Journal of Korean Medical Science
Vol. 8, No. 6, 471-475 December 1993

Jarcho-Levin Syndrome

— A report of an autopsy case with cytogenetic analysis —

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Jarcho-Levin syndrome (JLS) is a condition manifested by malformations of vertebral bodes and related ribs. There are two major subtypes spondylocostal dysostosis and spondylothoracic dysostosis, with different survival rates, associated malformations, and inheritance patterns.
We have experienced an autopsy case of a premature female fetus with multiple congenital anomalies. She was 30 weeks of gestational age, born as the second baby of twins and expired shortly after birth. A postmortem examination revealed multiple abnormalities including cervicothoracic hemivertebrae, a diminished number of right-sided ribs, and pulmonary hypoplasia with left diaphragmatic hernia.
In addition, there were anomalous rotation of the foregut, unfused pancreas and anomalous drainage of the superior vena cava. Chromosomal analysis showed 46, XX, del(4)(q ter).

Key Words: *Jarcho-Levin syndrome, Hemivertebrae, Chromosomal analysis*

INTRODUCTION

In 1938, Jarcho and Levin described two siblings with short trunks due to vertebral body and rib malformations. Similar cases have been described under a variety of names including Jarcho-Levin syndrome, spondylocostal dysostosis (SCD) or spondylothoracic dysostosis (STD), and costovertebral dysplasia. Many cases have been familial with variable inheritance patterns, apparently autosomal recessive or autosomal dominant (Rimoin et al.,1968; Moseley et al.,1969; Cantù et al.,1971; Franceschini et al.,1974; Solomon et al.,1978). Associated anomalies and clinical severity are also diverse.

We report an autopsy case of Jarcho-Levin syndrome associated with multiple congenital anomalies as well as chromosomal abnormality.

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CASE REPORT

A female infant was born as the second baby of twins at the 30th week of gestational age after an uneventful pregnancy. Her mother was 27 years old and had been healthy during the pregnancy. Apgar score was zero at one minute. after birth Despite neonatal intensive care, respiratory function was not recovered and the baby died at 4 hours after birth.

On autopsy, she weighed 1300 g, with a length of 35cm, a head circumference of 17cm, a thoracic circumference of 23.8cm and abdominal circumference of 19.8cm. Physical examination revealed a broad forehead and redundant occipital scalp, and low set ears. The neck was short. The thoracic cage was short and the left shoulder girdle was depressed. The digits of the left hand were long. Bilateral simian creases were also present. A single umbilical artery was present.

On infantogram, hemivertebrae were found in the 6th and the 7th cervical spine, and from the 1st to the 5th thoracic spine. Spina bifida were present from the 1st through the 5th cervical vertebra. The right upper five ribs were absent, howev-

