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Larsen's Syndrome*

(Report of a case with additional findings of urinary tract malformation)

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Larsen and his colleagues described six patients with multiple joint dislocations and a characteristc facial appearance in 1950, drawing attention to the possibility that this combination might represent a new syndrome.[1] All these were unrelated sporadic cases and shared the common findings of hypertelorism, a prominent forehead and a flattened nose, bilateral dislocations in the elbow, hip and knee joints and either equino-varus or equino-valgus deformity of the feet.

The limited number of reported cases in the literature of this skeletal dysplasia which has come to be known as Larsen's syndrome would suggest its rare occurrence. However, there is little doubt that some of these patients go unrecognized or are branded under various other disease entities. A review of the reported cases shows that in addition to the typical facial appearance and the joint dislocations of this entity, a few patients had another organ malformation as well. One patient had probable hydrocephalus while another one had congenital cataract andan undescended testis on one side.[2] In this paper we are going to present a case with postmortem examination and we are going to describe the major and minor malformations encountered outside the bones and joints.

Case Report: (M. T. Hosp. No. 253844) This 3 day old male infant was hospitalized on the 5th of May, 1971 because of deformities in his legs. His 23 year-old mother and 29 year-old father were not related. The infant was delivered in a normal way following a full term and uneventful pregnancy. A three and a half year-old female

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sibling was alive and healthy. Another sibling with no obvious skeletal anomalies had died of meningitis at 4 months. On admission the patient weighed 2700 gms. and had a height of 51 cms. The head circumference was 32.5 cms. and the chest circumference was 33 cms. Apart from experiencing slight hypoactivity, the baby appeared to be in good general condition. The scleras were icteric. The anterior fontanel appeared normal to palpation and its opening measured 4x4 cms. Hypertelorism, depression at the base of the nose, micrognatiha and small cystic structures over the upper lip were present. The high arched palate failed to disclose any defects on inspection. The shoulders appeared relatively wide in contrast to the narrow appearing chest. There was a medial angulation deformity of the distal phalanx of the fifth left finger. The lower extremities showed the presence of bilateral genu valgum, and pes varus deformities (Fig. 1). Sucking, moro and grasping reflexes were rather hypoactive, otherwise the physical examination showed no other abnormality.

