Piecing Together a Picture of Trisomy 8 Mosaicism Syndrome

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Relatively few cases of trisomy 8 mosaicism syndrome (T8mS) are documented in the medical literature. It is a rare genetic condition characterized by extreme phenotypic variability—ranging from severe congenital malformations to minute dysmorphic changes. The authors describe a case of T8mS in a man aged 33 years who presented with lumbar spine herniated nucleus propulsus. This case features some of the classic characteristics of T8mS and suggests an association between T8mS and herniated disks.


Trisomy 8 is defined as the presence of three copies of chromosome 8 in every cell of an individual’s body—a condition that is usually fatal.1 A variant of trisomy 8 is trisomy 8 mosaicism syndrome (T8mS)—also known as Workany syndrome. This condition occurs when a process called nondisjunction transpires during mitosis in the zygote phase of fetal development. In nondisjunction, a pair of chromosomes does not divide evenly, resulting in too few chromosomes in some cells and too many chromosomes in other cells. In T8mS, some of an individual’s cells contain the normal two copies of chromosome 8, while the other cells contain three copies of chromosome 8.1,2

The specific cells in which nondisjunction occurs and the timing of the nondisjunction in the developing zygote determine the particular tissues and cells affected in T8mS. As a result, T8mS is characterized by extreme phenotypic variability—ranging from severe congenital malformations to minute dysmorphic changes.3 The most common clinical features of this condition are thick lips, camptodactyly, clinodactyly, deep plantar and palmar skin furrows, vertebral or hip anomalies, and mental retardation.4

Because of its large phenotypic variability, the incidence of T8mS has been difficult to determine. However, the incidence of this condition in the general population has been estimated to be as high as 1 in 25,000 persons.2 A review of published studies found with the National Library of Medicine’s PubMed database, using the keywords trisomy 8 and trisomy 8 mosaicism,5-8 as well as other published texts,9,10 reveals that only about 120 cases of T8mS have been documented in the literature. Thus, further research is needed to characterize the phenotypic variability of T8mS.

In the present case report, we share observations of an individual with T8mS who presented with lumbar spine herniated nucleus propulsus. The case suggests an association between T8mS and herniated disks.

Report of Case
Medical History

The patient in the present case was born on June 16, 1975, at which time his primigravida mother was aged 25 years and his father was aged 29 years. His parents were unrelated and, at the time of the patient’s conception and birth, both parents were healthy. The pregnancy was uneventful, and the patient was born by spontaneous vaginal delivery at 37-weeks gestation.

At birth, the patient weighed 6 lb 8.5 oz (2.96 kg) and was 19.5 in (49.5 cm) in length. He had deep furrows in his hands and feet. While the patient was under neonatal clinical observation the day after birth, the pediatrician noticed that he was turning blue, at which time cardiopulmonary resuscitation was performed. The patient was then placed in the pediatric intensive care unit for 5 days. He was released from the hospital 2 weeks later. For the following 9 months, routine pediatric examinations of the patient were uneventful.

The first abnormal finding was related to the patient’s large head circumference, which was noted at 9 months of age. At that time, the patient was referred for a computed tomography cranial scan at Yale-New Haven Hospital in Connecticut. This scan revealed widening of the ventricles. Genetic testing was recommended because of the deep furrows on the patient’s hands and feet, as well as the additional findings at age 12 months of elongated facial features and developmental delays. Chromosomal analysis, conducted on the patient’s peripheral blood lymphocytes at age 15 months at Yale-New Haven Hospital, led to a diagnosis of T8mS. The extra chromosome 8 characteristic of T8mS is shown in the patient’s karyotype in Figure 1.
The patient received a variety of medical treatments throughout his life, beginning at age 3 years with repair of an inguinal hernia and an orchietomy to remove an undescended left testicle. As a toddler, the patient had recurrent otitis media infections, which led to a tonsillectomy and an adenoidectomy with insertion of myringotomy tubes. He also received bilateral strabismus surgery at an unknown age.

At age 6 years, the patient received a lingual frenectomy. His intelligence quotient as measured on the Stanford-Binet scale was found to be 61, suggestive of moderate mental retardation. Because of contracture of the great toe of the right foot, arthrodesis was performed on the toe’s interphalangeal joint at age 6 years. At age 10 years, the patient received arthrodesis and metatarsal reconstruction on both feet. In addition, he was diagnosed at age 10 years as having thoracolumbar scoliosis, with convexity to the left of approximately 20 degrees limited to vertebrae T10 to L5.

