Oral-facial-digital Syndrome, with Polycystic Kidneys and Liver: Pathological and Cytogenetic Studies

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In 1954 Papillon-Léage and Psamme (1954a, b) described 8 patients with a syndrome characterized by congenital anomalies of the face, oral cavity, and digits. Since then, several groups of patients have been reported (Gorlin, Anderson, and Scott, 1961; Ruess, Pruzansky, Lis, and Patau, 1962; Gorlin and Psamme, 1962; Kaplan, Vahar, Voorhess, and Gardner, 1962; Kushnick, Massa, and Baukema, 1963; Doege, Thuline, Priest, Norby, and Bryant, 1964) with this disorder, and the name 'oral-facial-digital syndrome' (OFD) has been suggested (Ruess et al., 1962).

Chromosome studies have been carried out on a number of patients with OFD. Patau, Therma, Inhorn, Smith, and Ruess (1961) described a mother and child who presumably had a 'partial trisomy' resulting from an insertion into a No. 1 chromosome (Denver classification). Gorlin (1961) also reported one of his six patients to have an abnormal No. 1, though no karyotype was published. However, the majority of patients studied have had normal karyotypes (Ruess et al., 1962; Gorlin and Psame, 1962; Kaplan et al., 1962; Doege et al., 1964).

Kushnick et al. (1963) described another chromosomal aberration in association with OFD. Their patient had 47 chromosomes, the extra chromosome matching best with group A, and the authors believed this probably was a trisomy for the No. 1 chromosomes. To our knowledge, this patient is the only male reported with OFD.

In a recent article Doege et al. (1964) described a family of 89 persons in which 15 females from 4 generations had OFD. The pedigree was compatible with a dominant mode of inheritance, and the male-female ratio (12:21) was noted to fit with the expected ratio (1:2), if this syndrome is lethal to males. In this series of patients, necropsies were done on 3 affected members. One of these had polycystic kidney disease, and one had polycystic liver and kidney disease. These patients had normal karyotypes in cells derived by culture of their peripheral leucocytes. It is of interest, however, that the patient with polycystic liver disease had an extra chromosome similar to group G in hepatic cells. The authors were unable to assess the significance of this finding.

Case Report

Clinical Findings. The patient was a newborn Caucasian female, dead at the time of examination. The mother, a 13-year-old unmarried girl, was physically normal and was thought by her teachers to have low-normal intelligence. Her expected date of confinement was estimated as April 14, 1965, but the infant was born on January 13. Pregnancy and delivery were otherwise normal as far as could be determined. The infant was severely malformed at birth and expired about 2 hours after delivery.

The mother was one of 16 children, 10 males and 6 females. Two male sibs died in infancy from unknown causes. Several of the sibs had children who were in good health. There was no history of malformations in any of the family members. The grandmother died at the age of 51 of cancer. The grandfather was 53 and was probably the father of the patient.

The female infant, who was 41 cm. in length, weighed 2440 g. She had hypertelorism, marked micrognathia, and webbed neck. The gums appeared thickened, and there were numerous thick frenula extending from the buccal to the gingival mucosa. The tongue was bifid. An omphalocoele was present posteriorly. There was a large omphalocoele, and a portion of colon was prolapsed through the anus. The abdomen was protuberant, and the genitalia appeared normal for a female infant. The right hand was everted to the ulnar side; there was a simian line and an extra digit, and only one flexion joint on the little finger. The left hand similarly had a simian line and one interphalangeal joint on the 5th finger. The fingers were tightly flexed but could be straightened with effort. Both wrists were flexed. There was bilateral talipes valgus, and the toes were short.
**Necropsy.** Inspection of the body confirmed the numerous developmental abnormalities previously noted in the physical findings. Examination of the liver and kidneys (Fig. 1a and b) revealed multiple variable-sized, multilocular thin-walled cysts containing serous fluid. The brain showed a pattern of microgyria throughout both cerebral hemispheres, hypoplasia of the medial portion of the right parietal lobe, a communicating channel between the subarachnoid space and the right lateral ventricle, and an encephalocele arising from the posterior mid-line of the cerebellum and communicating directly with the fourth ventricle. Aside from focal pulmonary atelectasis, the other organs showed a normal gross appearance.

The microscopical examination showed focal atelectasis and haemorrhage in the lungs, and mild pulmonary vascular hyperplasia. Cystic dilatation of intrahepatic bile-ducts throughout the portal areas accounted for the gross cystic changes of the liver. Multiple cysts lined by low cuboidal epithelium were seen in sections from both kidneys. There were no demonstrable glomerular or blastogenic zones, which gave the kidneys a microscopically...
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appearance similar to that described in failure of
development of the metanephrogenic renal anlage (Morris
and Johnson, 1961).

Cyogenetic Observations. All chromosome pre-
parations were made from cell cultures which were
derived from a pectoral muscle biopsy done at necropsy.
A previously described technique (Gustavson, Hagberg,
Finley, and Finley, 1962) was used for preparing the
material. A post-mortem blood specimen was also
obtained, but cultures were unsuccessful.

Twenty-three metaphase plates were counted and
photographed, and 23 karyotypes were prepared. The
majority (19) of the cells had 46 chromosomes. Four had
less than 46 and were presumed to be damaged, but an
analysis was carried out, because all the chromosomes in
group 1–3 (A) were present in these cells, and the
abnormality which has been described in OFD is in a
No. 1 chromosome. Both members of the No. 1 pair
were subjected to careful comparison, and in each of the
23 karyotypes there was no significant difference detected
between the pair members. The karyotypes were
interpreted as normal for a female.

Discussion

A number of patients with oral-facial-digital
syndrome have been reported, and the clinical
features of the disorder are fairly well established.
The aetiology remains less clear. Patau et al. (1961)
found in 2 patients a karyotype abnormality which he
interpreted as a partial trisomy resulting from the
insertion of a part of another chromosome into a
No. 1 chromosome. However, the published
results of chromosomal studies in patients with
OFD reveal the majority to be normal. Our patient
did not have a demonstrable chromosomal aber-
cation in cells derived by culture of pectoral muscle.

Only 3 of the previously reported cases of OFD
included a necropsy. Since 2 of these 3 had polycystic
disease, it is suggested by Doege et al. (1964)
that there may be a relation between OFD and
polycystic disease. The pathological findings in our
case substantiate this possibility.

The presence of polycystic disease in these 3
patients with OFD may have been coincidental or
these patients may have represented a more severe
form of the disease. The pathological study of
other patients with OFD will help clarify the
relationship. If polycystic disease proves to be a
consistent finding, the term ‘oral-facial-digital’ does
not adequately describe the clinical and pathological
features of this syndrome.

Summary

A newborn Caucasian female with oral-facial-
digital syndrome is reported. Chromosomal analysis
revealed a normal number and configuration of her
chromosomes. A significant finding on necropsy
was the presence of polycystic liver and kidneys.

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