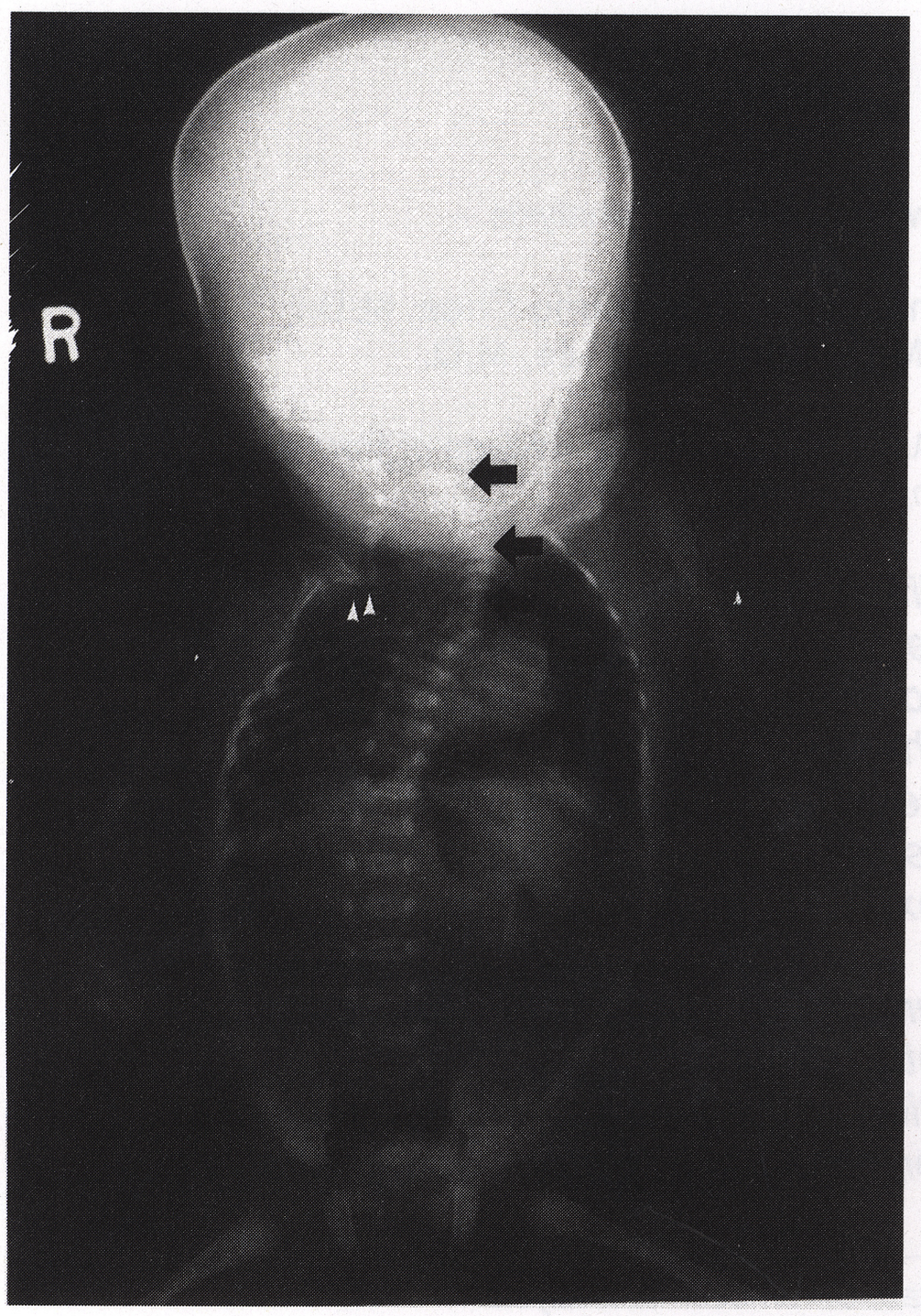

Fig. 1. Radiograph shows cervico-thoacic hemivertebrae (arrow) with spina bifida and absence of right upper five ribs (arrow head). There is a right-convex scoliosis.