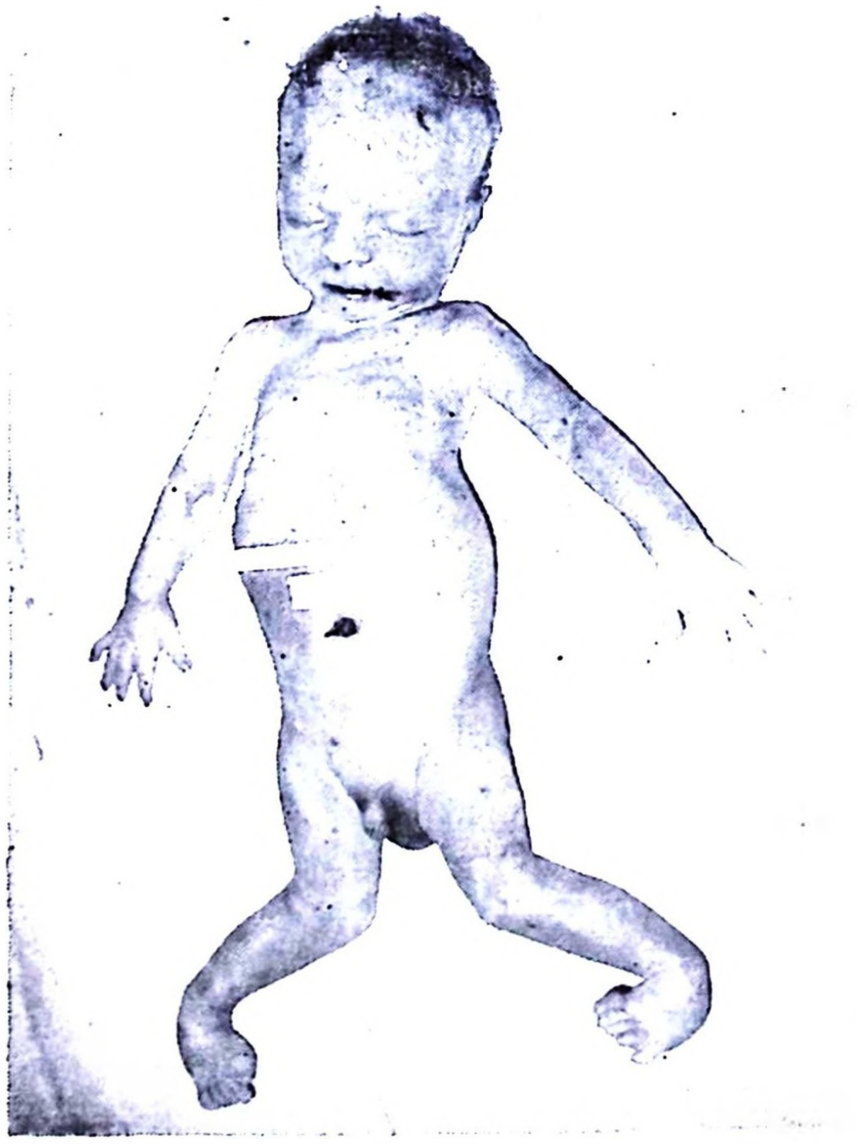

Figure 1

Laboratory Findings: These included a Hb. value of 23.4 gms 100 ml, white blood count of 15600 / mm3 with the peripheral blood smear showing dominance of segmented white cells, normal thrombocytes and normochrome normocytic red cells.

SGOT was 240 units, SGPT, 32 units and total bilirubin was 8.9 mgs / 100 ml. (1.2 mgs. direct bilirubin.)

Radiological examination of the patient showed bilateral dislocation of the hip joints. There was again bilateral dislocation of the proximal tibiae which were laterally displaced away from the distal femora. The feet showed varus deformity on both sides (Fig. 2). There was no frank dislocation at the upper extermities although the proximal humeri appeared rather hypoplastic. Radiograms of the skull revealed the micrognathia to be resulting from the hypoplasia of the mandibular rami and showed the presence of a midline cleft of the hard palate (Fig. 3). Slight hypertelorism was again noted. The vertebrae were seen to be normal.

