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MULTIPLE NEVOID BASAL CELL CARCINOMA, ODONTOGENIC KERATOCYSTS AND SKELETAL ANOMALIES

A Syndrome

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The syndrome consists principally of multiple nevoid basal cell carcinoma, cysts of the jaws and skeletal anomalies, most commonly bifid rib.

It was possibly described first by Jarisch (17) in 1894. In addition to multiple nevoid basal cell carcinoma, his Case II presented low mentality and marked scoliosis.

In 1939, Straith (24) described a family in which the grandfather had multiple cutaneous basal cell carcinoma, the mother had multiple raised lesions of the skin and jaw cysts and the son and daughter had numerous jaw cysts.

In 1951, Binkley and Johnson (1) reported a thirty-one year old woman with basal-cell nevi, agenesis of the corpus callosum and dental cysts. The skin lesions, appearing in childhood, extended to involve the neck, face, thorax, abdomen, upper arms and back. The jaw lesions, noted when she was about sixteen years of age, were diagnosed as dentigerous cysts. She was given roentgenotherapy to the jaw for seven years. Subsequently, fibrosarcoma developed in this area and metastasized to the lungs and vertebrae, resulting in death. A fibroma of the ovary was surgically removed, and bifid rib and absence of the corpus callosum were observed at autopsy. A daughter, six years of age, had "epithelioma adenoides cysticum" but no dental findings.

In 1952, Eisenbud, *et al.* (7) described a patient with what appears to be several of the same anomalies in spite of their diagnosis of Klippel-Feil syndrome.

Gross (13), in 1953, reported a similar clinical picture in a nine year old boy. Numerous papillary lesions, diagnosed as epithelioma adenoides cysticum, were present over the face, chest, back and legs. Retarded eruption of the teeth and swelling of the jaws resulted in the diagnosis of numerous cysts of the jaws. Roentgenograms of the chest demonstrated synostosis of the left first rib and bifid right and left sixth ribs anteriorly.

Howell and Caro (15) discussed 4 patients, two of whom had dental cysts. Their first, a fifty-nine year old man, had had multiple basal-cell nevi for at least 40 years. At thirty years of age, a mass diagnosed as sarcoma was removed from the antrum and he was treated by radium with apparent success. Numerous cysts were subsequently removed from the jaws. It was noted that he had brothers,

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nieces and nephews with the same symptom-complex. No mention was made of abnormal roentgenographic findings in the ribs.

Their case 3 was a ten year old girl who, at two and one-half years of age had over 100 basal-cell nevi on the neck and chest. Several cysts had been removed from the jaws during the intervening years.

Thoma (26) coined the word "polycystoma" to describe the multiple radiolucent lesions in both jaws of the thirty-nine year old woman. The cysts were both large and small, some being described as microcysts. Recurrence was noted two years after enucleation. Eighteen "basal-cell tumors" were removed from the skin of the jaw and neck. In addition, the patient complained of aching bones and joints, polyuria, nocturia and loss of weight. No mention was made of bifid ribs or agenesis of the corpus callosum. Personal communication with Dr. Thoma revealed that this information was not available.

Boyer and Martin (3) described a case of "Marfan's syndrome" associated with a "bone cyst of the mandible" and multiple (110) basal-cell carcinomas. Their patient, a fifty year old man, had a dolichocephalic head, prominent supraorbital ridges and frontal eminence, sunken eyes and curvature of the mid-lower dorsal spine. Inspection of the pictures of this patient strongly suggested a broad nasal root. It is of further interest that the brother of this patient had a "tumor of the jaw". Boyer and Martin (10), in December, 1959, revealed that their patient did, in fact, have a bifid third rib anteriorly on the right side and congenital fusion of the bodies of the sixth and seventh dorsal vertebras. Further information on the patients' brother was "unavailable".

Gorlin and Goltz (10), in 1960, felt that the combination of these signs was consistent enough to consider their occurrence a syndrome and presented two additional cases.

In 1960, Ward described a peculiar dyskeratosis of the palms and soles in association with the syndrome, a finding apparently identical to that noted by Calnan (4) in 1953.

Other cases have been recorded by Goldman (9), McKelvey, *et al.* (21), Kirsch (18), Lehnert (20), Thies (25), Hermans (14) and Jablonska (16).

A genetic pattern is suggested by the not infrequent occurrence of a *forme fruste* in parent, sibling, child or near relative. Gorlin and Goltz (10) suggested that the inheritance was autosomal dominant with poor penetrance.

We have seen several additional patients and have carried out chromosomal studies of two families.

Case Histories

Case 1. W. P., a fifty-six year old white male, was admitted to the Veterans' Administration Hospital in January, 1959 for excision of basal cell carcinomas of the face, chest and back. His past history, dating to 1952, indicated previous removal of similar lesions which arose in the same areas many years earlier. Dental records stated that cysts of the left mandible, first noted in 1946, were removed in January, 1953 and again in June, 1953.

Physical examination revealed a white male with a 1 × 1 cm. lesion of the right temporal area, a 2 × 3 cm. crusted nodule behind the right ear, a 0.5 × 0.5 cm. lesion in the left pre-auricular area and multiple smaller lesions about the nose and cheeks.

