A SYNDROME OF INFANTILISM, CONGENITAL WEBBED NECK, AND CUBITUS VALGUS[1]

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The triad, infantilism, webbing of the skin of the neck, and deformity of the elbow (cubitus valgus), occurring in the same individual is unusual, and, to my knowledge, has not been previously reported. It is sufficiently interesting to warrant this report, although the individual signs are perhaps not uncommon. Short neck, due to absence of the cervical spine, was first described by Klippel and Feil (1) in 1912. Only about 40 such cases have been reported to date, and these mostly in the French and German literature.

A similar condition (pseudo-Klippel-Feil syndrome) (2) has been reported, in which there was a numerical variation in, and more or less complete fusion of, the cervical vertebrae. Webbing of the neck was first described by Kobylinski (3) in 1882, and its relation to congenital short neck was suggested by Darchter (4) in 1922. Frawley (5) states that webbing is the most uncommon feature of congenital short neck, the most usual being the absence or fusing of the cervical vertebrae.

Sprengel's deformity (congenital elevation of the scapulae and other conditions, such as traumatic or spontaneous dislocation of the atlas on the axis (Frissell's disease), cervical Potts' disease, and sometimes torticollis) simulates congenital webbed neck. The classic objective signs of Klippel-Feil syndrome, as given by Bauman (6), are: *a)*, absence or shortening of the neck; *b)*, lowering of the hair-line on the back of the neck; *c)*, limitation of motion. Other signs occurring in a certain percentage of cases are: *a)*, torticollis, *b)*, mirror movement, *c)*, facial asymmetry, *d)*, dorsal scoliosis, and other deformities accompanied by difficulty in breathing or swallowing and shortness of breath.

The group of patients presented in this report cannot be classified under any of the above syndromes, inasmuch as the shortening of the neck is merely apparent, due to the webbing, and not real. There is no absence or fusion of the cervical spine in any of these patients. There is some lowering of the hair-line on the back of the neck, but no marked limitation of motion. Torticollis, mirror movements, facial asymmetry, and other signs and symptoms, such as difficulty in breathing or swallowing, shortness of breath, etc., are not present. There is no mental retardation. Deformity of the elbow, consisting of an increase in the carrying angle, or cubitus valgus, is constantly present.

All of my patients present osseous and sexual retardation similar to that

[1] Read before the 22d Annual Meeting of The Association for the Study of Internal Secretions, San Francisco, California, June 13-14, 1938.

