FOLLICULAR ATROPHODERMA AND PSEUDOPELAEDE
ASSOCIATED WITH CHONDRODYSTROPHIA
CALCIFICANS CONGENITA*

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In 1943 Miescher (1) reported peculiar atrophic changes of the skin of body
and scalp in a 7 year old Swiss girl. There were spots of atrophic alopecia on
the scalp, and on the extremities and trunk irregular zones in which dimple-like
depressions were found at the place of follicular orifices. The child was very
small and had thoracic kyphoscoliosis, lumbar lordosis, luxation of the right
hip, a considerably shortened right leg, and a moderately shortened left arm.
Five years earlier, Burckhardt (2) has described the skeletal condition of the
same child, then 2 years old, as chondrodystrophia foetalis calcarea. In the Eng-
lish speaking countries this disease is called chondrodystrophia calcificans
congenita, chondro-osseous dystrophy with punctate epiphyseal dysplasia, or
similar variations.

Several cases of this newly described syndrome of cutaneous and skeletal
changes have lately been seen in New York.

REPORT OF CASES

1. C. S. (3), an 8 year old Jewish girl, was born in the United States. The parents of the
child were born in Poland. They have three children, of whom the patient is the second.
The father, mother, a sister aged 10, and a brother aged 5, are small but do not present
the characteristic cutaneous or skeletal changes to be described.

The mother was well during her second pregnancy. The child was born spontaneously
at full term. Immediately after birth the mother noticed that large parts of the scalp and
body were covered by red crusts, some tiny, others confluent and forming large adherent
masses. The mother was told at the maternity hospital that this was eczema. After several
weeks the crusts fell off. The skin of the body looked normal except for “large pores”.
The scalp showed some bald spots. Neither the involved areas of the body nor of the scalp
have increased in size.

The child sat alone at the age of 7 months, and walked at 17 months. When she was
6 years old the mother noticed that her right heel did not touch the ground. The child was
treated by an orthopedic surgeon but the mother believes that the shortening of the right
leg has become more noticeable with passage of time. The child is the smallest in her class.
She does not suffer unduly in hot weather. She had chicken-pox at the age of 4 and measles
at 5. The mother sought dermatologic advice for the daughter's scalp condition.

The cutaneous changes were more widespread on the right than on the left side of the
body. They were found on the chest, right arm and forearm, dorsum of right hand, right
thigh, knee and tibia. The left arm and left knee were also involved. More or less sharply
circumscribed plaque- or band-like areas showed depressed pinhead-sized dimples with-
out lanugo hairs at the site of follicular orifices. Almost every follicle in involved areas
showed these changes while the skin between the follicles appeared normal. The dimples
formed a rather regular pattern, which made the skin look vermiculate (Fig. 1).

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Read before the Tenth Annual Meeting of the Society for Investigative Dermatology,
Atlantic City, N. J., June 12, 1949.
Scalp: Most of the scalp was covered by thick black hair, but on the frontal part and also near the crown there were large, poorly circumscribed areas of whitish or slightly reddened atrophic skin, without hair (Fig. 2), slightly more numerous on the right than on the left side. At the periphery of these bald spots crusts were attached to some of the hairshafts. No follicles were seen in the atrophic area but a few long, single hairs were found in the center with some broken-off hairs at the periphery.

Examination of the scalp with Wood's light was negative. Repeated examinations of the hair showed no fungi on slides or in cultures. Under the microscope the hairs from the periphery of the bald areas were torn in parts and the sheaths were encased by bacteria.

The eyebrows and lashes were normal.

The child had normal teeth. The finger- and toenails were undisturbed. The skin of the body in general was dry and there was slight keratosis pilaris present on the trunk. The child's face was freckled. Small spider nevi were seen below the left eye and on the left hand.

General examination in Babies Hospital revealed that the highly intelligent and very cooperative child was small, measuring only 119 centimeters in length (mean for her age: 128 centimeters). She had frontal bosses and a suggestive saddle nose. The eyes were hyperopic; the vision, however, could be corrected to normal with glasses.

All laboratory examinations including determinations of calcium, phosphorus and phosphatase, gave normal results. There was a trace of albumin in the urine. The urine contained no white or red blood cells.
The lower extremities measured 64 centimeters on the right and 67 centimeters on the left side, from anterior superior spine to heel. Most of the shortening on the right was in the femur. Because of this the child walked with pelvis tilted to the right.