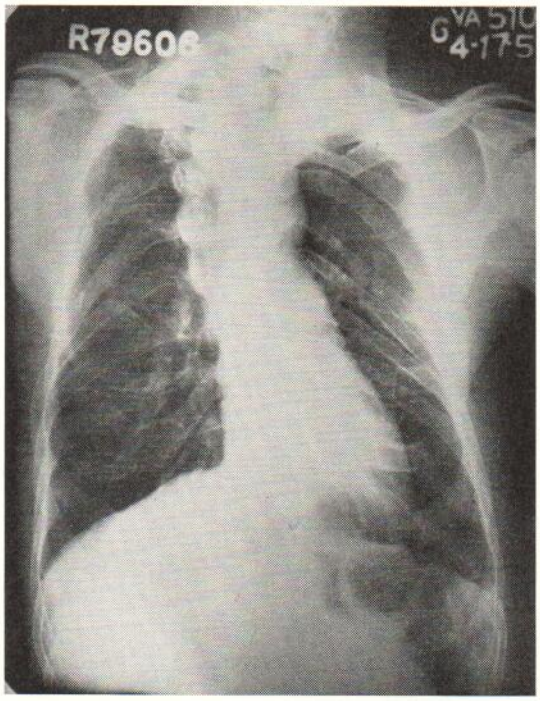

Fig. 1. — Case 1. Note rotoscoliosis and multiple rib anomalies including bifid fourth and fifth ribs on right and partial synostosis of fifth and sixth ribs posteriorly.

Also noted were multiple keratotic-like lesions of the skin of the abdomen and lower posterior thorax. Webbing between the second and third toes of the right foot extended from the distal interphalangeal joint to the metatarsal phalangeal joint. There was scoliosis of the upper thoracic spine to the right with a raised right scapula. Other findings included a corneal opacity of the right eye and a grade II systolic murmur in the mitral area. The remainder of the physical examination and laboratory findings were essentially normal.

A roentgenogram of the chest showed deformities of the thoracic cage with dextro-convex scoliosis of the upper thoracic spine. Calcified masses were seen in the upper anterior mediastinum on each side which were thought to represent thyroid adenomata. There was partial absence of the posterior portion of the right fourth rib. The anterior fourth and fifth ribs on the right were bifid and there was partial synostosis on the right between the fifth and sixth ribs posteriorly in the para-vertebral line. Roentgenograms of the lumbar spine and pelvis revealed marked rotoscoliosis of the lumbar spine with some hypertrophic changes. A slight amount of osteoporosis was noted with some cystic degeneration about both hip joints consistent with degenerative arthritis. Films of the mandible demonstrated large, sharply circumscribed cystic defects in the ramus bilaterally, the one on the right being about 4 cm. in diameter. The cysts had partially sclerotic borders. Each was explored and about 15 c.c. of yellowish content aspirated. Upon surgical intervention, the cyst wall was found to be thin and smooth and since it could not be removed in its entirety, an attempt was made to remove as much as possible.

Hospital Course: Seven basal cell carcinomas were excised from the face and behind

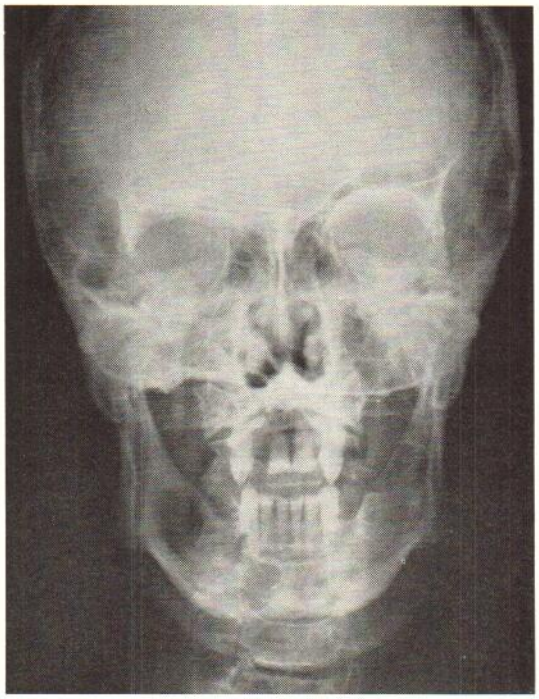

Fig. 2. — Case 1. Roentgenogram showing several large bilateral jaw cysts, those most evident being situated in the molar-ramus area.

the right ear. Two of the lesions were inadequately excised and, in February, were re-excised along with ten basal cell lesions from the posterior aspect of the neck and back.

Discharge diagnoses were: (1) multiple basal cell carcinomas of face, neck, back and epigastrium, (2) multiple senile keratoses, (3) corneal leukoma, right eye, (4) dextro-convex scoliosis of upper thoracic spine and rotoscoliosis of lumbar spine, (5) multiple jaw cysts and (6) multiple rib anomalies.

An attempt to reach the patient for further examination in October, 1961, indicated the patient had committed suicide.

Case 2. M. S., a 40 year old unmarried woman of Jewish extraction, had had multiple "dentigerous" cysts scattered throughout the jaws since the age of approximately 7 years. The cysts had been removed many times, but healing of the bony defects had been poor, with frequent recurrence of the cysts. Biopsy of these lesions revealed true cysts having a typical stratified squamous epithelial lining. At 20 years of age, a growth was removed from the neck that was diagnosed as basal-cell epithelioma, and another from beneath the left ear in 1953.

Difficulty with vision in the left eye had been experienced from birth, congenital cataract being diagnosed soon after birth, and exenteration of the left orbit was performed at 37 years of age. Pathological examination revealed congenital cataract, retinal atrophy secondary to glaucoma and coloboma of the choroid and optic nerve.

