

2. Palazzi DL, McClain KL, Kaplan SL. Hemophagocytic syndrome in children: An important diagnostic consideration in fever of unknown origin. *Clin Infect Dis* 2003; 36: 306-312.
3. Henter JI, Horne A, Arico M, Egeler RM, Filipovich AH, Imashuku S, *et al.* HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer* 2007; 48: 124-131.
4. Fisman DN. Hemophagocytic syndromes and infection. *Emerg Infect Dis* 2000; 6: 601-608.
5. Ramanan AV, Schneider R. Macrophage activation syndrome following initiation of etanercept in a child with systemic onset juvenile rheumatoid arthritis. *J Rheumatol* 2003; 30: 401-403.
6. Shaw PH, Brown D, Shulman ST. Tuberculosis-associated hemophagocytic syndrome in an infant. *Pediatr Infect Dis J* 2000; 19: 475-477.
7. Okascharoen C, Nuntnarumit P, Sirinavin S. Neonatal tuberculosis associated with shock, disseminated intravascular coagulation, hemophagocytic syndrome, and hypercalcemia: a case report. *J Perinatol* 2003; 23: 79-81.

Partial Trisomy 9q due to Maternal 9q/17q Translocation

SHEELA NAMPOOTHIRI
LAKSHMY R LAKSHMAN
ALKA ANILKUMAR
M V THAMPI*

ABSTRACT

Partial Trisomy 9q is a unique chromosomal anomaly with a distinctive phenotype. Only 5 cases have been reported in the literature till now. A large family with four affected children was studied in detail and was compared with the five previously reported cases. Determination of this novel balanced translocation in their family had helped us to offer prenatal diagnosis. This presentation is unique as even though partial trisomy 9q has been reported earlier with 9/17 translocations, our family is the first to have a translocation between q arms of chromosomes 9 and 17.

Key words: *Arachnodactyly, Camptodactyly, Contractures, Partial trisomy 9q.*

INTRODUCTION

Partial trisomy 9q is a distinct phenotype with severe psychomotor retardation, dolichocephaly, long fingers and toes, prominent beaked nose, deep-set eyes and camptodactyly(1,2). We present four children with this condition who are first cousins.

CASE REPORT

The proband (IV 5) was a 13 day old male baby weighing 2250 g born to a 30 year old second gravida mother by cesarean section. The parents were non consanguineous. On examination the baby had dolichocephaly, a prominent beaked nose with deep-set eyes, a small mouth, and ears with overfolded helices. The palate was narrow and high-arched. He fed poorly and had epiphora from both eyes due to associated trichiasis. He had prominent arachnodactyly. The fingers were flexed across the thumb bilaterally. He also had flexion contractures of both knees and left elbow. The limbs were extremely thin due to reduced muscle mass (dolichostenomelia). X-rays showed thin, osteoporotic long bones. He had bilateral undescended testes.

The trichiasis and flexion contractures improved gradually. At one year of age the only developmental

*From the Departments of Pediatric Genetics, and *Human Cytogenetics, Amrita Institute of Medical Sciences & Research Center, Elamakkara PO, Cochin 682 026, Kerala, India.*

Correspondence to: Dr. Sheela Nampoothiri, Department of Pediatric Genetics, Amrita Institute of Medical Sciences and Research Center, Elamakkara PO, Cochin 682 026, Kerala, India.

E mail: sheelaknpn@yahoo.co.in

Manuscript received: August 28, 2007;

Initial review completed: September 21, 2007;

Revision accepted: January 24, 2008.

milestones acquired were social smile and stranger anxiety. He had severe hypotonia and total head flop. CT scan showed ventriculomegaly; EEG was normal. At four years he weighed only 9 kg and was only able to crawl but had not acquired any language skills. The child died due to bronchopneumonia at the age of 4½ years.

The elder sibling (IV 4) also has global developmental delay and seizures. He too has long fingers and toes and flexion contractures of knees and elbows since birth, which improved with time. He cannot flex the index fingers bilaterally. He has associated microcephaly (48 cm) and a prominent fleshy nose. The mother's brother's daughter (IV 6) also has a similar phenotype with long fleshy nose, long fingers and toes, microcephaly, global developmental delay, bilateral low set flared pinna with bilateral alternating divergent squint (**Fig. 1**). The mother's sister (III 10) has a male child (IV 10) with the same phenotype, and additionally he has cleft palate, camptodactyly of the 2nd, 3rd, and 5th fingers on left side, contracture of both knees and right elbow joint, right inguinal hernia, right divergent squint and overfolded pinna on the left side. He had a birth weight of 2500 g, but at 3 months he weighed only 3 kg. Head circumference was 38 cm at 3 months of age.