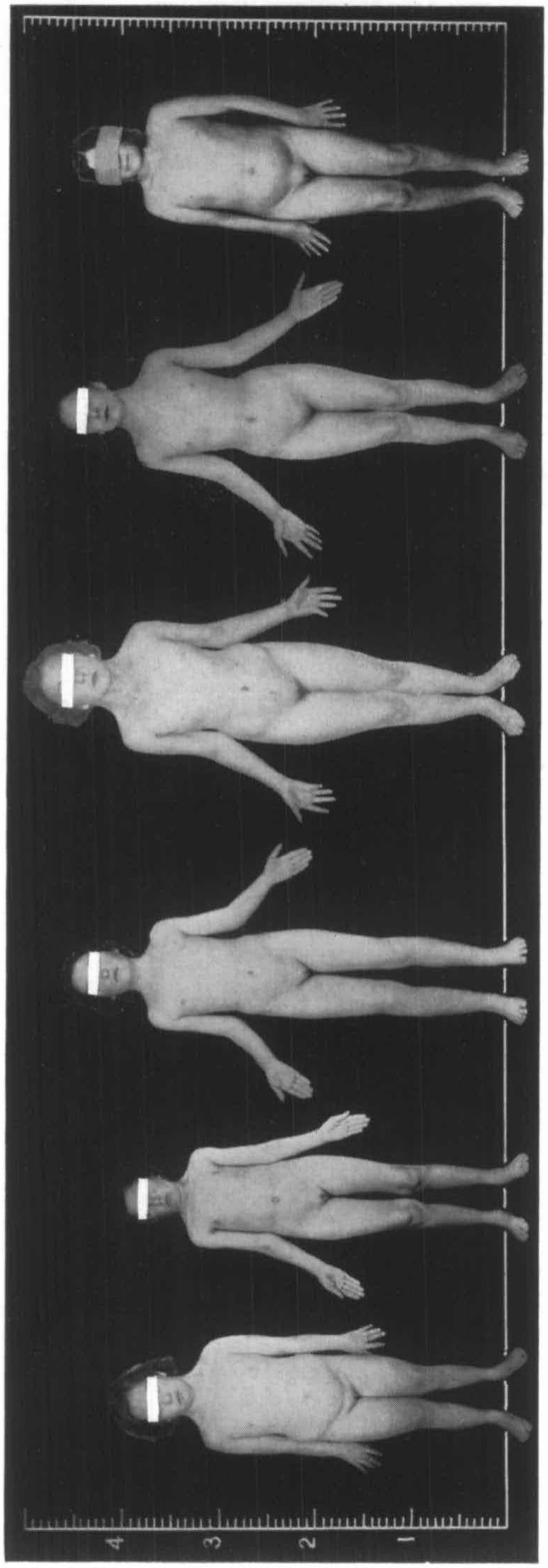

Fig. 1. Patients illustrating the syndrome of infantilism, webbed neck, and cubitus valgus.

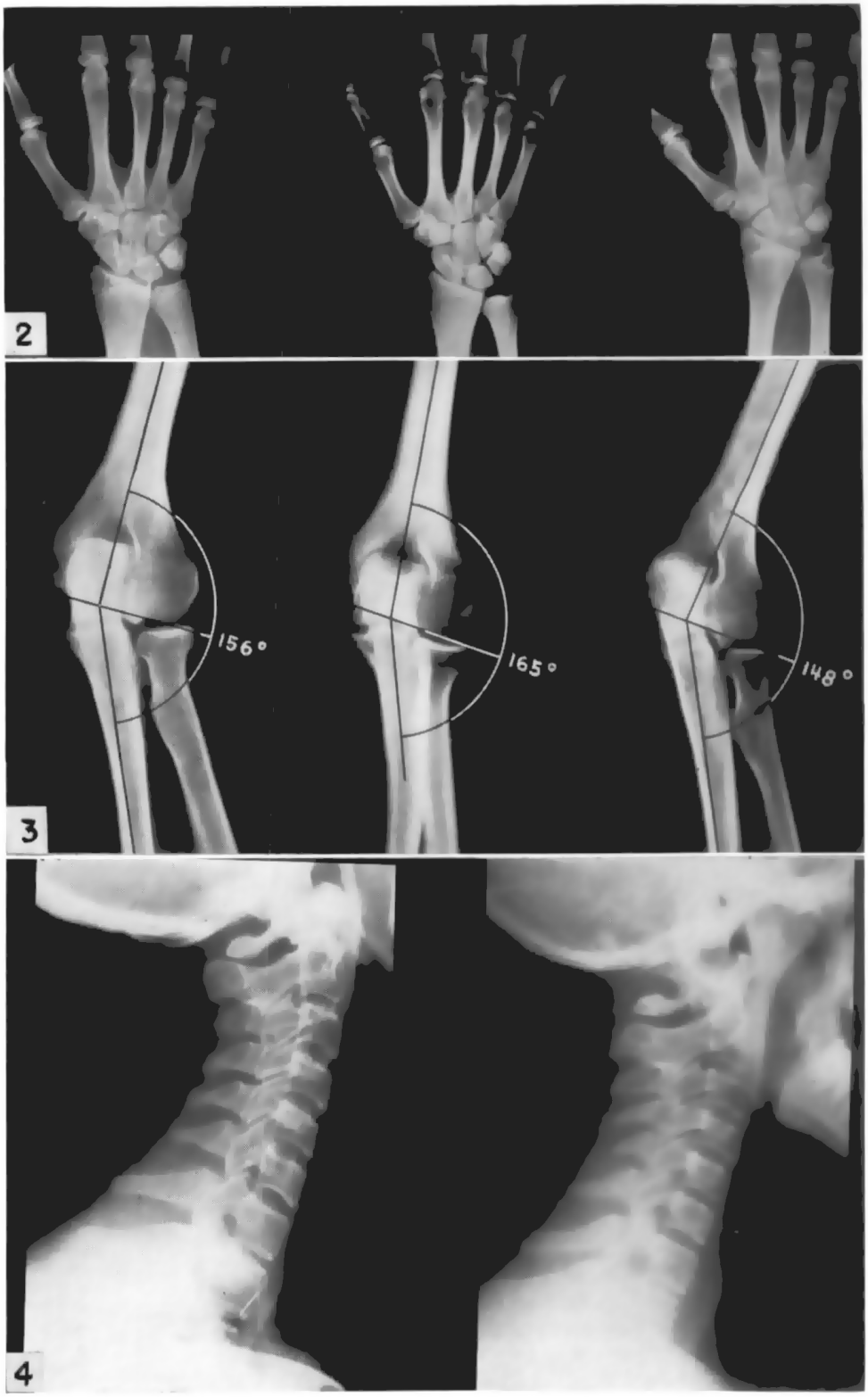

Fig. 2. *Case 1* (left) and *case 2* (right) compared with normal of same age. Note retardation of epiphyseal union.

