndrome is usually caused by spontaneous (de novo) errors early in fetal development that occurs (sporadically) for unknown reasons [1].

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***Corresponding Author**

Shahin Asadi

Medical Genetics-Harvard University. Director of the Division of Medical Genetics and Molecular Optogenetic Research.Division of Medical Genetics and Molecular Pathology Research, Harvard University, Boston Children's Hospital, USA

Email: shahin.asadi1985@gmail.com

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Clinical Signs and Symptoms of Circular Chromosome 9 Syndrome

As mentioned above, ring chromosome 9 syndrome may be characterized by various craniofacial abnormalities. However, in some cases, such features may not be obvious. Cranial and facial defects associated with ring chromosome 9 syndrome may include abnormally small head size (microcephaly) or premature fusion of the fibrous joint (suture) between the bones that make up the forehead (metopic suture), resulting in a narrow forehead. Pointed, "triangular" and eyes close together (ocular hypotelorism). Also, some people with this syndrome may have abnormal folds of the eyelids, slight protrusion of the eyes (exophthalmos), exaggerated arch to the eyebrows, small jaw (micrognathia) and small chin or short neck [1,2].

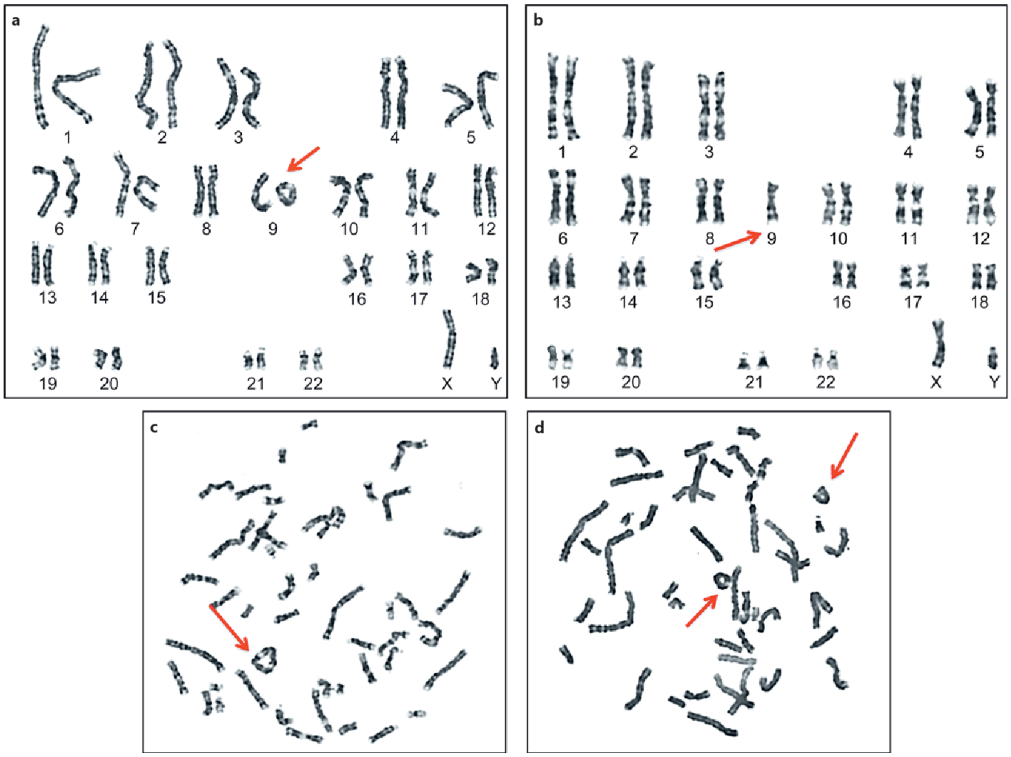

Figure 1: Illustrations of the karyotype of patients with circular chromosome 9 syndrome (a) and chromosome 9 deletion syndrome (b) [1]

In some cases, ring chromosome 9 syndrome may also be associated with growth retardation after birth. Various structural abnormalities of the heart (congenital heart defects), such as an abnormal opening in the partition (septum) that normally separates the lower chambers (ventricles) of the heart (ventricular septal defect) or variable skeletal abnormalities. Some affected men may also have genital abnormalities, including ambiguous genitalia or abnormal location of the urethral opening (hypospadias), below the penis. Additional physical abnormalities have also been reported in association with circular chromosome 9 syndrome. These include incomplete closure of the roof of the mouth (cleft palate), abnormal bending (clinodactyly) of certain fingers; a fold in the palms; or a disease known as gastric reflux. Gastric reflux is characterized by the abnormal backflow (reflux) of stomach acid into the esophagus, which causes inflammation and possible damage to the lining of the esophagus [1,3].