In roentgenograms the right tibia and fibula were distinctly shorter than the corresponding bones in the opposite extremity. The left tibial diaphysis measured 25.7 centimeters, the right 24.0 centimeters. The left femoral head and neck were larger than the right. The ossification center of the head of the left radius was tilted and hypoplastic. The shaft below was slightly expanded. There were no changes in the skull.

The diagnosis was: Follicular atrophoderma, pseudopelade and multiple shortening of tubular bones.

2. C. L., 9 year old girl, was born in the United States. The mother was born in Poland, and the father is of Polish parentage. The parents look very much alike but know of no consanguinity. The parents and all members of their immediate family are short.¹ A child of a cousin of the father was born without arms and legs. Each son of the mother's two brothers has an asymmetrical head, one side being larger than the other. The patient has 4 sisters and one brother. She is the fourth child.

The patient was born at full term and without instruments. The mother was well during the pregnancy. At birth shortening of the left arm and leg, a cataract of the left eye

¹ The patient and her family live 200 miles from New York City. An exact investigation of all family members is contemplated but has not yet been carried out.
and peculiar cutaneous changes on the scalp and body were noted. The scalp was partially covered with crusts. When they fell off after some weeks, hair was absent in these spots. At birth, large areas of the body showed dry scales. Later the mother saw "dimples" at areas where scales had been present. There also were many oddly-shaped dark and light patterns on the skin of trunk and extremities. While the bald areas of the scalp and the lesions of the body have remained unchanged, the discoloration has greatly improved.

The child sat up late and walked with a limp at the age of 2. She never complained of any pain and has not suffered unduly in hot weather. She is very active. At the age of 8 a cataract of the right eye was discovered. The child was admitted to Babies Hospital in October 1948.

![Figure 3](image)

**Fig. 3. Case 2. Shortened Left Femur, Flattened in Its Lateral Aspect, and Patella Dislocated Laterally and Dorsally**

General examination in Babies Hospital revealed an obviously deformed, moderately obese child with a saddle nose, frontal bosses and a high palate. The girl was of low average mentality according to the Stanford-Binet and Goodenough tests. There were numerous skeletal defects manifested by hemivertebal deformities in the thoracic, lumbar, sacral and possibly cervical segment of the spine, with a marked shortening deformity of all of the tubular bones in the left leg and left arm, the greatest shortening occurring in the bones of the forearm. The bones of the left hand and the left foot were as large as those of the right side. The distal epiphysis of the shortened left femur was flattened in its lateral aspect and the patella was dislocated laterally and dorsally (Fig. 3). There was hypoplasia of the left innominate bone and neck of the left femur and congenital dislocation of the left hip (Fig. 4). The depth of the left wrist was greatly diminished and there was no roentgen evidence of ossification centers in the naviculare and triquetrum. The skeletal meas-
urements of the two sides differed from 2.8 to 10 cm., the extremities on the left being the shorter. The standing height measured 16.5 cm. more on the right than on the left side.

The knee jerks and biceps reflexes of both sides could not be elicited. The Achilles tendon reflex was present only on the left side. The triceps reflex was present on the right and accentuated on the left side. There was a questionable Babinski reflex on both sides. Chaddock and Oppenheim reflexes could not be elicited.

The liver edge could be felt just below the costal margin. The results of blood counts, serologic tests, determinations of phosphorus and phosphatase showed no unusual features.

**Eyes:** There were more pronounced lens opacities in the left than in the right eye. When the pupils were dilated the cortex of the lens was hazy and there was nuclear sclerosis. The fundus gave a good red reflex but no details could be made out. The left eye presented a dense nuclear cataract. A red reflex was obtainable peripherally. The child had bilateral horizontal nystagmus.

![Figure 4. Case 2. Hypoplasia of the Left Innominate Bone and Neck of the Left Femur and Congenital Dislocation of the Left Hip](image)

**Teeth:** There appeared to have been some failure of development in the cuspid areas of both maxilla and mandible, resulting in some rotation and crowding of teeth in these segments. The upper incisor teeth were characterized by very prominent cinguli. Caries was present in many teeth.