Fig. 3. *Case 1* (left) and *case 2* (right) compared with normal of same age. Note increased carrying angle in both patients.

Fig. 4. *Case 1* (left) and *case 2* (right) showing normal cervical spine.

associated with hypoantuitarism, or the Lorain-Levi type of dwarfism. Funke (7) reported a case of 'pterygium colli,' which was somewhat similar to mine, in that the patient, aged 15 years, was retarded in growth and sexual development; however, no reference was made to any osseous deformaties.

CASE REPORT

Case 1. D. G., a female, aged 16 years 3 months, was first seen by me on March 28, 1932. She walked, talked, and teethed at the normal age. Her stature has always been less than that of her playmates of the same years. The patient showed somatic and sexual underdevelopment of the Lorain-Levi type. Her height was 53 in. (average 63.35 in.), and weight 78.25 lb. (average 118 lb.). There was no evidence of any secondary sex characters. Her breasts were quite masculine, and no glandular tissue was palpable.

Gynecological examination by Dr. J. B. Eskridge revealed greatly delayed development of the labia; the vagina barely admitted the index finger and was about 1.6 in. deep. The mucosa was dry and of the infantile type. The cervix was about the size of a pea, and there was an apparent congenital absence of the uterus and ovaries.

There was an internal squint of the right eye. The neck appeared very short, and there was a wing-like fold of skin extending from the mastoid region almost to the acromion. The hair-line was very low on the back of the neck. There was a marked deformity of the carrying angle of the elbow. No other abnormal physical findings were elicited.

Laboratory. The erythrocyte count showed a very moderate secondary anemia. The blood serology and chemistry gave normal reactions. The B.M.R. was +8 per cent. Roentgenograms of the skull and sella, cervical vertebrae, and hips indicated normal development. A retardation of the epiphyseal union on the metacarpals and phalanges was noted. The carrying angle at the elbow measured 156° (fig. 3).

Injections of the anterior-pituitary growth fraction, antuitrin-G, were begun, and over a period of 19 months she received 1600 cc. of this substance. Her height increased 1.75 in. (to 54.75 in.) during this period. Shortly after discontinuance of the growth hormone the patient left the city, and nothing further was heard from her until March, 1937. At that time, her height was 56.50 in. and her weight 88 lb. During the 3-year interval without treatment she had grown 1.75 in. and had gained 3 lb. There had been little, if any, change in her general appearance. The breasts and nipples continued very infantile, and there was no apparent change in her internal or external genitals. There was slightly increased hair growth over the lumbo-sacral region and over both trapezi down to the level of the scapulae. A great number of pigmented moles were noted over the trunk, with a few on the face, and there was some slight hair growth on the upper lip.

At this time, injections of 2½cc. anterior-pituitary gonadotropic (25 U)[2] were administered 3 times weekly and continued for 30 days. Then, injections of 1 cc. daily were begun and continued without interruption until Oct. 11, 1937. At this time, the gynecologist reported a scant growth of hair on the mons, with rather abundant growth over the labia majora; the vagina was much larger than on the previous examination, admitting one finger very easily, and if the vulvovaginal orifice were large enough, two fingers could be admitted. The vaginal length was

[2] Antuitrin-G, antuitrin-gonadotropic, and theelin generously supplied by Parke, Davis & Co.; progynon-B by Schering Corp.; anterior-pituitary sex hormone, and maturity factor by Ayerst, McKenna & Harrison.

3.5 in., rugae normal and moist. The probe passed through the cervical canal to a depth of 2.2 in. With the probe in the cervix, another attempt was made to locate the uterus, but the organ or adnexa could not be palpated. It was thought the probe passed through the Müllerian duct. The cervix was 0.75 cm. in diameter, very rudimentary and short. There was no evidence of development of the nipples or breasts. It is interesting to note that there had been a definite growth in the size and depth of the vagina, to the point that it would be possible for her to marry and carry on normal marital relations.