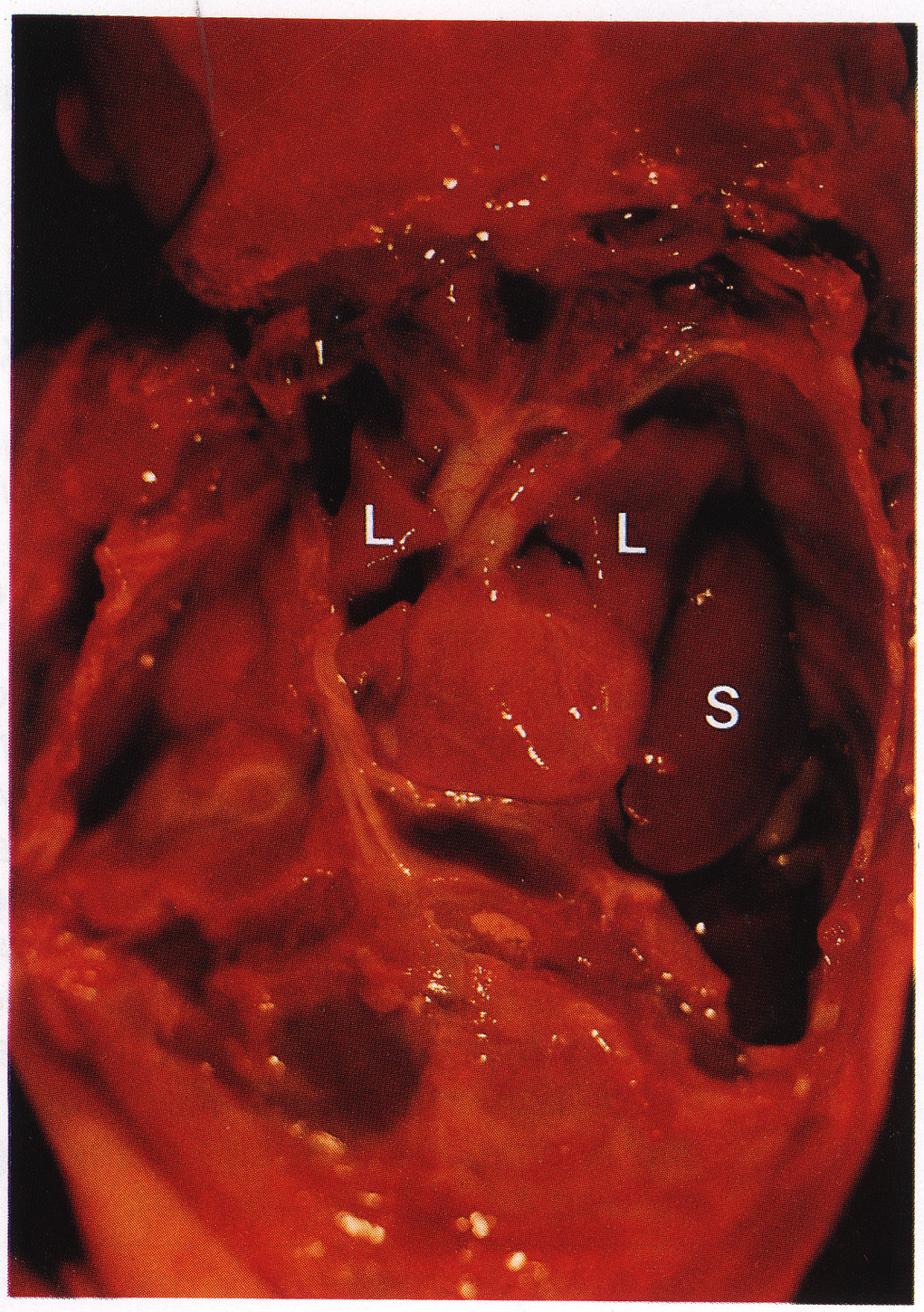

Fig. 2. Note left diaphragmatic hernia and bilateral hypoplastic lung (L). Abdominal organs including the spleen (S), the stomach and the intestine are seen in the thoracic cavity.

er, the left ribs were normal. There was a right-convex scoliosis (Fig. 1).

On opening of the thoracic cage, left diaphragmatic hernia was noted. In the left thoracic cavity, there were abdominal organs including the spleen, the stomach, and the small imtestine (Fig. 2.). The bilateral lungs were hypoplastic and incompletely lobated; right, two lobes and left, one lobe. Moreover, there was a superior vena cava traversing anterior to the right lung (Fig. 3). The foregut was anomalously rotated. The duodenum arose from the proximal portion of the stomach and the esophagus was very short and stenotic. The pancreas was unfused and attached to the stomach (Fig. 4). Meckel's diverticulum was also present.