**Skin—Scalp:** The hair was blond, dry, lusterless and sparse throughout, and there were many areas of baldness, especially in the frontal and temporal-parietal region and near the crown (Fig. 5) similar to those of Case 1. Examinations for fungi also were negative.

The eyebrows and lashes were present. The toe- and fingernails were normal with the exception of the left index finger which looked widened.

**Skin—Body:** Two kinds of disturbances were present, atrophic and pigmentary. Each formed an unusual and widespread pattern of irregular distribution. There was, however, no discernible relationship between the two. In the center of some depigmented whorls, an aggregation of atrophic spots could be found, but in other whorls such distribution was missing. The atrophic changes consisted of pinhead-sized depressions at the site of almost all follicles in involved areas. No lanugo hair protruded from these depressions. These
pitted areas formed irregular bands or patches and were located on both shoulders, arms, dorsal of hands and fingers (Fig. 6), lower legs, trunk, and very densely on the left buttock.

The pigmentary disturbance consisted of diffuse, irregularly almost bizarrely arranged, reticulated, gyrate and streaked patterns of alternating light-brown or white skin. The effect was somewhat like a melting ice-cream fudge sundae. These changes were found over the scalp, shoulders, trunk (Fig. 7), arms and lower extremities with a preponderance of darker areas on the lateral parts of the trunk.

The diagnosis was: Follicular atrophoderma, pseudopelade, incontinentia pigmenti, cataracts, kyphoscoliosis, congenital dislocation of left hip, hemivertebra deformities and shortening of many bones of the left side.

Fig. 5. Case 2. Scalp showing area of pseudopelade with central biopsy. The hair is blond, dry and lusterless

3. R. L., mother of Case 2. The 37 year old woman came to the United States from Poland at the age of 10. She has had 6 children and no miscarriages. She suffered from iritis of the left eye after the birth of her third child. She stated that direct sunlight did not agree with her skin and eyes.

The patient had blue eyes and blond hair. There were areas of bald atrophy on the anterior part of the scalp. She had the same kind of dimple-like changes as her daughter (Case 2). The lesions were arranged in patches or streaks, especially on the right arm and were found on both arms, back and axillae. There were no signs of incontinentia pigmenti. The right shoulder-to-finger distance was \(\frac{1}{4}\) inch longer than the left. The lower extremities were equal. No gross deformity was seen. Radiograms were not taken.

The diagnosis was: Follicular atrophoderma, pseudopelade, shortening of left arm.

The following information on the other children was obtained from the parents: An 18 year old daughter “has one rib higher than the other”. A 16 year old daughter “once had mild diabetes”. An 11 year old boy is tall and normal. The 9 year old daughter is described as Case 2. A 6 year old daughter is stocky but not exceptionally small. A sixth toe
of the left foot was amputated. B. L., a 4½ year old daughter, is a midget. She was born at full term and was jaundiced at birth. The mother had not been sick during this pregnancy. The child also showed at birth scaly areas covering large parts of the body. They were less numerous and smaller than those of her older sister. On the sides of the scalp were areas of baldness. Pigmentary disturbances like those of her sister have been present since birth but are more pronounced. Her right side—the opposite one from her sister's—was

Fig. 6. Case 2. Follicular Atrophoderma of Right Forearm, Hand and Fingers

the shorter one. Her eyes seemed normal. She still had her deciduous teeth. She was a bright child but limped considerably. A tentative diagnosis of pseudopelade, follicular atrophoderma, incontinentia pigmenti and multiple osseous changes resembling those of Case 2 was made.

Histologic examination

1. Follicular atrophoderma. Biopsy from right thigh, Case 1 (Fig. 8): The keratin layer was somewhat thickened and lamellated. There were several limited areas of epidermal
Fig. 7. Case 2. Incontinentia Pigmenti

Fig. 8. Follicular Atrophoderma. Biopsy from Right Thigh, Case 1
atrophy resulting from loss of rete pegs. The cutis showed in its upper layers a mild inflammatory reaction characterized by a slight perivascular infiltration of mononuclear cells some of which were lymphocytes. There was only one hair follicle present which showed some edema and questionable atrophy. The connective tissue sheath of this follicle was somewhat thickened. The coil gland ducts appeared as thin cellular cords. The acini of the few sweat glands were small and pale and probably atrophic although the cells were not extremely thin. Elastic tissue stain (orcein) showed some slight condensation of the elastic fibers which were arranged parallel to the epidermis.
2. Pseudopelade. Biopsy from scalp, Case 2 (Fig. 9). The epidermis was not remarkable. In the entire section only one hair follicle was seen. It was without hair, keratinized, and appeared to be a distorted remnant of an atrophic hair follicle.