In 1960, the patient presented numerous elevated skin nodules about the eyes, nose, ears, lips and chin. In addition, one was noted on the left 5th finger. They in-

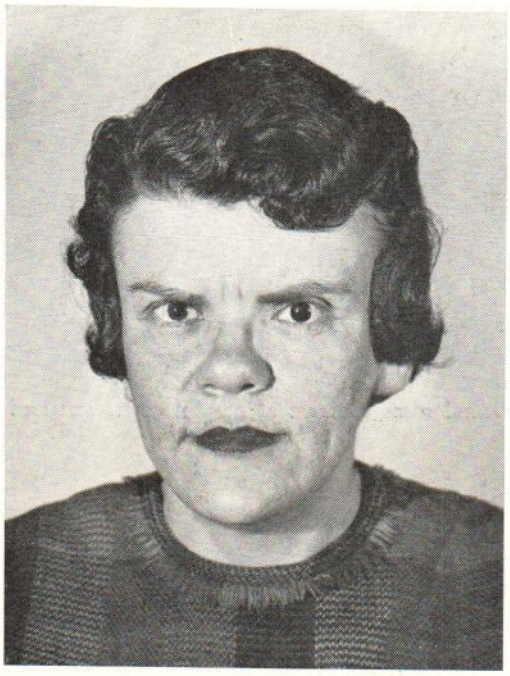

Fig. 3. — Case 2. Note frontal prominence, mild mandibular prognathism, increased distance between inner canthi, prosthetic left eye and basal cell cancer on lower lid. Patient has had at least a dozen basal cell cancers removed previously.

cluded basal-cell epithelioma of cystic and pigmented varieties and trichoepithelioma. Numerous reddish punctate lesions were present on the palms. The patient stated that these appeared in cold weather.

On roentgenographic examination of the chest, bifurcation of the 4th rib anteriorly on the left was noted as well as extremely broad 9th ribs posteriorly. A moderate degree of kyphoscoliosis was present. Frontal bossing was marked (head circumference 23.5 inches) and measurement of her intercanthal and interpupillary distances revealed dystopia canthorum. There was mild mandibular prognathism. Roentgenograms of the hands demonstrated progressively shortened metacarpals and scattered sub-cortical defects in several phalanges.

If view of the absence of any neurologic signs or symptoms, pneumonencephalography and myelography were not attempted. Electroencephalographic tracings, although exhibiting moderate diffuse and localized abnormalities were not diagnostic. There was an excessively slow background, scattered temporal spikes on the right and focal mid-temporal spikings in sleep on the right. X-ray study of the teeth showed radiolucent cystic areas on both sides.

Gynecologic examination was negative for ovarian masses.

Within the past two years, the patient has been seen on several occasions. She has had several recurrences of facial basal cell carcinomas and new ones have appeared on her legs. New jaw cysts have been discovered.

Buccal smear revealed a normal female pattern. A peripheral blood sample processed for chromosome study exhibited a normal chromosome count but an abnormality in one of the chromosomes No. 1 (Denver nomenclature). One arm of one of the No. 1

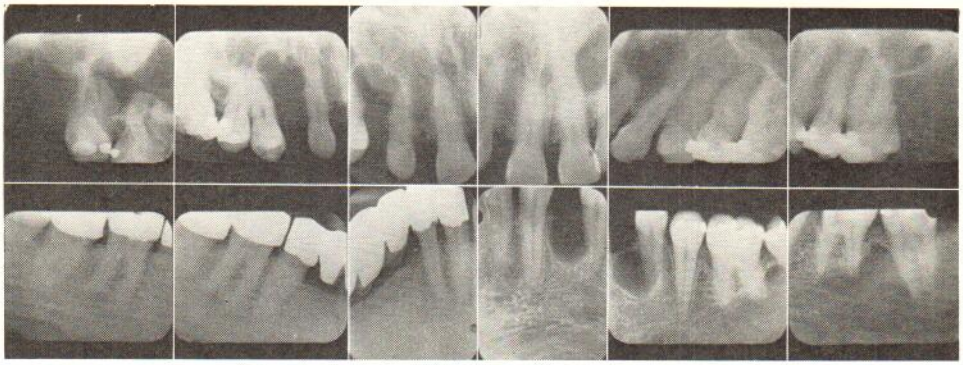

Fig. 4 A. — Case 2. Dental roentgenogram of multiple cysts scattered throughout both jaws.

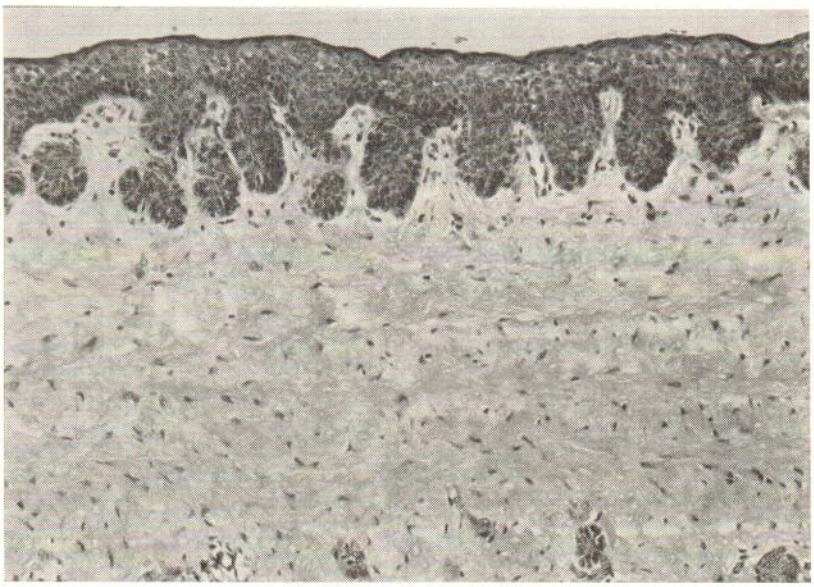

Fig. 4 B. — Case 2. Photomicrograph of one of the cysts taken from jaw of patient.

pair was longer than that of the corresponding arm in the other No. 1 chromosome. This was present in a large number of mitoses.