Peripheral blood samples were obtained from the proband (IV 5) and subsequently from his mother (III 4), III 6, III 8 and III 10 and II 6 (**Fig. 2**). Metaphase chromosomes were analyzed by standard trypsin-giemsa (GTG) banding. Chromosome analysis of the proband's (IV 5) lymphocytes showed a derivative chromosome 17. Subsequently, a balanced translocation was demonstrated in the mother's lymphocytes (III 4) between chromosome 9q and 17q. The break points were 9q34 and 17q25. Thus, the maternal karyotype (III 4) was determined as 46,XX, t(9; 17) (q34; q25). Consequently, the proband's (IV 5) chromosomal imbalance was interpreted as partial trisomy 9q34@qter and monosomy for region 17q25@qter (46,XY,der (17)t(9;17)(q34;q25) and the same unbalanced chromosomal anomaly were noted in IV 4, IV 6, IV 10. III 6, III 8 and III 10 who were siblings and parents of these children with unbalanced karyotype showed a balanced translocation, 46,XX,t(9;17)



FIG. 1. IV 6 with beaked nose, flared pinna and strabismus.

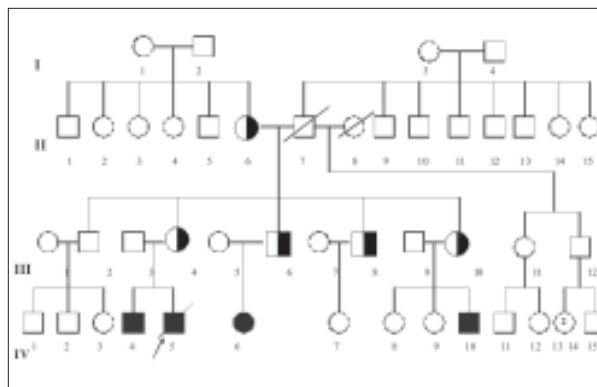


FIG. 2. Pedigree showing proband (IV5), IV 4, IV 6 and IV 10 with partial trisomy 9q. III4, III6, III 8, III 10 and II 6 are balanced translocation carriers.

(q34;q25) as III 4 (**Fig. 3**). Cytogenetic studies revealed that the translocation was inherited from the maternal grandmother (II 6).

DISCUSSION

Partial trisomy 9q is rare; and only 5 cases are reported till date. Chromosomal analysis of the proband and three other children with similar

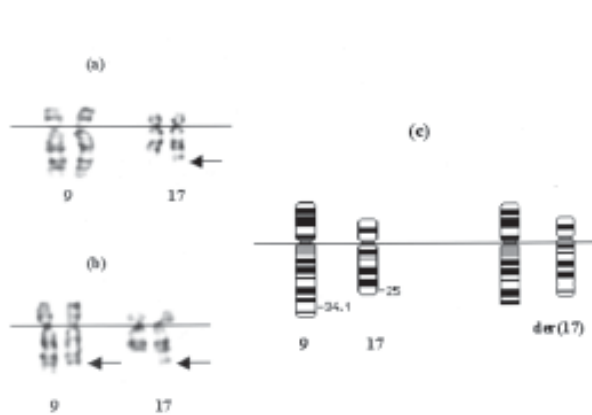


FIG. 3. (a) Partial karyotype of the boy with partial trisomy 9q34 showing normal chromosomes 9, 17 and a derivative chromosome 17 (arrow); (b) partial karyotype of the mother with balanced $t(9;17)(q34.1;q25)$ showing normal and derivative (arrows) chromosomes 9 and 17; (c) Ideogram of $t(9;17)(q34.1;q25)$.

phenotype showed that all four of them have partial trisomy 9q and had inherited this unbalanced chromosome from their respective parents who were siblings and were carriers of a balanced $t(9;17)(q34;q25)$ (III 4, III 6, III 10). The break point in our family was in q 34 and q25 in chromosomes 9 and 17 respectively. If the translocated segments were very small in genetic content, the resulting unbalanced gametes would lead to viable pregnancies leading to children with malformation and would not end up in miscarriages. On the contrary if the translocated segments are very big, the unbalanced gametes cannot be viable and this would lead to spontaneous abortions. In our case the translocated segments in 9q and 17 q were very small and hence it had led to birth of children with partial trisomy 9q. Even though five cases of partial trisomy 9q have been reported earlier, this is the first case where there was a balanced translocation between q arms of chromosome 9 and 17(1).

The sibling (III 8) who was also found to be a carrier of this translocation. All these four siblings had inherited the translocation from their mother (II 6). This information helped III 8 to opt for prenatal diagnosis and karyotyping was performed in the amniotic fluid at 16 weeks. The fetus had a normal karyotype and they later had a normal female baby.

Partial trisomy 9q usually result from unbalanced meiotic segregation of parental balanced translocation involving chromosome 9 and an autosome(1,3-5). Duplication of 9q segment due to balanced rearrangement as an inverted insertion of 9q 34.3 segment in q arm of chromosome 9 has been reported to produce the phenotype of partial trisomy 9q(6). *De novo* tandem duplication of 9q 22.2-q 31.1 has also shown to produce a phenotype consistent with partial trisomy 9q(7). It is highly pertinent to do a meticulous search for the trisomic segment in a patient with compatible features of partial trisomy 9q as the trisomic segment can be very small which is corresponding to the segment q 31-32(8).