3. Incontinentia pigmenti. Biopsy from trunk, Case 2 (Fig. 10). There was mild hyperkeratosis. Great variations in the amount of pigment existed in the epidermis. At the periphery of the section there was a moderate to large amount of melanin pigment in the basal layer, but in the center there appeared to be a relative loss of pigment. Occasionally very few chromatophores were seen in the cutis.

COMMENT

Bones: In none of my cases were the characteristic calcium deposits of the bones seen. They have been observed in babies suffering from chondrodystrophia calcificans congenita at birth but disappeared between the ages of 12 months and 3 years (Borovsky and Arendt (4), Hünermann (5) and Raap (6)). The osseous changes seen in my patients were compatible with the end results of chondrodystrophia calcificans congenita.

The primary disturbance of this disorder consists in severe degenerative changes of the basic cartilage (Hilliard (7) and Bureckhardt (2)) which does not offer homogeneous material for ossification. In histologic studies Bureckhardt (2) and others saw short and irregular formation of columns of cartilage. The disturbance involves mostly the enchondral zone with the result that periosteal growth may become preponderant. Shortened and plump bones result and since the process does not affect the bones equally, some are more involved than others. Shortening or deformity is not limited to one side of the body although one side is usually more involved than the other. The calcareous deposits are found at the site of the degenerative changes. After a while they are again resorbed. They do not denote disturbance of the calcium metabolism, and this is borne out by the normal values of calcium in the blood of these patients. The disturbance, with or without other congenital defects such as cataracts and cardiac lesions, has been seen in several members of families (Raap (6), Resnick (8) and Maitland (9)). Systematic family research of cases suffering from the disease would determine the genetic pattern.

Skin: Follicular atrophoderma and pseudopelade: While the histologic picture showing agenesis of hair follicles and other appendages, some atrophy of the epidermis and slight changes in the cutis is not striking, the clinical picture of the end stage of the lesions on the body is rather unique. Plaques or bands on trunk or extremities, with uniformly depressed follicular orifices containing no hair, cannot easily be mistaken for any other cutaneous disorder. Diagnostic difficulties, however, have been encountered in babies in whom a rash was present at birth and persisted for several weeks or months. This process has in all cases been considered some form of eczema. Satisfactory biopsies were not performed. They might have revealed atrophic changes co-existing with a superficial inflammatory process. It seems obvious that inflammation alone, terminating in crusts and scaling, cannot account for agenesis of certain parts of the skin. Atrophy of the skin of the scalp is easily recognizable clinically; the skin between the follicles of the body, however, does not give the impression of atrophy in these cases.
Coexistence of pseudopelade and follicular atrophoderma occurred in every case reported. In instances in which osseous disturbances are slight, the presence of the characteristic cutaneous lesions would call for roentgenograms of the bones.

My cases and the patient described by Miescher (1) and Burckhardt (2) were not the only ones in which the typical bone disease was accompanied by skin changes. Vychytil (10) noted in a female baby almost generalized cutaneous changes including the scalp, and scar-like depressions on ulnar region and elbow. Bloxsom and Johnston (11) observed horny plaques of hyperkeratosis and red and thickened skin covering body and scalp of their patient. At 5 and 7 months of age the skin had cleared considerably. Conradi (12) mentioned a new-born girl whose body was covered by scaly, thickened skin. Bateman's (13) and Lightwood's (14) patient showed dry and rough skin of the body. An unusual picture is also described by Bateman (13) in another patient whose palmar skin was found to be furrowed and adherent to deep tissues.

All patients suffering from the complete cutaneo-osseous syndrome were girls. In several other reports on the bone disease of older children, boys as well as girls, there were no accompanying cutaneous changes. They could easily have been overlooked, or might not have been present. All cases showing the cutaneous changes, on the other hand, have also exhibited more or less pronounced osseous disturbances.