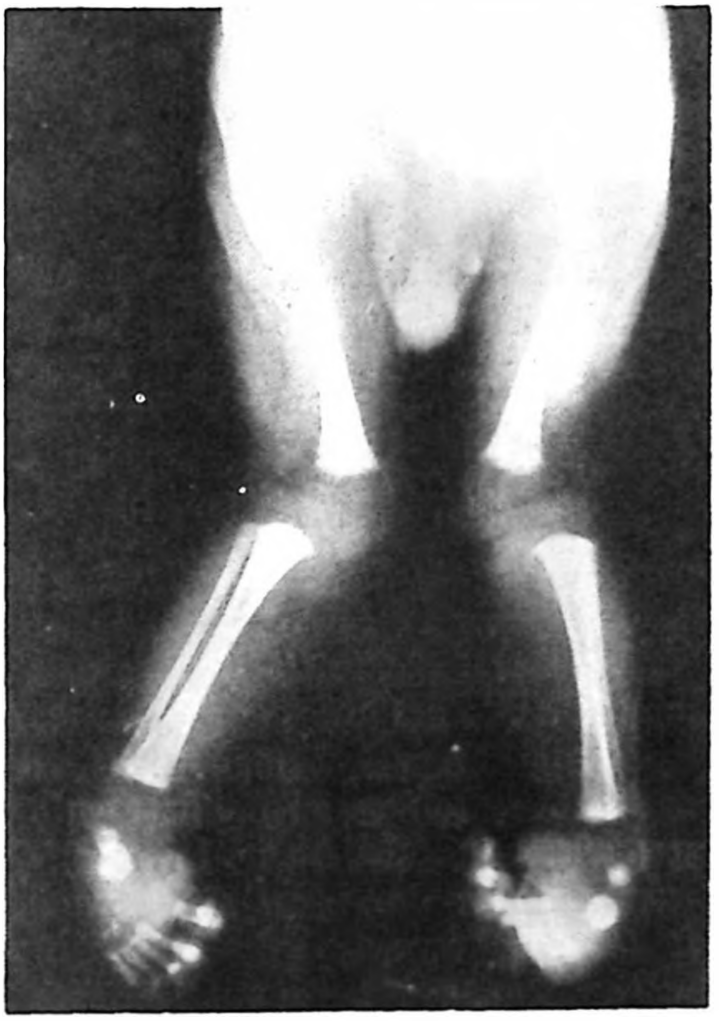

Figure 2

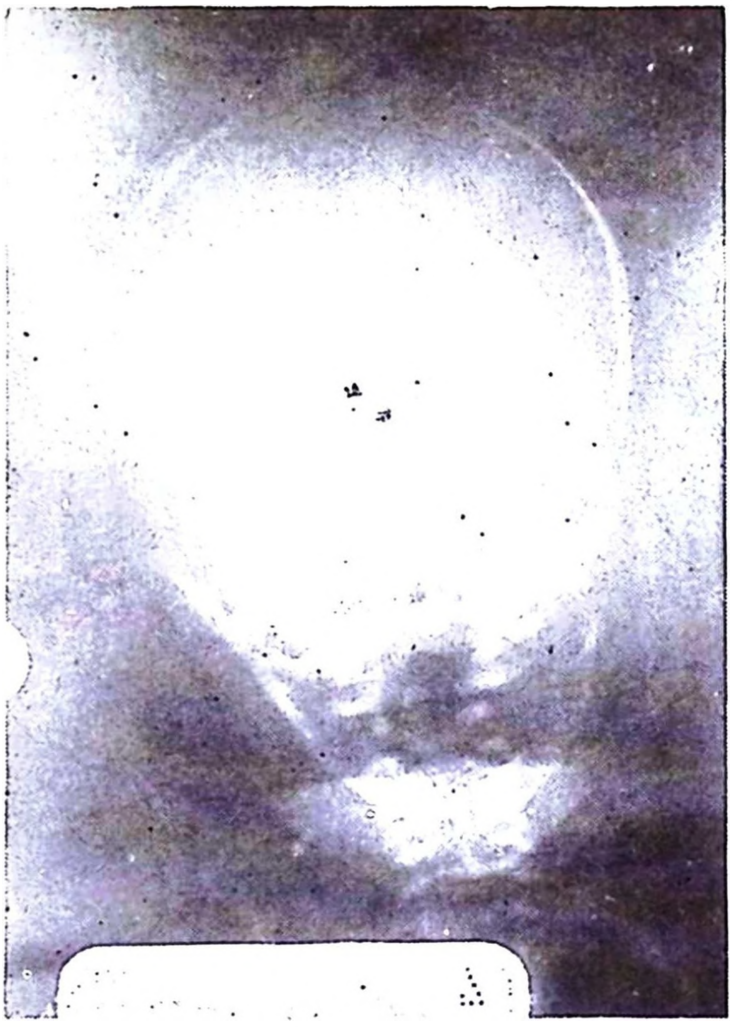

Figure 3

The infant's general condition deteriorated rapidly during the short period he remained in the hospital. His icterus increased, and petechiae developed over the abdomen and the posterior chest wall. The patient became cyanotic and died on the fourth day following admission to the hospital. A complete postmortem examination was performed.

In the postmortem examination, the following macroscopic and microscopic findings were noted in addition to the above-described typical facial appearance and skeletal malformations: The lungs showed evidence of intrauterine as well as postnatal aspiration pneumonia and bacterial necrotising bronchopheumonia. There were multiple extra fissures over the lower surface of the liver with the gall-bladder appearing almost totally embedded in the liver which showed active and passive congestion. There was bilateral hydrocele with the testes having completely descended into the scrotal sacs. The central nervous system revealed edema and subarachnioid hemorrhage. The spleen showed findings encountered in the presence of sepsis. Microscopic