In spite of a negative family history for any of the signs exhibited by the patient, chromosome investigation was carried out on some of her close relatives (Figs 5 + 6). Her mother, one sister and a male child of this sister exhibited a virtually identical chromosome pattern. These findings are being reported in detail in a subsequent paper (28).

Case 3. A. P. a 29 year old white female, gravida 7 para 5 ab-2, was admitted to University Hospital for treatment of uterine prolapse in June, 1959. Two of her

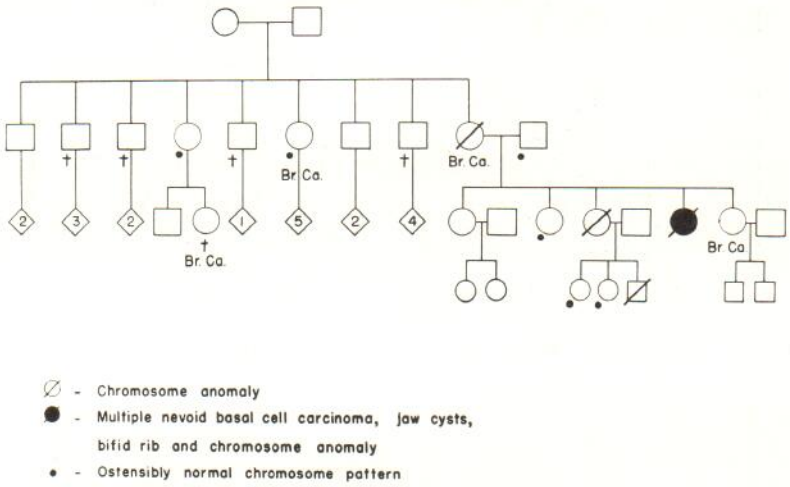

Fig. 5. — Case 2. Hereditary pattern of chromosome anomaly seen in Figure 6. The chromosome anomaly appears as an autosomal dominant characteristic and is probably inherited separately from the syndrome.

children are reported here as Cases 4 and 5. All of her living offspring are female. Her two abortions occurred at one and two months, respectively.

Family history revealed that her mother had jaw cysts and basal cell skin cancer. Attempts to secure an accurate history from her physician were unfruitful.

Physical examination revealed a well-developed white female in no acute distress. Several nodulo-ulcerative basal cell cancers were noted at the right outer canthus and at the right lateral border of the nose. Severe keratoderma palmaris ws noted bilaterally. Pelvic examination revealed normal external genitalia, a grade III uterine descensus and a moderate urethrocystocele and rectocele. The rest of the physical examination was essentially negative except for mild mandibular prognathism.

Roentgenographic findings, apart from multiple jaw cysts involving both jaws in the molar ramus area and four bifid ribs, (fourth and fifth ribs, bilaterally), were essentially normal except for a hydroureter and hydronephrosis on the right.

In 1959, one week following vaginal hysterectomy and anterior and posterior colporrhaphy, she had a course of radiation therapy to the involved skin of the face, receiving a total dosage of 5,000 r. in air. In March, 1962, she was re-admitted to the University Hospital with recurrence of several basal cell epitheliomas of the face. Upon excision, a full thickness skin graft was placed to cover the defect. In addition to the fourth and fifth ribs being bifurcated bilaterally, the cervical spine x-rays revealed narrowing of disc spaces between C 5, 6 and 7 with somewhat undulant opposing vertebral surfaces. There was minimal scoliosis in the lower thoracic area with convexity to the right. IVP showed a minimal to moderate degree of hydronephrosis and hydroureter on the right with an essentially normal upper collecting system on the left. Roentgenograms of the pelvis showed calcification compatible with leiomyoma. Laboratory studies were not remarkable. Eye examination demonstrated slight right supranuclear gaze paralysis. There was mild mental retardation. The EEG showed a mild, diffuse, low abnormality in the waking record; the sleeping record was normal. There was no activation with premarin.

Chromosome studies of this patient and two of her daughters revealed no detectable chromosome abnormality.