Incontinentia pigmenti: Typical incontinentia pigmenti was seen in Case 2 and seems to be present in her younger sister. The bizarre shape of the lesions and their aggregation on the sides of the trunk are characteristic. The usual gradual improvement was noted by the mother, which may explain why the pigmentary disturbance is more pronounced in the younger girl. Whether the mother of the two in earlier years showed signs of incontinentia pigmenti is not ascertainable. The intolerance to direct sunlight of eyes and skin, and the light color of her eyes and hair would not speak against such assumption. Even without examination of all family members, it can be said that incontinentia pigmenti was a familial trait and that at least two female members were involved.

Have previously reported cases of incontinentia pigmenti perhaps contained descriptions of accompanying cutaneous or osseous disturbances suggestive of the category under discussion?

With regard to scalp lesions, Sulzberger (15 a and b) observed scleroderma-like spots both in the case of incontinentia pigmenti originally reported by Bloch and in his own case, the first to be reported in this country. The scalp changes seem indistinguishable from the ones I have noted.

Follicular atrophoderma, however, has not been described in connection with incontinentia pigmenti. There is, however, one report by Schuermann (16a, b and c) of cutaneous changes which makes me think that the author observed follicular atrophoderma rather than depigmented areas of incontinentia pigmenti. In describing a 1½ year old child who suffered from incontinentia pigmenti, he says "There are lesions which show very slight atrophy if tension is applied. Under a magnifying glass the pigmentation does not appear to be evenly
distributed, but a distinct absence at the follicular orifices can be made out.”
Since one main characteristic of incontinentia pigmenti is its bizarre, haphazard
pattern, lesions which are distributed in an orderly and even manner, and which
are limited to the follicles, would be an unusual feature of the pigmentary dis-
ease. On the other hand, the altered reflection of light caused by the depression
of the atrophic follicular orifices could have given the impression of depigmen-
tation. Radiograms of the bones were not made. Bloch (17) and Sulzberger (15)
noted that at birth their patient showed inflammatory redness of the legs as
well as pigmented spots.
In no other case of incontinentia pigmenti were the osseous disturbances so
pronounced as in my second patient. Detailed roentgenograms were not taken
in most instances but one may assume that they would have been if deformities
had been obvious. However, some descriptions of cases of incontinentia pigmenti
suggest shortening or hypoplasia of the bones. In a 30 year old woman recently
shown at Duke Hospital (18) the right lower extremity was slightly shorter than
the left and slight atrophy of the right arm and right leg and a stippled appear-
ance of the skull roentgenogram were noted. The skull and bones of the hands
of Sulzberger’s (15) American case were small and of dwarf type, but apparently
no difference existed between the right and left sides. Siemens’ (19) patient was
microcephalic.
There was, however, no evidence that incontinentia pigmenti was present
early in the life of Miescher and Burckhardt’s case or in my first patient. The
syndrome under discussion can therefore occur with and without incontinentia
pigmenti.

SUMMARY
Pseudopelade and follicular atrophoderma, in combination with skeletal de-
formities such as have been described as end results of chondrodystrophia cal-
cificans congenita were observed in one member of one and in several members
of another family. In addition, other congenital defects such as incontinentia
pigmenti, cataracts and polydactylyia were seen in some members of the family.
The syndrome is caused by fetal inherited hypoplastic changes of the cartilage
and skin. Great variation in the degree of bone involvement has been observed
in the various cases. Lesions resembling eczema are present at birth on body and
scalp. These, as well as the disturbance of the cartilage, undergo various post-
natal stages. The syndrome has been observed only in females.

