Brief Clinical Report: Trisomy 18 and Hepatic Neoplasia

Majed Dasouki and Mason Barr, Jr.

Division of Pediatric Genetics, Department of Pediatrics and Communicable Diseases (M.D., M.B.), University of Michigan, Ann Arbor, Michigan

A 2 9/12-year-old girl with trisomy 18 presented with a 3-week history of low grade fever, abdominal distention, and hepatosplenomegaly. Abdominal cytometry (CT) scan showed hepatic infiltration with a tumor mass presumed to be hepatoblastoma. She deteriorated rapidly and died 3 weeks later. No autopsy and/or biopsy could be done.

Key words: trisomy 18, hepatic tumor, multiple congenital anomalies/mental retardation (MCA/MR) syndrome

INTRODUCTION

Trisomy 18 is a well-recognized aneuploidy syndrome with reduced survival. About 30% of newborns with this condition die before the age of 1 month, while 90% die during the first year of life [Gorlin, 1977]. Survival of one affected individual for 15 years has been reported [Hook et al, 1965]. Malignancy is rarely described in trisomy 18. Only two patients with Wilms’ tumor [Geiser and Schindler, 1969; Karayalcin et al, 1981] and one with neurogenic tumor [Robinson and McQuorquodale, 1981] have been reported. Anderson et al [1977] reported a papillary tumor of the tricuspid valve in a 6-day-old infant with trisomy 18. Histologically there was no evidence of malignancy.

Hepatoblastoma is the most frequent malignant hepatic tumor in the pediatric population, presenting usually during the first 3 years of life as an abdominal mass [Exelby et al, 1975]. Major and minor congenital anomalies have been recognized in patients with hepatoblastoma [Fraumeni et al, 1968; Kobayashi et al, 1968] which ranks second to Wilms’ tumor in the prevalence of associated congenital anomalies. Here we describe a patient with trisomy 18 and hepatic tumor presumed to be hepatoblastoma.
CLINICAL REPORT

This patient was born to a 32-year-old, primigravid white woman at 42 weeks gestation with evidence of intrauterine growth retardation detected by prenatal ultrasoundography. Delivery was by cesarean section for breech presentation. Birth weight was 1,860 g (< 5th centile). Congenital anomalies included: microcephaly, wide anterior fontanel, hypoplastic orbital ridges, small palpebral fissures, depressed nasal bridge, anteverted nares, posteriorly rotated ears, micrognathia, and left sided torticollis. Her nipples were widely spaced. Cardiac anomalies were membranous VSD, thickened right ventricle, and pulmonary hypertension. Limb anomalies included broad clenched hands, simian creases, proximal thumbs, subluxable hips, genu recurvatum, left calcaneovalgus foot, and bilateral syndactyly of the second and third toes. She also had pseudoarthrosis of the right clavicle, partial hemivertebra (T11), reduced disc space between C5 and C6, and thoracolumbar scoliosis. Both cranial and renal ultrasounds were normal. Chromosomes showed trisomy 18 (47,XX,+18).

At age 2 9/12 years she presented with a 3-week history of low-grade fever, abdominal distension, and hepatosplenomegaly. Her hemoglobin was 9.8 g/dl, hematocrit 30%, WBC 18500/μl with 82% neutrophils. The liver enzymes, SGOT and LDH, were elevated (183, 692 IU/l, respectively). Serum alphafetoprotein was not measured. Abdominal CT scan with contrast showed a large cystic tumor infiltrating nearly all the liver (Fig. 1) and questionable pulmonary metastasis. No calcifications or renal or adrenal anomalies were seen. Her condition rapidly deteriorated and she died 3 weeks later. Permission for autopsy and/or biopsy was refused.

DISCUSSION

In addition to hepatoblastoma, the differential diagnosis of childhood hepatic tumors includes: hepatocellular carcinoma, hemangioendothelioma, mesenchymal hamartoma, and metastatic neuroblastoma [Amendola et al, 1984]. These conditions can be distinguished by clinical data, serum alphafetoprotein, abdominal CT scan, and histological examination. Hepatoblastoma is malignant with a high mortality and tendency to metastasize to the lungs [Exelby et al, 1975]. On abdominal CT scan, it has lower attenuation than normal liver which is accentuated by injection of urographic contrast medium. Also, calcifications may be seen in about 50% of those scans. The CT scan appearance (Fig. 1) and clinical course in our patient are most suggestive of hepatoblastoma rather than of other tumor types found in this age group.

Kobayashi et al [1968] found that 45% of hepatoblastoma patients had congenital anomalies while 58% of Wilms’ tumor patients had major congenital anomalies. Among 76 children with primary hepatic tumors, Fraumeni et al [1968] found 7 children with hepatoblastoma. Four had major anomalies; one child had hemihypertrophy and genitourinary abnormalities, two children had renal anomalies, and a fourth had an absent right adrenal gland. Renal abnormalities that were reported included glomerular and tubular changes, early polycystic changes, and duplication of the collecting system. In our patient there was no hemihypertrophy or macroglossia and neither renal nor adrenal abnormality was seen on CT scan. Hemihypertrophy and genitourinary malformations were the most common anomalies seen in a survey of 547 patients with Wilms’ tumor [Pendergrass, 1976]. Although Wilms’ tumor and hepatoblastoma have embryologically different origins, some similarity in the type of congenital anomalies associated with each is seen, and we find that both can be seen in trisomy 18. It is possible that trisomy 18 may have an oncogenic effect (direct or
Trisomy 18

Fig. 1. Abdominal CT scan with contrast showing a large cystic tumor is infiltrating the liver. No calcifications are seen.

indirect) on both mesenchymal and endodermal cells in addition to the teratogenic effect [Kobayashi et al., 1968; Bolande, 1977]. The nature of this relationship needs to be examined as more cases of malignancy with trisomy 18 are seen. Also, direct cytogenetic analysis of tumors in such patients is recommended.

REFERENCES


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