The main differential diagnoses of partial trisomy 9q include congenital contractural arachnodactyly (CCA) and Marfan syndrome. In partial trisomy 9q, patients do not have the characteristic cardiac anomalies and upward dislocation of the lens, which are the hallmarks of Marfan syndrome, and they also lack the “crumpled pinna” which is typical of CCA(9,10). Marfan syndrome and CCA are autosomal dominant conditions and these conditions can be diagnosed by prenatal molecular studies. This case highlights the importance of detailed pedigree analysis while encountering patients with unbalanced chromosomal anomalies.

Contributors: SN diagnosed the condition, evaluated the family tree and has picked up other affected members and drafted the article. She will act as the guarantor of the manuscript. LRL helped in the clinical evaluation of the family. MVT performed the cytogenetic analysis for the confirmation of the diagnosis and helped in the drafting of the manuscript. AA was involved with MVT for the cytogenetic analysis.

Funding: None.

Competing interests: None stated.

REFERENCES

1. Aftimos SF, Hoo JJ, Parslow MI. Partial trisomy 9q due to maternal 9/17 translocation. *Am J Dis Child* 1980; 134: 848-850.
2. Subrt I, Janovsky M, Jodl J. Partial trisomy 9q-chromosomal syndrome. *Hum Genet* 1976; 34: 151-154.

CASE REPORTS

3. Soltan HC, Jung JH, Pyatt Z, Singh RP. Partial trisomy 9q resulting from a familial translocation t (9:16) (q32;q24). *Clin Genet* 1984; 25: 449-454.
4. Penehaszadeh VB, Coco R. Partial 9 trisomy by 3:1 segregation of balanced maternal translocation (7q+; 9q-). *J Med Genet* 1975; 12: 301-305.
5. Ten SK, Chin YM, Tan SK, Hassan K. Three cases of partial trisomy 9q in one generation due to maternal reciprocal t (6;8;9) translocation. *Clin Genet* 1987; 31: 359-365.
6. Allderdice PW, Eales B, Onyett H, Sprague W, Henderson K, Lefeuvre PA, *et al.* Duplication 9q34 Syndrome. *Am J Hum Genet* 1983; 35: 1005-1019.
7. Utine GE, Melotte C, Vermeesch JR, Fryns JP. Partial trisomy 9q syndrome with a de novo tandem duplication of 9q22.2-q31.1. *Genet Couns* 2005; 16: 407-412.
8. Turleau C, de Grouchy J, Chavin-Colin F, Roubin M, Brissaud PE, Repessé G, *et al.* Partial trisomy 9q: a new syndrome. *Hum Genet* 1975; 29: 233-241.
9. Ramos Arroyo MA, Weaver DD, Beals RK. Congenital contractural arachnodactyly. Report of four additional families and review of literature. *Clin Genet* 1985; 27: 570-581.
10. DePaepe A, Devereux RB, Dietz HC, Hennekam RC, Pyeritz RE. Revised diagnostic criteria for the Marfan syndrome. *Am J Med Genet* 1996; 62: 417-426.

Cerebral Salt Wasting Syndrome Following Neurosurgical Intervention in Tuberculous Meningitis

L NAGOTKAR
P SHANBAG
N DASARWAR

ABSTRACT

Cerebral salt wasting is characterized by inappropriate natriuresis and volume contraction in the presence of cerebral pathology. Diagnosis can be difficult and therapy is challenging. We report two children with tuberculous meningitis and hydrocephalus who developed cerebral salt wasting following neurosurgical intervention. The first patient was managed with rigorous salt and water replacement whereas the second patient required the addition of fludrocortisone for control of salt-wasting.

Key words: Cerebral salt wasting; Hydrocephalus; Tuberculous meningitis.

INTRODUCTION

Hyponatremia frequently develops in patients with a variety of acute central nervous system diseases. Two pathophysiological mechanisms have been

suggested to cause non-iatrogenic hyponatremia: cerebral salt wasting syndrome (CSWS) and the syndrome of inappropriate secretion of antidiuretic hormone (SIADH)(1-4).

Considering the divergent nature of treatment and the potential adverse effects of improper fluid therapy, it is important for the treating clinician to be able to differentiate between SIADH and CSWS, since therapy of SIADH is fluid restriction whereas in CSWS, rigorous salt and volume replacement are necessary. We describe two patients with tuberculous meningitis and hydrocephalus who developed cerebral salt wasting syndrome following neurosurgical intervention.

CASE REPORT

Case 1: A 4-year-old boy was transferred to the Pediatric Intensive Care Unit (PICU) following

From the Pediatric Intensive Care Unit, Lokmanya Tilak Municipal Medical College & General Hospital, Sion, Mumbai 400 022, India.

Correspondence to: Dr Leena Nagotkar, 9458/242, Kannamwarnagar 2, Vikhroli(E), Mumbai 400 083, India. E-mail: nagotkar.leena@gmail.com.

Manuscript received: August 6, 2007;

Initial review completed: August 29, 2007;

Revision accepted: January 28, 2008.