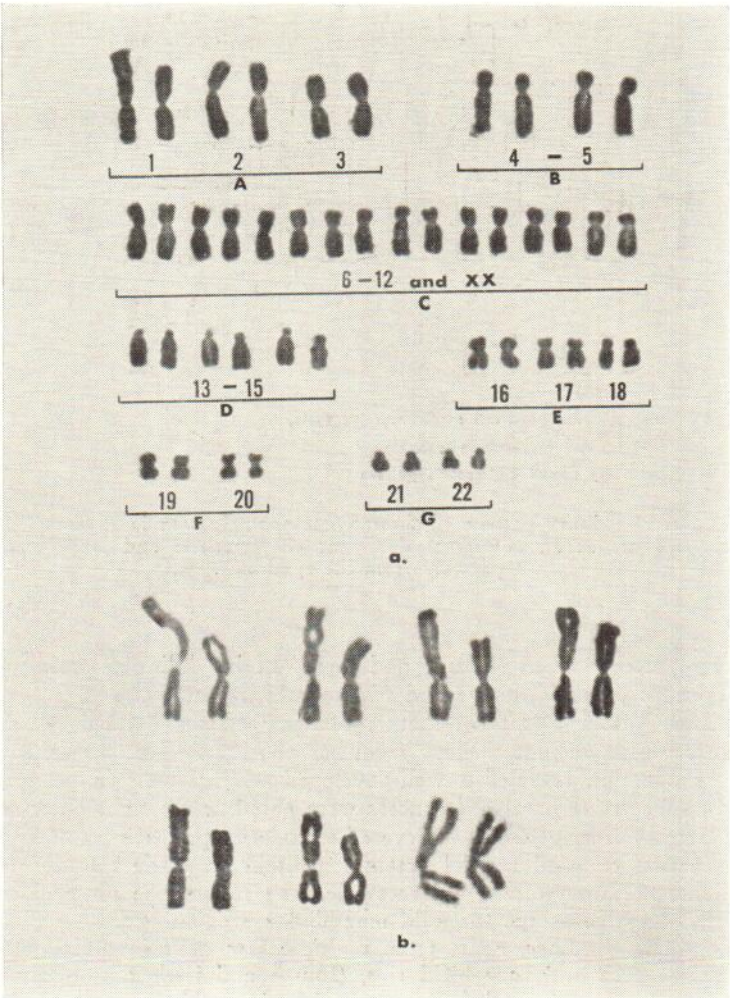

Fig. 6. — Case 2. Note above the abnormal length of one arm of one of No. 1 chromosomes. Below are several No. 1 pairs from different cells exhibiting same change.

Case 4. L. P., a 8 year old daughter of A. P., was a product of a 37 week pregnancy. The mother was advised to have cesarean section because of cephalopelvic disproportion. Upon refusal, a forceps delivery was carried out and the child was cyanotic and limp at birth. Her birth weight was 9 lbs., 15 oz. Her head was large early in life and operation was considered but was not carried out due to her poor general condition.

The patient's motor and mental development was retarded. She sat at 2 years, talked at 2.5 years and began walking at 4 years. At age 5, the child was 39 inches long, weighed 42 pounds and had a head circumference of 23.5 inches and a chest circumference of 24.5 inches. Mild mandibular prognathism was present. Funduscopic examination was normal. Her tendon reflexes were somewhat hyperactive but there was no clonus. A pronation deformity of both feet was marked. She was noted to

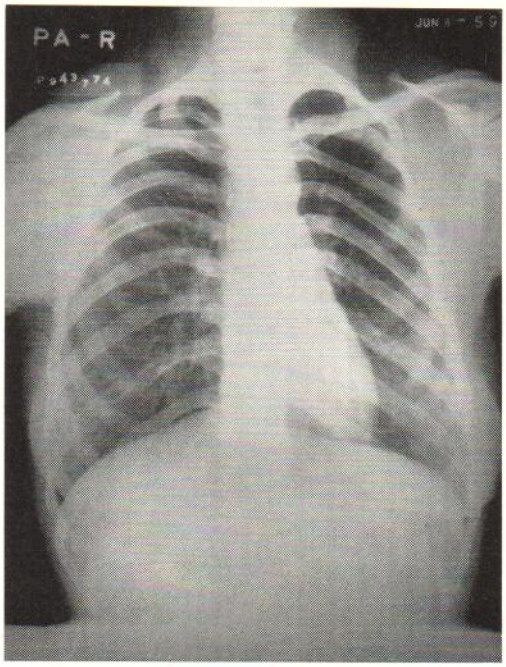

Fig. 7. — Case 3. Roentgenogram of chest showing fourth and fifth ribs bifurcated bilaterally.

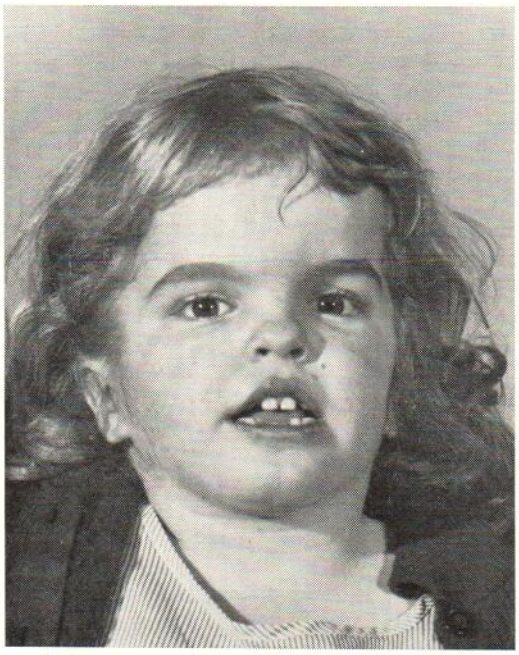

Fig. 8. — Case 4. Daughter of Case 3. Note frontal bossing and general increase in size of skull. Also increased distance between inner canthi.

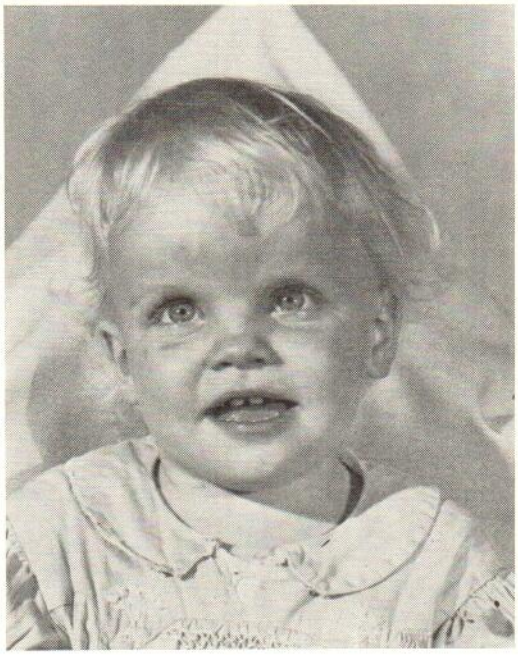

Fig. 9. — Case 5. Daughter of Case 3. Note similar changes to those seen in Fig. 8.

