Spina bifida occulta-a diagnostic feature of the trisomy 8 syndrome

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INTRODUCTION

Introduction. Clinical manifestation of the trisomy 8 syndrome are craniofacial abnormalities, skin manifestations, heart and renal malformations, skeletal abnormalities and mental retardation. Case report. We present a case of spina bifida occulta in the child with full trisomy 8. On physical examination there were signs of dysmorphic features in the girl, deep creases on palms and soles, camptodactyly, corneal opacities, cleft palate, agenesis of the corpus callosum and spastic quadriplegia. Clinical examination revealed a subtle protrusion covered by skin in the midline thoracic region of the back, which was confirmed to be a lipoma with an intact spinal cord and spina bifida occulta. Meningocele was eliminated and no surgical intervention was needed. Conclusion. Chromosomal abnormalities including trisomy 8 syndrome occur in patients with spina bifida. It is important to detect small subcutaneous lesion which require no specific treatment, but must be differentiated from small meningocele.

Key words: trisomy 8 syndrome; spina bifida occulta; neural tube defects; neurological features.

Trisomy 8 is a chromosome abnormality where an extra chromosome 8 exists in every body cell. If apart from trisomic cells there are normal cells, the person has a trisomy 8 mosaicism. Trisomy 8 mosaic syndrome is more frequent finding than full trisomy 8 and usually has better prognosis. There is no clear correlation between the phenotype and the percentage of trisomic cells. Full trisomy 8 very often has lethal outcome in first years of life and could also be responsible for spontaneous abortions. It is known that full trisomy 8 is responsible for spontaneous abortions in about 12% of autosomal trisomies.

Mosaic trisomy 8 syndrome is one of the most common autosomal trisomies after chromosome 21, 18 and 13. An estimated incidence is 1 of 35,000 live births. The male to female ratio is 5 to 1. Clinical manifestations in this syndrome are craniofacial abnormalities, skin manifestations, heart and renal malformations, skeletal abnormalities and mental retardation. Craniofacial abnormalities include abnormal head shape with prominent forehead, deep set eyes, hypertelorism with broad nasal root and prominent nares, full lips, everted lower lip, micrognathia, high arched palate, cleft palate and prominent ears with thick helices. Skeletal abnormalities are long and slender trunk, slender pelvis, camptodactyly, major joint contracture, absent patellae and spina bifida occulta. Skin manifestations include deep creases on palms and soles and widely spaced nipples. Occasional abnormalities are hemathological abnormalities like coagulation factor VII deficiency and malignant myeloid disorders. Central nervous system manifestations include mental retardation, agenesis of the corpus callosum and delayed motor development.

Trisomy 8 can be associated with neural tube defects including spina bifida occulta. Spina bifida occulta is a defect in the posterior bony components of the vertebral column without herniation of the cord or meninges. It is usually asymptomatic. This defects is often found incidentally on radiographic studies or is diagnosed because of a subtle clinical finding such as hair, angioma or lipoma in the midline of the back marking the location of the defect. The presence of such a cutaneous lesion is associated with spina bifida occulta in about 10% of cases.

Meningocele, a protrusion of meninges without accompanying nervous tissue, is not associated with neurologic deficits. The mass could be usually evident as a fluid-filled protrusion covered by skin or membrane in the midline. Meningomyelocele is the most complex of
congenital spinal anomalies, involving all tissues and leading to herniation of cord elements and nerve roots. The birth prevalence rate for spina bifida, which has steadily declined because of improved methods of prenatal diagnosis, has been estimated to be 4.6 cases per 10,000 births.

We presented a case of spina bifida occulta in the child with full trisomy 8. Computed tomography (CT) was helpful in determining the contents of a mass along the spine in our reported case and in differentiating spina bifida occulta from meningocele. We reviewed the genetic and environmental factors associated with neural tube defects.

CASE REPORT

The patient, a female infant, was born at 36 weeks’ gestation with a birth weight of 2500 g by spontaneous delivery. The pregnancy was complicated by umbilical cord around baby’s neck and partial placental abruption prior to delivery. Apgar score was 8 at 5 minutes of life. Her parents were nonconsanguineous, and both parents and two brothers, 10 and 8 years of age, were healthy. Family history was unremarkable with no history of mental retardation, learning deficits, birth defects, or genetic syndromes. The mother was aged 35 years and the father 42 years at the time of birth.