Over 30 metaphases of peripheral blood lymphocytes were analysed. The terminal deletion of the long arm of chromosome 4 (46, XX, del(4)(q ter) was seen (Fig. 5).

DISCUSSION

The major congenital anomaly of Jacho-Levin syndrome (JLS) is vertebral malformation. Associated anomalies as well as inheritance pattern, clinical manifestation and severity are variable. Therefore, several attempts have been made to classify JLS on the basis of the anomalies and clinical manifestations.

In 1968, Rimoin et al. suggested the term "spondylocostal dysplasia" for this syndrome and proposed two types according to inheritance pattern and severity: Type I includes cases with an autosomal recessive inheritance and early death, and type II is inherited as an autosomal dominant pattern with less severe involvement and a better life expectancy. Solomon et al. (1978) classified cases of this syndrome into two groups, SCD and STD, based on the presence or absence of rib malformations. Individuals with SCD had vertebral anomalies, intrinsic rib malformation (broadening,

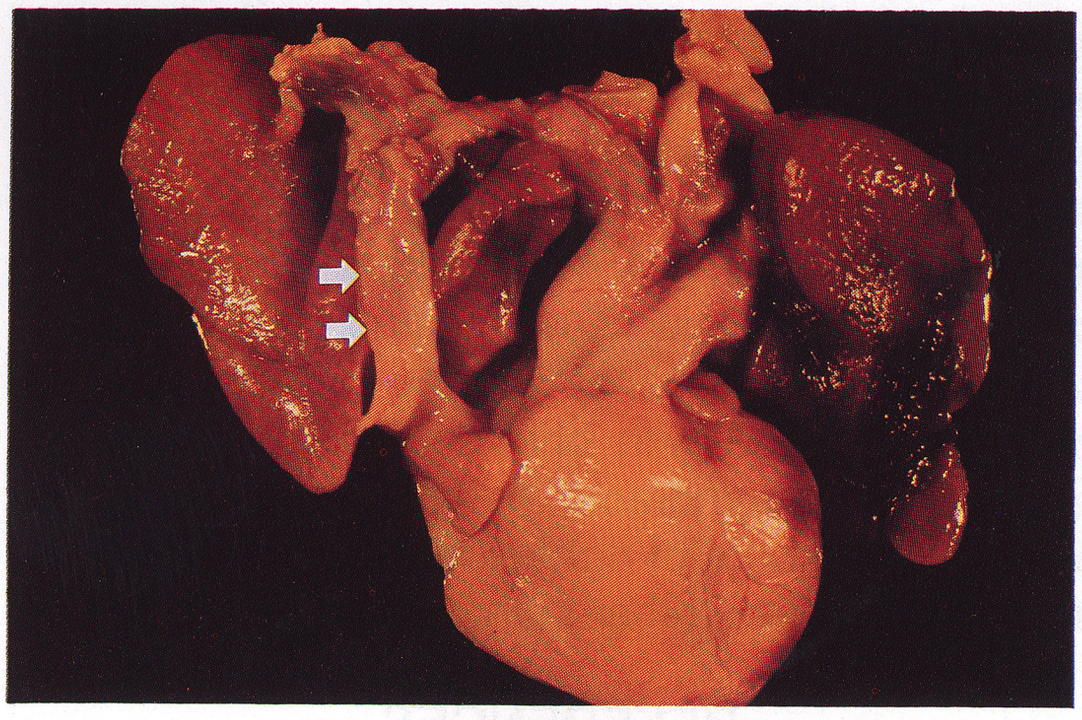

Fig. 3. Fixed en bloc section of cardiopulmonary organs; note bilateral hypoplastic lungs with indistinct lobations and superior vena cava traversing anterior to the right lung (arrow).