walk with a rather waddling gait, abducting the left leg. She was able to count and distinguish colors, but could not draw a circle. She could dress herself, but could not manipulate buttons. Laboratory studies were within normal limits. Skull x-ray showed marked disproportion in the size of the cranial vault compared to the facial bones. The chest x-ray was normal except for a posteriorly broad and distorted third rib on the right. An electroencephalogram showed a mild abnormality background and low voltage for her age. There were some focal very slow waves in the left central area. Ventriculographic and air studies revealed congenital hydrocephalus of the communicating type. Except for mild myopia and dystopia canthorum (Inter inner canthal — 35.5 mm., interpupillary — 55 mm.), the eyes were negative.

Case 5. R. P., a 2 year old daughter of A. P., was born one month prior to the expected date of confinement with a birth weight of 9 lbs., 10 oz. Her development up to the age of 6 months was very slow. She first followed with her eyes at 5 months and by 6 months did not roll, grasp or support her head.

At first admission, the child was noted to be wasted, irritable and pale with enlargement of the head. Occipitofrontal circumference was 45.2 cm. and chest circumference was 37.0 cm. There was mild mandibular prognathism. The extremities were slightly wasted and muscle tone and grasp were poor. The neck and back were held in hyperextension.

Roentgenograms at that time showed no evidence of suture widening of the skull or unusual prominence of the anterior fontanel. However, there was a definite increase in the size of the cranial vault in relation to the facial bones and overall skeletal maturation. Bone age was considered within normal limits. A soft systolic murmur was heard over the 3—4 intercostal space at the left sternal border with no transmission.

During certain phases of respiration there was a musical quality to the systolic murmur. The pulmonary second sound was normal. The EKG and x-rays and cardiac fluoroscopy were also normal. A ventriculogram showed evidence of moderately dilated ventricles with no evidence of intracranial tumor and there was good communication between the ventricles and the spinal system. The patient was discharged and followed in the pediatric clinic. It was noted that within 11 months her head size had slowly increased 5 cm. more than it had been upon discharge, but with normal ventricular pressures. She was not able to sit, use a spoon, or feed herself at that time. Hydrocephalus was quite obvious and the same systolic murmur previously described was still present. Estimated developmental age at that time was approximately 10—11 months, the chronological age being 16 months. By June, 1961, no progressive hydrocephalus had occurred and the patient could now sit with support as well as stand with some aid. Her grasp had improved somewhat and she had begun to use a few simple words. She followed simple commands and brushed her own teeth. Eye examination revealed alternating esotropia and dystopia canthorum.

Laboratory examination was essentially negative. Roentgenograms of the chest revealed a bifid fourth rib on the left.

Review of the literature and our own cases has yielded the following analysis:

Systemic Manifestations:

Facies. — There is a certain degree of frontal and temporoparietal bossing, giving the skull a pagetoid appearance. The supraorbital ridges in several patients have been well developed, giving the eyes a sunken appearance (10, 14, 16, 24, 25). A broad nasal root was noted by several authors (1, 3, 10, 13, 15) and Gorlin and Goltz (10) suggested that it is part of the syndrome. Measurement of several of our patients revealed that it is dystopia canthorum. In addition, several of our patients have exhibited mild mandibular prognathism. The dystopia canthorum and mandibular prognathism may also be seen in pictures of patients of Howell and Caro (15) and Kirsch (18).

Skin. — Multiple nevoid basal cell carcinomas usually appear in childhood, more frequently about puberty, and most often involve the nose, upper eyelids, cheeks, trunk, arms and neck. However, any part of the skin may be involved. They appear as flesh-colored to pale brown papules.

Microscopically, the tumors cannot be differentiated from the ordinary basal cell carcinoma (a histochemical investigation is certainly desirable). Multiple lesions taken from the skin of our patients have presented a wide spectrum. Some are superficial and multicentric, some are pigmented, some are solid, others cystic, still others lattice-like and, rarely, one finds one to be trichoepitheliomatous in appearance.

Milia are often present, intermixed with the epitheliomata (4, 5, 10, 15) and comedones have been noted by others (5, 19). Cysts of the skin were also noted by Straith (22).

Calnan (4) and Ward (27), in addition to the usual anomalies, described a palmar-plantar dyskeratosis, the central plug of which falls out. This was seen in our Case 2.

Skeletal System. — Bifurcated rib has been found to be associated with the skin tumors by several investigators (1, 2, 3, 10, 13, 22, 27). This may involve

more than one rib and may be bilateral. All our patients had rib anomalies. Case 3 had four such bifid ribs and Case 1 had multiple rib anomalies.

Kyphoscoliosis has been observed by Boyer and Martin (3) and others (5, 10, 11, 17), and was seen in several of our patients (Cases 1—3). Fusion of the vertebrae has been noted (7) and cervical rudimentary ribs have recently been reported by Kraus and Vortel (19) and Ward (27).

Shortened metacarpals have been found in one of our patients and in one patient by Block (2).

Central Nervous System and Mental Development. — The patients of four observers (1, 2, 3, 17) and three of our patients have been mentally retarded.

Binkley and Johnson reported partial agenesis of the corpus callosum found at autopsy (1). Straith (24) reported calcification of the dura in the left parietal region and in the falx cerebri. We have also noted this finding.

Other Systems. — Binkley and Johnson's (1) patient was found to have an ovarian fibroma and Block (2) noted pelvic (ovarian or uterine) calcifications. Our Case 3 also had pelvic calcification.