Cytochromosome 9 syndrome is usually characterized by moderate to severe intellectual disability. However, some affected individuals may have low intelligence within the normal range. Those suffering from this disorder may also show variable delays in acquiring skills that require coordination of mental and physical activities (psychomotor retardation) or behavioral abnormalities, such as irritable or excited behavior [1,3].

Etiology of Circular Chromosome 9 Syndrome

Ring chromosome 9 syndrome is caused by the removal of chromosomal material from the end (distal) regions of the short arm (p) and long arm (q) of chromosome number 9 and connecting its ends to form a ring. Chromosomes are found in the nucleus of all cells in the body. They have the genetic characteristics of each person [1,4].

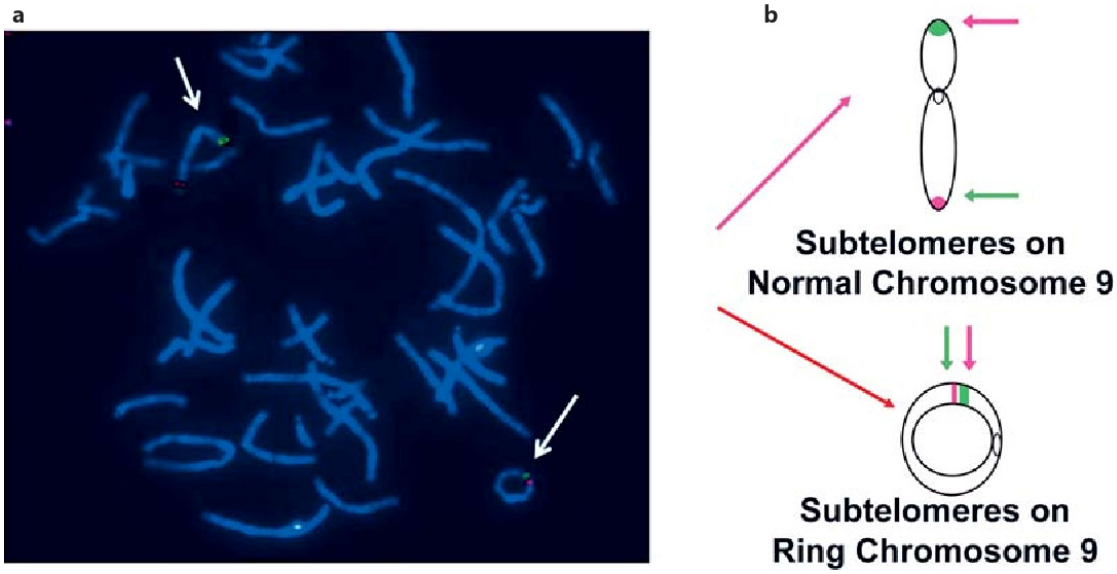

Figure 2: Microscopic image of circular chromosome 9 [1].

As mentioned above, in those with ring chromosome 9, associated symptoms and findings may vary from case to case. Such clinical variation may depend on the specific amount and location of missing material from chromosome 9, the stability of the circular chromosome during subsequent cell divisions, or other factors. For example, in some cases, only a certain percentage of an affected person's cells may have circular chromosome 9, while other cells may have the normal chromosomal composition (a finding known as "chromosomal mosaicism"), which A variety of associated and physical symptoms are affected. Circular chromosome 9 syndrome is usually caused by spontaneous (de novo) errors very early in fetal development. In such cases, the parents of the affected child usually have normal chromosomes and have a relatively low risk of having another child with a chromosomal abnormality. However, it is theoretically possible that one of the parents of the affected person also has circular chromosome 9 in all or some cells with few symptoms. In such cases, it is believed that ring chromosome 9 may be inherited and the likelihood of having another child with the chromosomal abnormality is higher [1,5].

Frequency of Circular Chromosome 9 Syndrome

Circular chromosome 9 syndrome is a rare chromosomal abnormality that is thought to affect males and females in relatively equal numbers. Since the description of this disorder, more than 12 cases have been reported in the medical literature [1,5].

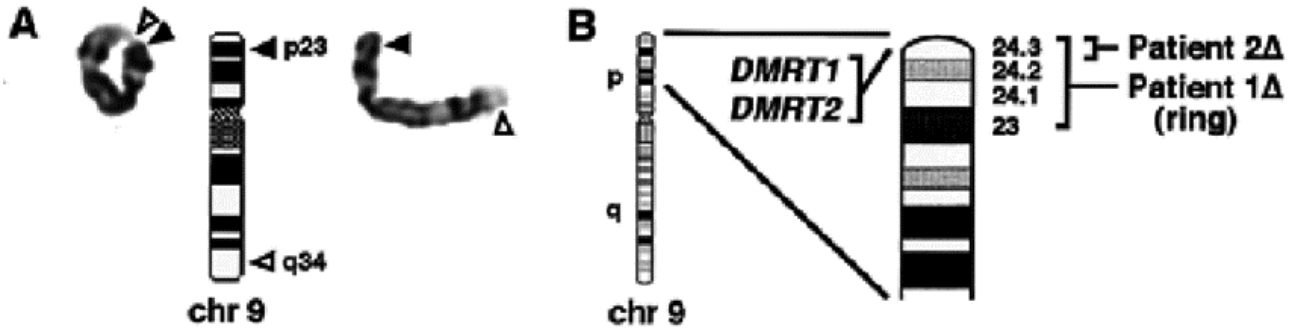

Figure 3: Schematic of circularization of chromosome number 9 [1].