Anterior-pituitary sex hormone (330 U maturity factor, and 75 U thyrotropic), 1 cc. daily, plus 40,000 U of theelin per week were given until Feb. 1938, at which time it was noted that the pubic hair had increased; a small uterus about the size of a pecan was palpated, and glandular tissue could be palpated in the breasts. Her weight was 94 lb., and height 57 in.

Because of the multiple injections and the fact that the buttocks were becoming quite infiltrated, it was decided to discontinue the daily injections of anterior-pituitary sex hormone but continue the 10,000 U of theelin 4 times weekly. Following the injection of a total of 170,000 U of theelin during the next four weeks, dosage was increased to 50,000 U of progynon-B 3 times weekly. Following the 6th injection, an apparently normal menstrual flow began and lasted for 3 days. She stated that the flow was moderate in amount and no pain was experienced. The injections were discontinued during this week of flow and then continued as before. Following 7 injections, or a total of 350,000 U of progynon-B, and after a rest period of 7 days, a second menstrual flow began, with an average amount of discharge for 2½ days, then scant for 3 days. No pain was encountered. Whether or not the two periods of bleeding were the true menstrual type or result of the large doses of estrin I am unable to say.

To date, she has received a total of 17 injections (850,000 U) of progynon-B. Her height is 57 in., and weight 99 lb. Pubic hair is increasing. Labia minora are still small, but showing definite evidence of development. Labia majora are small, but appear normal. The vagina easily admits one finger and is about 2.4 in. long and considered normal in size and shape for a person of this age. The cervix is about 1 inch across and much larger than on previous examination. A fundus uteri can be definitely palpated, being 1 inch across and about 1 inch thick, and approximately 2 in. long. The cervix forms about one-half of the uterus. Glandular tissue is now palpable in both breasts, and they are assuming an adolescent contour.

Case 2. O. D. L., a female, aged 18 years, was first seen on Sept. 7, 1934, because of statural underdevelopment and non-appearance of the secondary sex characters. Her height was 55 in. (average 65 in.), weight 86 lb. (average 126 lb.). There was nothing unusual in her history during infancy or childhood, with the exception that she had always been smaller than other children. She had always made excellent grades in school and at this time was taking a secretarial course. There had never been any serious illnesses. One brother, aged 15 years, and one sister, aged 25 years, father and mother, are all of average height and weight. Her general appearance was that of an anterior-pituitary dwarf of the Lorain-Levi type. There was complete absence of any secondary sexual characteristics. The breasts were flat, with no glandular tissue palpable, and the nipples were rudimentary. The neck appeared quite short, and on either side the skin appeared as a wing-like fold, extending from the mastoid almost to the acromion process. There was an abundance of black hair on the scalp, extending down the back of the neck to a point slightly below the first dorsal vertebra. The remainder of the body was devoid of hair, with the

exception of very scant growth in the axillae and a few scattered over the pubis. The facial features were small, clear-cut, and there was no obvious asymmetry of the face. The eye muscles were intact. There was a marked increase of the carrying angle of the elbow.

Vaginal examination by Dr. Eskridge disclosed the labia markedly underdeveloped, and an absence of hair on the mons, with very scant growth over the labia. The vagina was too small for digital examination, and the uterus and adnexa could not be palpated. A small structure about the size of a pea was believed to be a rudimentary cervix.

Laboratory. The blood cytology, serology, and chemistry were all within normal limits. B.M.R. was +7 per cent. Chemical and microscopical examination of the urine revealed no abnormal constituents. Roentgenograms showed retardation of epiphyseal union on metacarpals and phalanges; very marked cubitus valgus; small and shallow sella; a slight osteoporosis of the spinal column; and separate ossification centers on both transverse processes of the first thoracic vertebra. The carrying angle of the elbow measured 148° (fig. 3).

Anterior-pituitary growth hormone, 2 cc. 3 times weekly, was prescribed, and injections were continued for approximately 5 months without any appreciable increase in her height. In Oct., 1936, injections of 1 cc. maturity factor (200 U) 3 times weekly were begun and continued until April 1, 1937. Examination at this time revealed increased growth of hair on the labia and scanty growth on the mons. The labia minora were rudimentary and small. The vagina barely admitted the index finger, but the rugae were normal and moist. The cervix, about 1 cm. in diameter, did not admit a probe. The uterus and adnexa were not palpable.