The patient reported by Gorlin and Goltz (10) (Our Case 2) had congenital cataract, glaucoma and coloboma of choroid and optic nerve of the left eye. Our Case 1 had corneal leukoma of one eye, possibly congenital.

Oliver (22) noted "congenital blindness" of the left eye in his patient and Hermans, *et al.* (14) thought the eye changes so characteristic as to include it as a fifth type of phakomatosis.

Oral Manifestations. — Scattered throughout the jaws are numerous cysts that vary in size from microscopic to several centimeters in diameter. These cysts are lined by epithelium that runs from a simple to a thickly keratinized stratified squamous variety. They may appear for the first time as early as 7—8 years or as late as the thirties. In our experience there is a marked tendency for these cysts to recur, possibly from adjacent microcysts, in spite of thorough curettement.

Many cysts arise in juxtaposition to the teeth, causing dilaceration of the roots, if the teeth are in that developmental stage. The uniform stratified squamous epithelial lining with the thin keratinized layer suggests a primordial cyst or keratocyst. Some cysts show budding, reminiscent of embryonal skin (Fig. 4 B) and one we have seen appears to have exhibited signs of early ameloblastoma formation.

The question of sarcoma arising in the jaws in relation to the cysts seems quite germane. It is not unlikely in the case described by Binkley and Johnson (1) that the fibrosarcoma arose as a post-irradiation lesion but this argument is certainly not valid for the first case of Howell and Caro (15). If, indeed, the antral lesion was a true sarcoma (and these authors seem to have some reservations), close observation and conscientious follow-up study must be carried out on all patients.

Discussion

The syndrome is far more complex than heretofore supposed, involving many organ systems and merits considerable further investigation.

The most constant features of the syndrome are: multiple nevoid basal cell car-

Table 1.

Signs and Symptoms	Relative Frequency
A. *Skin*	
1. Multiple nevoid basal cell epithelioma	+++
2. Palmar dyskeratosis	++
3. Milia	++
B. *Oral Manifestations*	
1. Multiple jaw cysts	+++
2. Mild mandibular prognathism	++
3. Fibrosarcoma of jaws (?)	+
C. *Skeletal System*	
1. Rib: bifid, synostosis, partial agenesis or cervical rudimentary	+++
2. Vertebrae: scoliosis, cervical fusion	++
3. Frontal bossing	++
4. Shortened metacarpals	++
D. *Central Nervous System*	
1. Mental retardation, variable	++
2. Congenital hydrocephalus	++
3. Calcification of dura	++
4. Agenesis of corpus callosum (?)	+
E. *Eye*	
1. Congenital blindness, coloboma of choroid and optic nerve	+
2. Dystopia canthorum	++
F. *Other*	
1. Pelvic calcification (?)	+
G. *Inheritance*	
1. Autosomal dominant, poor penetrance	
2. Possible associated chromosomal anomaly (No. 1 — Denver nomenclature) appears doubtful	

cinoma, multiple jaw cysts and skeletal anomalies. However, several other components appear rather frequently and are probably part of the symptom complex: palmar dyskeratosis, milia, mild mandibular prognathism, frontal bossing, congenital hydrocephalus dural calcification, scoliosis and eye anomalies including dystopia canthorum and colobomata (Table 1).

Of questionable importance at this time are: fibrosarcoma of jaws, agenesis of corpus callosum, and pelvic calcification. More cases need to be analyzed before a conclusion may be reached. The high incidence of breast cancer in the family of Case 2 is interesting but is probably not related (Figure 5). The jaw cysts appear to be odontogenic keratocysts and it is rather likely that eventually a case will be reported in which a true ameloblastoma has developed.

The syndrome seems to be transmitted as an autosomal dominant trait with poor penetrance.

Dystopia canthorum and mild mandibular prognathism are also seen in the Waardenburg syndrome (6). The former observation is well-documented, the latter is our own.

The association of shortened metacarpals and calcifications in various parts of the body suggests abnormal calcium and/or phosphorus excretion, a problem which should be investigated.

The incidence of bifid rib, rudimentary rib and synostosis of ribs unassociated with this syndrome appears to be 6.2, 2.0, and 2.6, respectively, per 1,000 live births (8). This would make a fortuitous association in this syndrome highly unlikely. The absence of jaw cysts and multiple nevoid basal cell carcinomas in the children of Case 3 is not surprising considering their age at this time.

In one affected individual (Case 2), her unaffected mother, sister and a male child of this sister a chromosomal anomaly was noted. One arm of one of the chromosomes No. 1 was longer than that of its homologue. The chromosomal anomaly seen in Case 2 and her relatives appears to resemble the chromosomal anomaly described by Patau, *et al.* (23) in association with oro-digital-facial dysostosis. On the other hand, another family (Cases 4—6) affected with the syndrome, has demonstrated no detectable chromosomal abnormality.

One may consider possible alternatives:

a) Partial trisomy for a small chromosomal segment in which the segment is too small to be diagnosed in other cases. One must further suppose that in Case 2 the extra length is irrelevant and there are modifying factors (genetic or environmental) which permit expression in Case 2 but not in others in her family.
b) Chromosomal anomaly not related to syndrome, but transmitted independently in an autosomal dominant manner. If so, it is interesting that such a sizeable extra piece has no phenotypic effect. At this time, we would favor this view.

These and other possibilities are discussed by Yunis and Gorlin (28).