On physical examination there were signs of dysmorphic features in the girl: prominent forehead, expressionless facies with a deep-set eyes, a broad upturned nose with prominent nares, and prominent, low set ears. She had cleft palate and full lips. Other abnormalities included camptodactyly, deep creases on palms and soles and widely spaced nipples. She had poor visual tracking of the moving objects because of congenital corneal opacities revealed by ophthalmological examination. There was no cardiac abnormalities and the echocardiographic findings were normal. She was hypotonic with reduced motor activity, and had brisk deep tendon reflexes. Ultrasound of the brain and computed tomography (CT) of the brain revealed agenesis of the corpus callosum and mildly dilated lateral ventricles. There was a presence of a subtle protrusion covered by a skin in the midline of the back in the thoracic region of the spine. The remaining results of her systemic examination were normal. Genetic testing revealed trisomy 8 syndrome, specifically 47, XX, +8, while those of the parents and both brothers were normal.

At the age of 9.5 months the girl was suffering from poor visual tracking, cleft palate and malnutrition, spinal deformity and seizures. She was admitted to the hospital for a further evaluation of her neurological and physical status. Neurological examination revealed abnormal head shape, flaccid quadriplegia and severe developmental delay. She was not able to sit or to control her head. Focal seizures appeared two weeks earlier and interictal electroencephalography (EEG) recording showed focial activity in the left fronto-temporal region. The complete control of seizures was achieved by carbamazepine and she was seizure-free later. Computed tomography (CT) of the brain confirmed abnormal head shape, ventriculomegaly and agenesis of the corpus callosum (Figure 1).

Spinal clinical examination showed a small, cherry-like mass covered by a skin, which was palpable in the thoracic area of the back. This protuberant and fluctuant protrusion looked like a lipoma. Ultrasonography showed homogeneous signal within the lesion confirming the diagnosis of lipoma. Computed tomography imaging findings facilitated the diagnosis, detecting spina bifida occulta. There was no progressive symptomatology and suspicion on meningocele was eliminated.
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Hydrocephalus requires ventriculoperitoneal shunt. Prenatal diagnosis is possible by fetal ultrasound starting from 13th week of gestation, and measurement of elevated level of alpha-fetoprotein in the maternal serum.

Spina bifida seems to be determined by many genes and environmental factors that might affect susceptibility independently or through interactions. A family history of spina bifida or anencephaly is one of the strongest risk factors for these disorders. Neural tube defects have been reported in children with various karyotype abnormalities, including trisomy 13, 18 and 8. Because of the profound effect of folate on the risk of myelomeningocele, polymorphisms in the methylenetetrahydrofolate reductase (MTHFR) gene were evaluated as a risk factor. In general, most neural tube defects are multifactorial disorders that may be secondary to either genetic or environmental factors or a combination of both. Chromosomal abnormalities, family history of neural tube defects and mutation in MTHFR gene are predisposing factors for neural tube defects.

The present report is a case of a patient with full trisomy 8 syndrome, who presented with psychomotor retardation and spina bifida occulta. Our patient is also of interest, having survived the neonatal period with complete trisomy 8, which is usually lethal. Only a few cases of complete trisomy 8 have been described, the majority of patients having the mosaic form. The intellectual and physical abnormalities in trisomy 8 (complete or mosaic) are variable. Patient usually present with delayed psychomotor development and failure to thrive, similar to our patient. A few cases with normal development, phenotype and intellectual function have been described. In contrast to other autosomal trisomies, there is no association with advanced parental age, while birth weight and length are usually normal for gestational age.

Mosaic trisomy 8 is usually underdiagnosed because of a highly variable phenotypic expression. Some patient are asymptomatic, while others have multisystemic involvement. Neurological features of mosaic trisomy 8 syndrome include agenesia of the corpus callosum, mental retardation and predisposition to language delay and spina bifida occulta.

Our patient had many of the described phenotypic findings, namely abnormal head shape, expressionless facies, deeply set eyes, broad upturned nose, prominent ears, prominent lower lip, cleft palate, conical opacities, deep skin furrows on palms and soles, camptodactyly and nipples widely spaced. Neurological features include psychomotor retardation, agenesia of the corpus callosum, seizures and spina bifida occulta.