Injections of antuitrin gonadotropic, 2½ cc. 3 times weekly, were then begun, and over a period of 7 months she received 70 injections, or a total of 4,375 U. At the end of the treatment period no development of the breast tissue was evident. However, the pubic hair was becoming more abundant. The vaginal canal was moist and admitted the index finger very comfortably. The uterus and ovaries still could not be palpated. At this time, her weight was 85 lb., and height 55.75 in.

Anterior-pituitary sex hormone, 2 cc. twice weekly, was begun Oct. 11, 1937, and continued to date (76 injections). At the present time her height is 56 in., and weight 91 lb. There is definite development of the labia majora. Introitus admits one finger snugly. The cervix is palpable, although still infantile, but the uterus has not yet shown signs of developing.

Case 3. V. C., a female, aged 15 years 4 months, was a normal full-term baby who had her first tooth at 9 months. She walked and talked at 13 months. Her statural development was apparently normal until the age of 9 years, but she had matured very little since then. There was no mental retardation.

The patient's general somatic development was definitely retarded, although proportional. Her height was 50 in. (average 62.27 in.), and weight 74 lb. (average 115 lb.). The upper, lower, and half-span measurements were 25 in., respectively. The neck was short and wide, and the hair-line low posteriorly. There was a moderate increase in the carrying angle of the elbow, and an internal squint of the right eye. There was no obesity. The extremities were quite acrocyanotic. The skin and hair were of normal texture. A slight hypertrichosis of the forearms was present. No breast development was evident. There were a few scattered hairs over the mons veneris. Rectal examination revealed a very infantile uterus, but no adnexa were palpated.

Laboratory. The blood count, Wassermann reaction, and chemical examinations,

including serum calcium and phosphorus determinations, were all within normal limits. The urinalysis was normal. B.M.R. was +9 per cent. Roentgenograms of the wrists, shoulder, knee, skull and sella turcica, cervical spine, and elbows revealed normal osseous progress.

She received anterior-pituitary growth hormone (10 R.U.), 3 cc. subcutaneously every other day over a period of three months, with an increase in her height of 1.3 inches (theoretical normal increment 0.15 in.). Further treatment during the following 6 months, interspersed with rest periods, resulted in no further growth. In a letter received March, 1938, the mother stated that the patient's height was the same as when the growth hormone was discontinued 2½ years previously, and that sexually she remained quite infantile.

Case 4. M. B., a female, aged 16 years, consulted me first in Sept., 1934, because of dwarfism and sexual underdevelopment. Her height was 53.75 in. (average 65 in.), and weight 69 lb. (average 128 lb.). She was the second child in a family of 5, and had always been smaller than other children of her age. Examination revealed a definitely underheight and undernourished girl, with no visible evidence of secondary sex development. The neck was short and somewhat broad at the base, although there were no marked folds of skin comparable to the cases reported above. The facial features were very delicate. There was a normal amount of brown hair on the scalp, but none in the axillae or on the pubis. There was a marked increase in the carrying angle of the elbow, as observed in the other individuals of this series.

A scanty growth of hair appeared on the labia majora only. The labia minora were rudimentary, and the vagina would not admit the index finger. On rectal examination the broad ligament was found to be indistinct. There was a small mass about 0.5 in. in diameter, which was interpreted to be the cervix. The corpus uteri and ovaries were not palpable.

Roentgenograms of the skull showed an increased deposition of calcium along the coronal sutures. The sella turcica was well within normal limits, and there was no erosion of the clinoid processes. A rather marked degree of demineralization of the carpals and metacarpals, and the distal end of the ulnae and radii was demonstrated. The epiphyseal lines of the ulnae and radii and proximal ends of the metacarpals were quite visible, showing some delay in the union of the epiphyses. The cervical vertebrae were of normal number and appearance. No other laboratory procedures were recorded. No treatment.

Case 5. M. T., a female, aged 23 years, was referred to the Endocrine Clinic, University Hospital, Feb., 1935, because she was under height and had not developed sexually. She stated that she stopped growing at the age of 8 years, and was considerably disturbed because of the fact that her associates treated her as a little girl and because she feared she would never be able to marry and have a home. Her height was 52.25 in. (average 65 in.), and weight 76.75 lb. (average 130 lb.). She presented a typical picture of somatic and genital retardation with a rather oldish face. She had a very short, broad neck, with folds of skin extending from the mastoid to a point just proximally to the acromion. The hair-line extended well down the back of the neck. There was a very small amount of axillary hair, and none on the pubis. The breasts were flat with underdevelopment of the nipples. There was a marked increase in the carrying angle of the elbow.