bifurcation, abnormal orientation, and fusion), and flaring of iliac bones. Cases with STD had vertebral anomalies and a "fanlike" rib configuration but no intrinsic rib malformation. In 1986, Aymé and preus indicated the existence of three phenotypic groups. The first group comprises those with autosomal recessive inheritance, severe thoracic lordosis, early respiratory failure and death within the first few months of life. The second group includes cases with mild clinical features of autosomal recessive transmission and those cases with an autosomal dominant mode of inheritance. The third group consists of those patients with the clinical features corresponding to the COVESDEM syn-

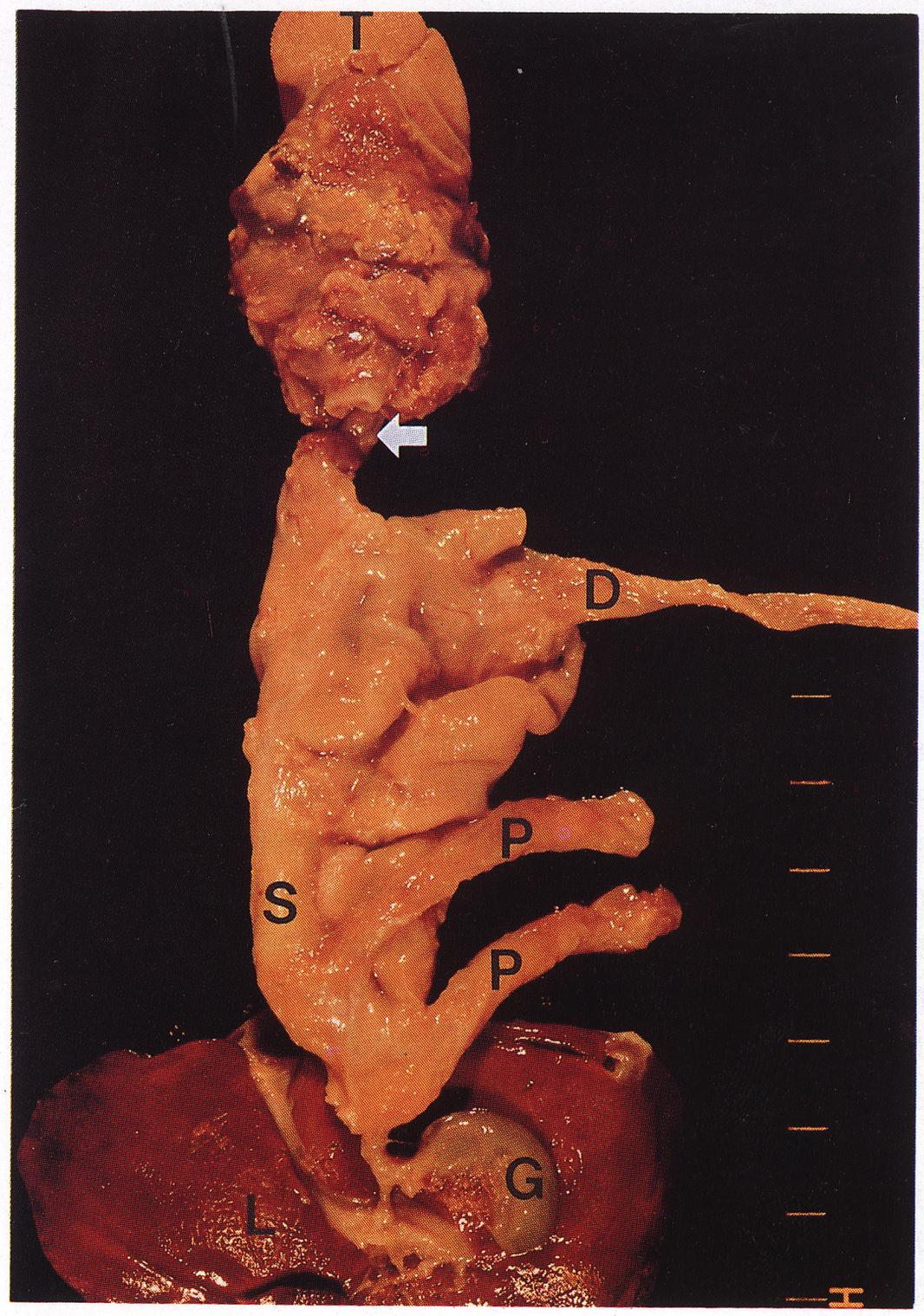

Fig. 4. The esophagus is very short and stenotic (arrow). The stomach displays indistinct greater and lesser curvature. The duodenum arises from the proximal portion of the stomach. The unfused pancreas is attached to the distal portion of the stomach. Bile drains directly to the stomach. The liver shows equal sized right and left lobe. T; tongue, S; stomach, D; duodenum, P; pancreas, L; liver, G; gallbladder.