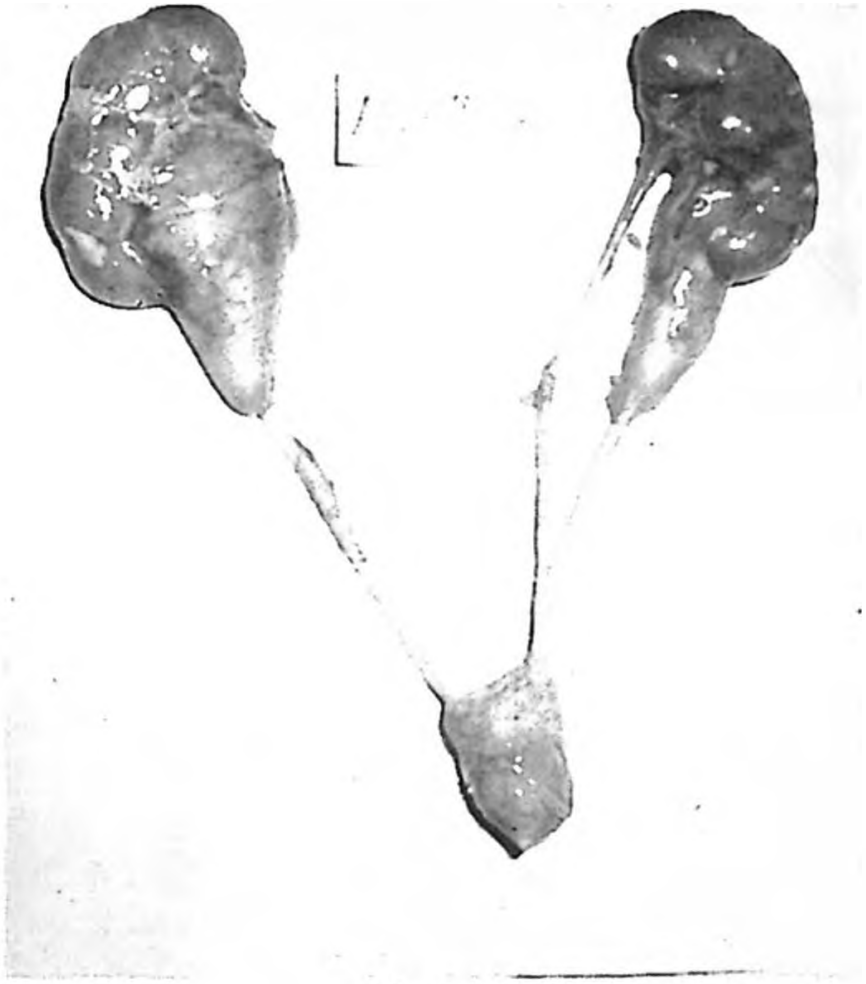

Figure 4

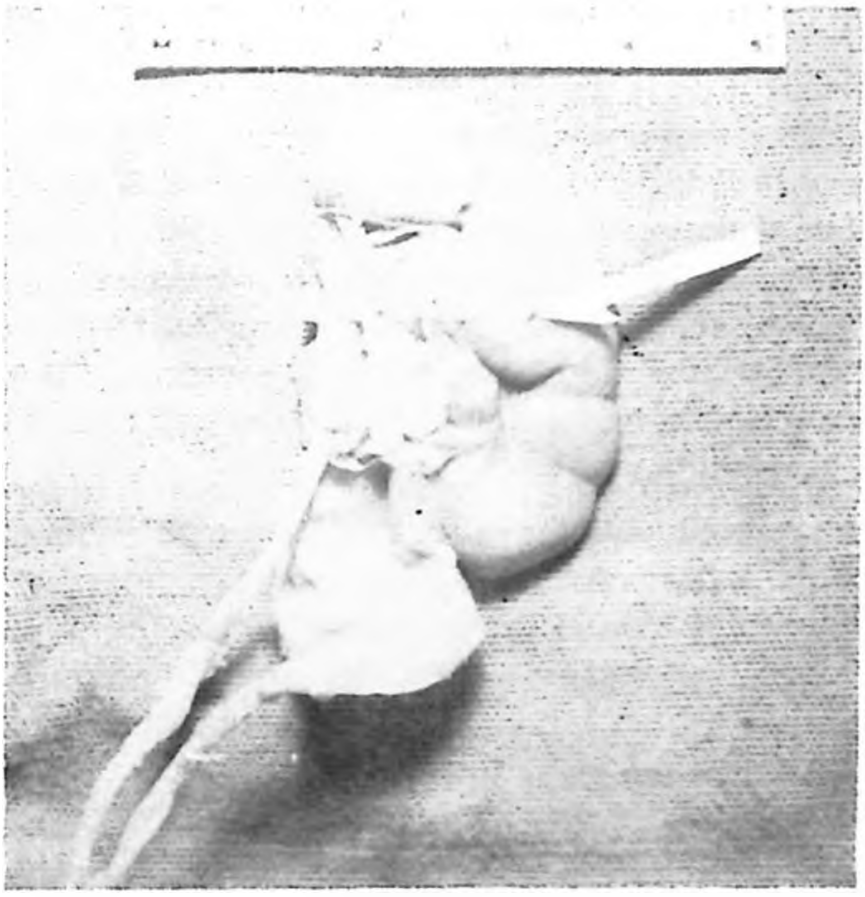

Figure 5

examination of striated muscle and cartilage removed from the costochondral junction failed to disclose any abnormality. There was macroscopic abnormality of the urinary tract with multiple subcapsular cysts measuring 1-2 mm. in diameter being observed on both kidneys. There was marked narrowing of the ureteropelvic junction on both sides and kidney pelves were noted to be extra-renal. Double pelves and double ureters were present on the left side (Fig. 4). The calysces showed cystic changes. On microscopic examination, this kidney was classified as cystic kidney meeting the criteria of Type IV of Potter's classification (Fig. 5).

Discussion

Although this combination of multiple joint dislocations, flat nose and short nails were first recognized as a distinct entity in 1950, a review case reported by McFarland in 1929 also represented the same syndrome.[3] Patients with Larsen's syndrome have characteristic facial features. The base of the nose is flat, the distance between the eyes is wider than normal and the forehead is prominent. Elbow, hip and knee dislocations as well as equino varus or equino valgus deformities of the feet are present. In contrast to the long and cylindriical fingers, the thumb displays a distal flattening and widening like a spatula. Metacarpal bones are relatively short. There may be abnormal segmentation of the thoracic vertebrae. A cleft palate usually not associated with cleft lip may be present. Rarely the cleft palate is seen to be of the incomplete type. In some cases, there is an adjoining cleft in the soft palate or uvula. Fraser has described micrognatihia as a component of this syndrome.[4] No abnormality of the teeth has been reported. Only in one of the reported cases, a complete postmortem examination was carried out and this failed to demonstrate any abnormalities, other than those described above. Striated muscle was seen to be normal. One of Larsen's original patients had a muscle biopsy examination and displayed no histological abnormality.