In our patient’s case the question arose as to whether the lipoma in thoracic region were a part of meningocele. Computed tomography of the thoracic spine showed that the spinal cord is intact without signs of herniation and the diagnosis of spina bifida occulta was confirmed. Very small subcutaneous lesion may remain undetected for prolonged periods and typically require no specific treatment, but must be differentiated from small meningocele. Myelomeningocele require surgical intervention because

FIGURE 3.
COMPUTED TOMOGRAPHY OF THE SPINE SHOWED SPINA BIFIDA OCCULTA.

Neuroradiological results determined the content of a mass along the spine and helped in differentiating spina bifida occulta from meningocele (Figure 2 and 3).

Three months later, after ophthalmological operation, the patient could fixate well with both eyes. Cleft palate was operated and feeding was much easier. The girl is now 4.5 years old and show severe delay in psychomotor development and gross motor and intellectual handicap. She could sit only with support and cannot change from the lying position to the sitting without help.

DISCUSSION

Failure of the posterior neuropore, the terminal location of the neural tube fusion, to close at approximately day 29, cause a range of spinal defect. They include failure of vertebral closure without herniation of neural elements (spina bifida occulta), herniation of meninges alone (meningocele) and herniation of cord elements and nerve roots (meningomyelocele). Most defects are lumbar-sacral in location but may occur in the thoracic or cervical region. The type II Chiari malformation is always associated with meningomyelocele; aqueductal stenosis with hydrocephalus is common.

The cause of these defects are not established, but dietary supplementation with folic acid before and during pregnancy is prophylactic. An increased risk of spina bifida is associated with an utero exposure to different antiepileptic drugs (valproic acid or carbamazepine, at the first place). The mechanism by which valproic acid and carbamazepine increase the risk of spina bifida has not been established, but these drugs may affect the folate pathway, too. Folic acid deciency and antiepileptic drugs are the most common environmental risk factors that are associated with neural tube defects. Meningomyelocele is managed by preserving residual function. Early closure of the open defect is desirable.
death results from hydrocephalus, meningitis, and renal failure.

Longo and Maccani reported a case of myelomeningocele associated with trisomy 8\(^1\). Mosaic trisomy 8 has been associated with spina bifida\(^1\). Chromosomal abnormalities have been reported in 2.5-10% of fetal and newborn patients with common neural tube defects\(^30,31,32\). Chromosomal abnormalities occur in 4-17% of patients with spina bifida\(^30,31,32\). Trisomy 18 and trisomy 13 are the most common chromosomal abnormalities associated with neural tube defects, and there is a predominance of spina bifida. Trisomy 8 is also associated with neural tube defects, like in our case.

**CONCLUSION**

Taken together, we would like to stress the need for multidisciplinary assessment of children with “multiple congenital malformation-intelectual disability” syndromes (e.g. trisomy 8), including comprehensive clinical and genetic evaluation, which could provide early management of complications, timely rehabilitation, and proper genetic counselling.

The goal of this paper is to help in better understanding, counselling and management for the families that are affected with different chromosomal abnormalities.

**SUMMARY**

Uvod. Klinička slika sindroma trizomije 8 hromozoma uključuje kraniofazijalne abnormalnosti, kožne manifestacije, srčane i bubrežne malformacije, skeletne poremećaje i mentalnu retardaciju. Prikaz bolesnika. Prikazujemo slučaj spine bifide okulte kod deteta sa kompletom trizomijom 8 hromozoma. Kliničkim pregledom su otkriveni dismorfički poremećaji, naglašeni i duboki dermatoglifi na šakama i stopalima, katarka, rasecp nepca, agenezija korpusa kalozuma i spastična kvadruprezja. Uočeno je postojanje male subkutane protruzije u središnjem torakalnom delu kćeri, koja je dijagnostikovana kao lipom i koja ne komunicira sa kćerim kanalom i postojanje spine bifide okulte. Meninjogelka je isključena, kao i potreba za hiruškom intervencijom. Zaključak. Hromozomski poremećaji uključujući trizomiju 8 hromozoma se javljaju kod bolesnika sa spinom bifidom. Važno je dijagnostikovati male subkutane lezije koje ne zahtevaju hiruško lečenje, ali se moraju diferencirati od meninjogelika.

Ključne reči: trizomija 8 hromozoma; spina bifida okulta; defekti neuralne tube; neurološki poremećaji.

**REFERENCES**