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DISCUSSION

Dr. Hermann Pinkus: It is remarkable how in the well spaded field of clinical dermatology once in a while new diseases or syndromes turn up which give a new meaning to previously known, but seemingly unrelated odd rarities. When Bloch and Sulzberger first described incontinentia pigmenti more than twenty years ago this seemed to be a rare oddity, and only a few cases were reported at long intervals. Sulzberger later pointed out the connection of the pigmentedary disturbance with other congenital malformations. Now Dr. Curth's thorough investigation fits incontinentia pigmenti, follicular atrophoderma, and other cutaneous defects into the much more inclusive pattern of a congenital abnormality which affects several systems of the body.
Dr. Curth's presentation also may throw new light on cases described as congenital dermatitis herpetiformis (Wilson, Arch. Dermat. and Syph. 44: 58, 1941). Dr. Stephan Epstein (Marshfield, Wis.) has been studying such a case for some time, and being unable to be present today has given me permission to mention it here. The baby developed large bullae twenty-four hours after birth. After some weeks the blisters gave way to papillary verrucous lesions in irregular patterns. As these subsided, the typical bizarre pigmentation of incontinentia pigmenti developed. Several biopsies which I had the opportunity to examine showed at first intraepidermal bullae crowded with eosinophils, later epidermal hypertrophy and inflammatory infiltrate in the corium, and gradually developing melanophore pigmentation in the subpapillary layer. At all times, the epidermis contained peculiar centers of cornification, somewhat resembling abortive sweat ducts. Sweat glands, and possibly hair follicles were completely absent in the affected areas. This baby probably represents another variant of the syndrome outlined by Dr. Curth. The baby is of small stature, but at two years of age has not yet shown any osseous abnormalities.

Dr. Marion B. Sulzberger: I enjoyed this presentation very much. We all know how carefully Dr. Curth has been working not only on this syndrome, but on several other peculiar combinations of nevoid anomalies or of several systems, including the skin. As far as I can recall, no cases observed by Bloch or myself had the severe changes in the bones, although we might have missed minor bony changes. However, many of our cases did have other changes showing that this, too, was a nevoid anomaly, including gliomas, changes in the eyes and pseudo-pelade-like alopecia. I should like to ask Dr. Curth to say a word about another syndrome, osteopoikilosis with dermatofibrosis lenticularis disseminata. She once mentioned to me that this could be distinguished very readily from the combination she has described today.

Dr. Murray C. Zimmerman: Dr. Curth has given us an excellent and detailed description of this syndrome, which appears to be a diathesis like other eponymic syndromes which people studying for the boards learn the night before examinations. Vogt-Koyanagi, Lawrence-Moon-Biedl, Rothmund's, Werner's, etc., for that matter, diabetes, or the eczema-asthma-hay-fever-rhinitis-migraine complex, all seem to be something that "runs in the family". We may expect to see more of such anomalies in the future for several reasons. One is the latent effect of gamma and X-radiation on the germ plasm, which Muller predicts will cause genetic changes from the 3rd generation on.

A second reason is the improved medical treatment of this generation. Within the last two years, the lay press has hailed as medical triumph that for the first time a severe diabetic could carry thru a successful pregnancy. Since, according to White, diabetes is eight times as prevalent in the families of diabetics as in the general population, I wonder just how beneficial this contribution of medicine is to society. The eczema-asthma-hayfever diathesis in my own family killed a cousin twenty years ago, of broncho-pneumonia following status asthmaticus. Today, with penicillin, he would have lived to have asthmatic children, just as the diabetic is living to have diabetic children.

It seems to me that many of these eponymic syndromes could be lumped together under the heading, "Here is another individual conceived of defective germ plasm", and the time spent in detailed description of such cases better spent in discovering how better to predict their occurrence and stop their conception.

Closing Discussion by Dr. Helen O. Curth: I believe that all the lesions which either precede, accompany or follow incontinentia pigmenti should be reviewed in the light of follicular atrophoderma. I myself have been guilty of what the Chairman has called "descriptive dermatology", but this has been remedied by Doctors Pinkus and Epstein. I have one excuse: I saw the children when they showed the end results of the condition. It is entirely possible that the baby Doctors Pinkus and Epstein examined suffered from
the syndrome. It was a small baby. It should be examined for involvement of the scalp, and roentgenograms of the bones should be made.

I intended to speak of dermatofibrosis lenticularis disseminata. This cutaneous disease together with osteopoikilosis represents another cutaneo-osseous syndrome. The cutaneous changes consist of skin-colored, elevated lenticular lesions which show histologically foci of fibromatous thickening. The spotted osseous changes consist of areas of condensation at the end of the long bones. The explanation which I promoted years ago that we are dealing with an hereditary mesenchymal disturbance seems to have been generally accepted by now.

I did not go into the genetics of these cases as I did not examine the family histories thoroughly enough to be sure of the pattern.