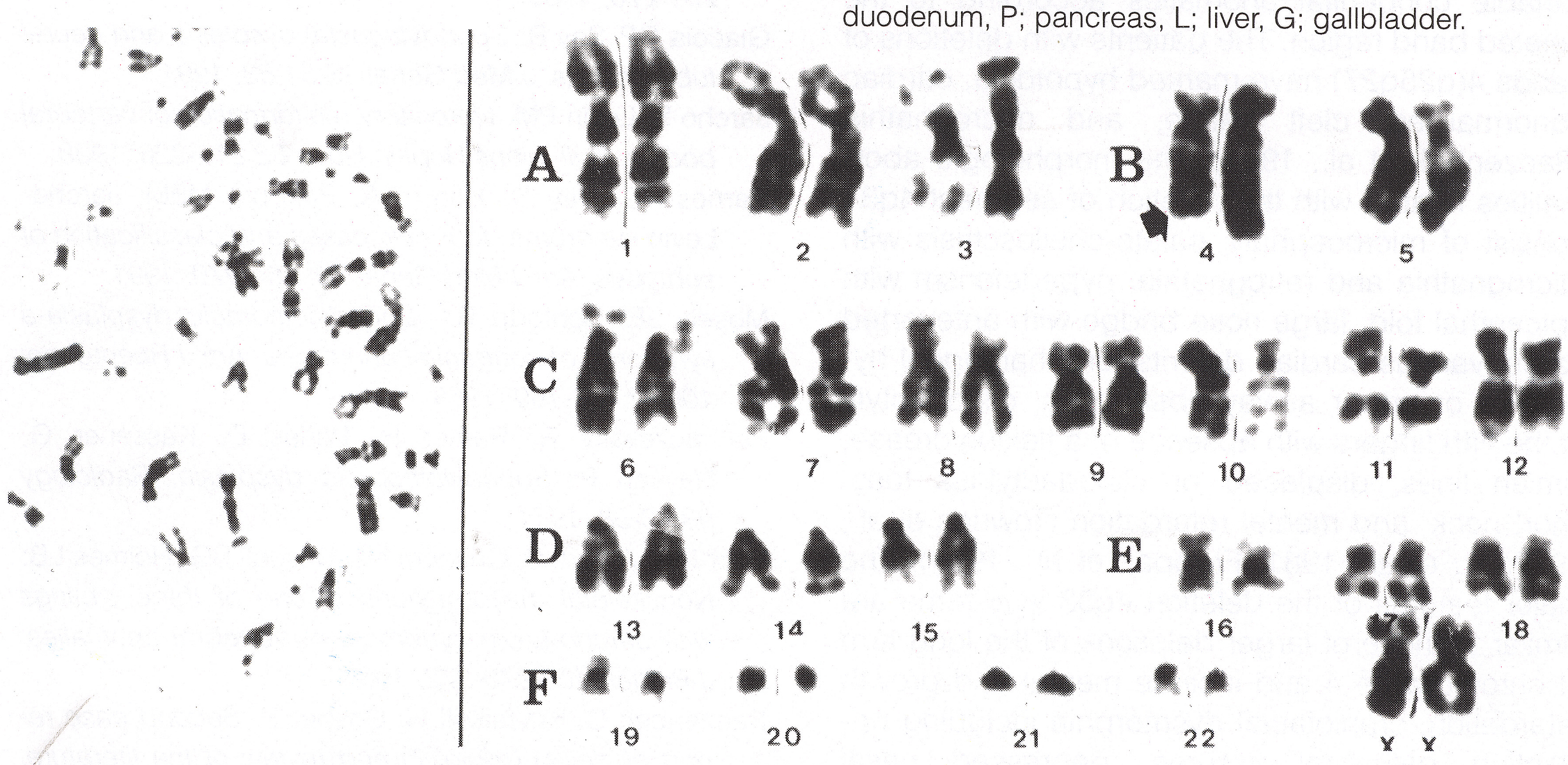

Fig. 5. Chromosomal idiogram shows terminal deletion of the long arm of chromosome 4 (arrow).

drome which includes multiple costo-vertebral defects, mesomelia, peculiar faces and short upper limbs. The life expectancy is normal and it is transmitted through an autosomal recessive pattern. In 1991, Karnes et al. suggested that individuals with vertebral and rib malformations with absence of fanlike chest configurations are more often short-statured, have almost double the survival rate, are less likely to have neural tube defects (spina bifida), and may inherit the disorder in autosomal recessive or autosomal dominant pattern. Individuals with a fanlike rib configuration and posterior tethering characteristic of STD have a higher mortality rate and a higher incidence of neural tube defects, and inherit the disorder in an autosomal recessive manner. This autopsy case had hemivertebrae and absence of ribs. In addition, spina bifida and other congenital anomalies of internal organs as well as chromosomal abnormality are also associated. This case has a broad spectrum of anomalies as in SCD and the high mortality rate of STD.

No case of Jarcho-Levin syndrome in which cytogenetic analysis has been done has shown any chromosomal abnormality (Rimoin et al.,1968; Moseley et al.,1969; Pochaczevsky et al.,1971; Franceschini et al.,1974; Casamassima et al., 1981; Poor et al., 1983; Young et al.,1983; Aymé et al.,1986; Romero et al.,1988; Giacoia et al.,1991; Karnes et al 1991). However this case revealed 46, XX, del(4)(q ter). The patients with a terminal deletion of the long arm