SUMMARY

The authors have described a well-defined syndrome that consists of multiple nevoid basal cell carcinoma, multiple jaw cysts and rib anomalies, the most common of which are bifurcation, synostosis and partial agenesis. Less frequently palmar dyskeratosis, milia, mild mandibular prognathism, vertebral anomalies, frontal bossing, calcification of dura, shortened metacarpals, dystopia canthorum and congenital hydrocephalus have been seen, frequently enough in association with the triad to suggest they are part of the syndrome. Other signs such as mental retardation, agenesis of corpus callosum, eye colobomata and pelvic calcification must wait for further case reports for evaluation of their significance.

Inheritance is autosomal dominant with poor penetrance and variable expressivity.

The association of an anomaly of the No. 1 chromosome (Denver nomenclature) in one patient and several members of her family appears to be fortuitous but raises fascinating questions concerning the presence of an added chromosome segment *without* phenotypic expression. This may be identical to the finding described by Patau, *et al.* in patients with orodigitofacial dysostosis. The present authors suspect that the chromosome changes described in the latter syndrome may be fortuitous as well.

RÉSUMÉ

Les auteurs ont décrit un syndrome bien défini, composé de multiples carcinomes basocellulaires naevoïdes, de kystes multiples de la mâchoire et d'anomalies costales; les plus fréquentes de ces anomalies étant les côtes bifurquées, la synostose et l'agénésie partielle. Moins fréquemment, on a observé une dyskératose palmaire, des miliums, un léger prognathisme mandibulaire, des anomalies vertébrales, une bosse frontale, la calcification de la dure-mère, des métacarpiens raccourcis, une dystopie des angles oculaires et une hydrocéphalie congénitale; ces anomalies sont assez souvent associées, à la triade du syndrome, et permettent de penser qu'elles en font bien partie. En ce qui concerne les autres signes, tels que le retard mental, l'agénésie du corps calleux, le colombe oculaire et la calcification du bassin, des études ultérieures sur ces cas seront encore nécessaires pour préciser leur signification.

La transmission héréditaire se fait selon le mode dominant autosomique, la pénétrance est faible et l'expressivité variable.

L'association à ce syndrome d'une anomalie du chromosome No. 1 (selon la nomenclature de Denver) existant chez une de ces patientes, ainsi que chez plusieurs membres de sa famille, semble être due au hasard; mais ce fait soulève cependant des problèmes intéressants, concernant la présence d'un segment de chromosome supplémentaire, *sans* aucune expression phénotypique. Ce fait semble être identique au phénomène décrit par Patau et coll. chez des patients atteints de dysostose oro-digito-faciale. Les auteurs pensent que les modifications chromosomiques décrites dans ce dernier syndrome peuvent tout aussi bien être dues au hasard.

ZUSAMMENFASSUNG

Die Autoren beschreiben ein wohldefiniertes Syndrom, das sich aus multiplen naevoiden Basalzellcarcinomen, multiplen Cysten an den Wangen sowie aus Rippenanomalien zusammensetzt. Bei den letzteren handelt es sich im allgemeinen um Bifurkation, Synostosen und partielle Agenesie. Weniger häufig wurden Dyskeratosen des Gaumens, Milien, mässige Prognathie, Wirbelanomalien, Stirnhöcker, Calcification der Dura, verkürzte Metacarpalknochen, Dystopia canthorum und angeborener Hydrocephalus beobachtet; jedoch waren diese Merkmale häufig genug, um sie als Teil des Syndroms zu betrachten. Andere Zeichen, wie geistige Retardierung, Agenesis des Corpus callosum, Kolobom der Augen und Calcifikation des Beckens sind in ihrer Bedeutung noch nicht zu übersehen; weitere Beobachtungen müssen abgewartet werden.

Der Erbgang ist autosomal dominant mit geringer Penetration und variablem Ausdruck.

Die Verknüpfung einer Anomalie des Chromosoms Nr. 1 (Denver-Nomenklatur) bei einer Patientin und verschiedenen Mitgliedern ihrer Familie scheint zufällig zu sein, wirft aber interessante Fragen hinsichtlich der Gegenwart eines zusätzlichen Chromosomsegmentes *ohne* phänotypische Expression auf. Dieses könnte mit den von Patau *et al.* bei Patienten mit orodigitofacialer Dysostosis beschriebenen Befunden identisch sein. Die Autoren vermuten, dass die bei diesem Syndrom beschriebenen Chromosomenveränderungen ebenfalls zufällig sein könnten.

RESUMEN

Los autores han descrito un síndrome bien definido que consiste en carcinoma basocelular nevoide múltiple, quistes múltiples de maxilar y anomalías de

costillas, siendo las más corrientes bifurcación, sinostosis y agenesia parcial. Menos frecuentes son: disqueratosis de paladar, milia, prognatismo mandibular discreto, anomalías vertebrales, abultamiento frontal, acortamiento de metacarpianos, «dystopia canthorum» e hidrocefalia congénita, pero no rara vez asociados con la triada, lo que hace suponer que forman parte del síndrome. Otros signos tales como retraso mental, calcificación de la dura, agenesia del cuerpo calloso, coloboma ocular y calcificación pelviana, precisan mayor casuística para poder valorar su significación.

La herencia es autosómica dominante con débil penetración y expresividad variable.

La asociación de una anomalía del nº 1 (nomenclatura de Denver) en un paciente y varios miembros de su familia parece ser fortuita, pero plantea preguntas fascinantes concernientes a la presencia de un segmento cromosómico adicional *sin* expresión fenotípica. Esto puede ser idéntico al hallazgo descrito por Patau y als. en pacientes con disostosis orodigitofacial. Los autores actuales sospechan que las alteraciones cromosómicas descritas en el último síndrome puedan ser también fortuitas.

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