The patient’s scoliosis improved during his adolescent years. At age 14 years, he received radical mandibular reconstruction. He also started physical therapy for hip flexion contractures. At age 18 years, he was diagnosed as having bilateral osteoarthritis of the knees. Six years later, at age 24 years, the patient was diagnosed as having severe tendonitis in both legs and both feet. At age 28 years, he received a pilonidal cystectomy.

Presentation of Case
At age 33 years, the patient presented at the Sierra Vista Regional Medical Center in Arizona with the chief complaint of low back pain. He weighed approximately 280 lb (127 kg) and was 6 ft 7 in (2.0 m) tall with a marfanoid habitus body type. He described symptoms of numbness and tingling radiating from his lower back to his left lower extremity.

The patient experienced great difficulty in ambulating, and his parents, who were much smaller than the patient, had substantial difficulty in transporting him. In addition, the patient described a progressive weakness of his left ankle dorsiflexion with complete drop foot.

Upon initial interview, the patient denied any bowel or bladder changes. However, during the following hours in the emergency department, he began to feel constipated and had some liquid fecal incontinence.

Magnetic resonance imaging (MRI) of the patient’s lower back was performed. The MRI results at the L3-L4 level are shown in sagittal view in Figure 2 and in cross-section in Figure 3. These results revealed L3-L4 central disk herniation of approximately 8 mm, with some calcification within the disk itself. The herniation was causing marked compression of the thecal sac at this level. The MRI results also showed signs of stenosis at the L2-L3 and L4-L5 levels.

Diagnosis and Treatment
The patient was diagnosed as having cauda equina syndrome. He was transferred to a facility with neurosurgical services, where a laminotomy, partial facetectomy over L3 and L4, and microdiskectomy of L3-L4 were performed. He was then referred to intense inpatient physical therapy for 6 weeks to restore his ability to walk.

Several months later—after continued physical therapy—the patient became able to ambulate without pain.

Discussion
The present case illustrates a number of characteristic features associated with T8mS that have been previously reported in the literature. In addition to the patient’s classic features of trisomy 8 (ie, furrows in the palms and feet, elongated facial features, low-set and abnormally shaped ears, strabismus, developmental delays, and mental retardation), the patient also had a marfanoid habitus body type.

In a previously documented case of T8mS with similar body type, the individual was treated for Marfan syndrome until age 15 years.11 Physicians should consider T8mS in the differential diagnosis of individuals with mental retardation and tall stature—especially when there is also evidence of such skeletal abnormalities as joint contractures and scoliosis.

In addition to having these abnormalities, the patient in the present case was diagnosed as having a herniated disk at L3-L4 and cauda equina syndrome. Because of the extreme phenotypic variability associated with mosaic genetic disorders.
had cauda equina syndrome, suggesting an association between that condition and T8mS. We believe that the patient’s spinal abnormalities and marfanoid habitus secondary to T8mS placed him at increased risk of herniated disks.

Our literature review revealed many documented cases of vertebral anomalies in individuals with trisomy 8. Approximately 71% of patients with T8mS are estimated to have some form of vertebral anomaly. Therefore, vertebral anomalies could increase patient risk of herniated disks. Nevertheless, further research is needed to establish a firm association between T8mS and herniated disks.

Certain aspects of T8mS are particularly relevant to osteopathic medicine. The majority of patients with T8mS have musculoskeletal complaints. Thus, osteopathic manipulative treatment can play an important role in the treatment plan for these patients. In addition, many patients with T8mS require a number of surgeries, and osteopathic manipulative treatment can be used to expedite their recovery and rehabilitation.

Conclusion
The present case demonstrates some of the classic features of T8mS—features that healthcare providers should be aware of in order to conduct early chromosomal analysis of patients. In addition to these classic characteristics, the patient in this case had cauda equina syndrome, suggesting an association between that condition and T8mS. We believe that the patient’s spinal abnormalities and marfanoid habitus secondary to T8mS placed him at increased risk of herniated disks.

References