of chromosome 4 have variable congenital anomalies according to the deleted band region. The patients with deletions of bands 4(q25q27) have marked hypotonia, cardiac abnormalities, cleft palate, and micrognathia (Raczenbek et al., 1991). The morphologic abormalities related with the deletion of segment 4q31 consist of microcephaly, palato-cheiloschisis with micrognathia and retrognathia, hypertelorism with epicanthal fold, large nose bridge with anteverted nares, various cardiac defects, oropharyngeal hypotonia or upper airway obstruction, clinodactyly of the fifth fingers with absence of a flexion crease, simian lines, displaced or clinodactylous toes, short neck, and mental retardation (Townes et al., 1979; Yu et al., 1981; Frappaz et al., 1983). The major features of the deletion 4q33 syndrome are similar to those of larger deletions of the long arm of chromosome 4 and include mental and growth retardation, craniofacial dysmorphia including upslanting palpebral fissures, depressed nasal bridge, anteverted nares, abnormally shaped ears and cardiac defects (Tomkins et al., 1982). However, the characteristic vertebral and rib anomalies of Jarcho-Levin syndrome are not associated with these syndromes of terminal deletion of the long arm of chromosome 4. With autopsy findings and cytogenetic analysis, it is assumed that multiple congenital anomalies of internal organs may be partly associated with chromosomal abnormality, however cervicothoracic hemivertebrae with diminished numbers of right-sided ribs are developmental anomalies rather than genetic defects.

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