The first reported patients with this syndrome were not related. But later McKusick has reported the occurrence of this disease in more than one sibling in the same family according to the observations o Steel in 1966 and Rimoin in 1970.[2] Latta and his group reported in 1971 that the presence of a juxtacalceneal accessory bone was rather specific for this syndrome and also added their observations of a decreased cartilage rigidity and increased finger folds in their patients. The absence of other affected members in the families of the six patients in Larsen's original report appears in favor of a single dominant gene

or a new mutation in the inheritance of this disease. Although the number of reported cases is rather limited it may be a safe guess to assume that a number of these patients might have been misdiagnosed as arthrochalosis or arthrogyroposis.7 On the other hand, we have to take into account that because of the decreased cartilage rigidity, possibly quite a few of these patients are lost in early infancy as they might develop serious respiratory problems similar to our patient.

The patient presented meets the diagnostic criteria for Larsen's syndrome with his typical facial appearance and the multiple joint dislocations. He has an added internal organ malformation in the form of double renal pelves and double ureters combined with a cystic kidney of Potter Type IV. This combination has not been reported previously.

The recognition of the syndrome is important for the prognosis. Available experience shows that these patients are mentally normal and have no pathology in the central nervous system. The cause of this disease is not known. That an aberration in the mesenchymal tissue is the leading factor, resulting in the various pathological manifestations seen in this disease, appears to be the most plausible explanation. Surgical correction of the joint abnormalities and mechanical aids for the joints have been successfully used as palliative measures in some patients.

Summary

A three day-old male infant with Larsen's Syndrome is presented. The patient is presented with the typical facial appearance of this disease consisting of a flat nose, hypertelorism, a prominent forehead as well as multiple joint dislocations. A complete postmortem examination was carried out which revealed the added organ abnormality of a cystic kidney of Potter's type IV combined with double kidney pelves and double ureters.

Various features of the disease are discussed with a brief review of the literature.

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