Disorders Associated with Circular Chromosome 9 Syndrome

The symptoms of the following disorders may be similar to those of ring chromosome 9 syndrome. Comparison may be useful for differential diagnosis of this syndrome:

Circular chromosome 9 syndrome is a chromosomal disorder characterized by the deletion (monosomy) of a portion of the distal (distal) short arm (p) of chromosome 9 (eg, the breakpoint is usually at band 9p22). Characteristic features include variable degrees of mental disability, malformations of the skull, face, limbs, heart or reproductive system, or other physical malformations. Common craniofacial defects include a "triangular" or "spiral" forehead, a short nose, flat nasal bridge and upturned nostrils, prominent eyes with upward-sloping eyelid folds, vertical skin folds that may covers the inner corners of the eyes (epicanthal folds), highly arched eyebrows, small jaw (micrognathia); Short and wide neck or other features [1,6].

Additional chromosomal disorders may have symptoms and findings similar to those potentially associated with ring chromosome 9 syndrome. Chromosomal testing is necessary to confirm the specific chromosomal abnormality present [1,6].

Diagnosis of Circular Chromosome 9 Syndrome

In some cases, ring chromosome 9 syndrome may be suggested before birth (fetal) with specialized tests such as ultrasound, amniocentesis, or placental villus sampling (CVS). During fetal ultrasound, reflected sound waves create an image of the developing fetus, potentially revealing certain findings that indicate chromosomal abnormalities or other developmental abnormalities. With amniocentesis, a sample of the fluid that surrounds the developing fetus is removed and analyzed, while CVS involves taking tissue samples from part of the placenta. Chromosomal analysis performed on such fluid or tissue samples may reveal the presence of circular chromosome 9 [1,7].

In most cases, chromosome 9 ringing is diagnosed after birth (after delivery) based on careful clinical evaluation, specific physical findings, and chromosomal analysis. Various specialized tests may also be performed to help diagnose or describe some of the abnormalities associated with this disorder. For example, a complete cardiac evaluation may be recommended to evaluate any cardiac abnormalities that may be present. These evaluations may include a thorough physical examination, evaluation of heart and lung sounds through the use of a stethoscope, and special tests that enable doctors to evaluate the structure and function of the heart (eg, X-ray studies, electrocardiography [EKG]), Echocardiography [1,7].

Treatment Paths for Circular Chromosome 9 Syndrome

The treatment of circular chromosome 9 syndrome is directed towards specific symptoms that are specific to each individual. Management of this condition may require the coordinated efforts of a team of medical professionals, such as pediatricians, doctors who diagnose and treat disorders of the skeleton, muscles, joints, and related tissues (orthopedics), cardiologists, or other health care professionals [1,8].

For some affected people, doctors may recommend surgical repair or correction of some abnormalities of the skull, genitals, or other abnormalities related to this disorder. In addition, for those with congenital heart defects, treatment with certain medications, surgical intervention, or other procedures may be necessary. The specific surgical methods performed depend on the severity and location of the anatomical abnormalities, their accompanying symptoms, and other factors [1,8].

Early intervention may also be important in ensuring that disadvantaged children reach their potential. Special services that may be helpful include special education, speech therapy, physical therapy, or other medical, social, or occupational services. Genetic counseling will also be helpful for affected individuals and their families. Another treatment of this disorder is symptomatic and supportive [1,9].

DISCUSSION

In some cases, ring chromosome 9 syndrome may also be associated with growth retardation after birth. Various structural abnormalities of the heart (congenital heart defects), such as an abnormal opening in the partition (septum) that normally separates the lower chambers (ventricles) of the heart (ventricular septal defect) or variable skeletal abnormalities. Cytochromosome 9 syndrome is usually characterized by moderate to severe intellectual disability. However, some affected individuals may have low intelligence within the normal range. In most cases, chromosome 9 ringing is diagnosed after birth (after delivery) based on careful clinical evaluation, specific physical findings, and chromosomal analysis. Various specialized tests may also be performed to help diagnose or describe some of the abnormalities associated with this disorder. For some affected people, doctors may recommend surgical repair or correction of some abnormalities of the skull, genitals, or other abnormalities related to this disorder. In addition, for those with congenital heart defects, treatment with certain medications, surgical intervention, or other procedures may be necessary [1,10].

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