The vaginal examination revealed very small, underdeveloped labia. The vagina admitted one finger. The uterus was about the size of that of a 6 or 7-year-old child. The ovaries could not be palpated.

Roentgenograms of the skull and sinuses revealed no apparent pathology. The

epiphyses of the femurs were demonstrated. A considerable lack of calcium in the bones of the pelvis and thighs, and a demineralization in the distal end of the humerus and proximal ends of the ulna was evident, with an apparent beginning cystic degeneration in the right and left ulna. Anteroposterior and lateral views of the cervical spine revealed a spinabifida of the first cervical vertebra. The bodies of the vertebrae, however, were of normal size and position. Further laboratory investigation was refused by the patient. No treatment.

Case 6. M. A. S., a female, aged 15 years, was seen in the out-patient department of the Endocrine Clinic, University Hospital, March 1, 1937, because of her dwarfism and sexual underdevelopment. She was 51.75 in. in height (average 62.27 in.), and weighed 69 lb. (average 115 lb.). She was a normal full-term baby, and walked, talked, and teethed at the usual age, but had always grown very slowly. She was mentally alert and ahead of her class in school—an honor student.

Physical examination revealed evident infantilism, with very short neck and wing-like folds of skin extending from the mastoid region to the acromion. The hair-line was very low. There was no axillary or pubic hair. The increased carrying angle of the elbow was quite marked. Vaginal examination could not be made because of the infantile vagina. Rectal examination revealed a minute mass which was interpreted as an infantile uterus. The ovaries were not palpable.

Laboratory. The blood cytology, serology, and chemistry were all within normal limits. Roentgenograms of the cervical spine and pelvis, including both hip joints, were normal. The radial deviation of both elbows was quite prominent. The radii appeared shorter than normal, and the heads were deformed. The right wrist showed an absence of the distal epiphyses of the radius, and the carpal bones were atrophic. There was also a flattening and partial sclerosis of the epiyhpses of the left ulna and radius. These observations indicated a growth disturbance; however, it was not determined whether this was of nutritional or endocrine origin. Chondrodysplasia did not seem likely. No treatment was given.

Case 7. M. B., a female, aged 16 years, was referred to the Endocrine Clinic, University Hospital, Dec. 27, 1935, because of her short stature and lack of sexual development. She was 48.50 in. in height (average 63.35 in.), and weighed 46.50 lb. (average 118 lb.). Her twin sister, who was with her, was 63 in. in height, and weighed 125 lb. The history was rather interesting, in that the patient weighed 2½ lb. at birth, while her twin weighed 5 lb. Her weight at one year was 5 lb., and that of her sister 15 lb. She had one brother and one other sister of average height and weight for their age. The parents stated that she had gained none in height or weight during the past 5 or 6 years, and that she grew very slowly before that time. She presented a rather typical picture of infantilism with congenital webbed neck and cubitus valgus. Her sister was normally developed sexually, and normal menarche was established at the age of 12 years.

Routine laboratory examinations gave essentially normal findings. Roentgenograms of the skull and sella turcica appeared normal, except for some slight demineralization. X-rays of the extremities revealed normal osseous progress, but evidence of osteoporosis. The cervical vertebrae were normal in number and appearance. No treatment was given.

SUMMARY

Infantilism with webbing of the neck and deformity of the elbow (cubitus valgus), occurring in the same individual is extremely rare, and, to the author's knowledge, has not been previously described. This unusual phenomenon was

observed exclusively in seven female patients, aged 15 to 23 years. Among the characteristic signs were retardation in growth and sexual underdevelopment. Webbing of the skin of the neck was slight to marked. Absence or fusion of the cervical vertebrae was not demonstrated, and the shortening of the neck was merely apparent, due to the webbing, and not real. The posterior hair margin extended well down on the neck. Deformity of the elbow, consisting of an increase in the carrying angle, or cubitus valgus, was constantly present. Movements of the head and arms were not hindered. Fascial asymmetry, dorsal scoliosis, and other deformities, mirror movement, difficulty in breathing and swallowing, shortness of breath, or mental retardation were not present in this group of patients.

Laboratory examinations of the blood and urine showed findings that were entirely within normal limits. Roentgenograms of the skull, cervical spine, elbow, wrist, and pelvis showed no abnormalities with the exception of demineralization and evidence of delayed union of the epiphyses in 6 cases. Treatment with pituitary growth hormones has been unsatisfactory. There was definite genital development following administration of the anterior pituitary gonadotropic hormone in the two cases treated.

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Addendum. Since this paper was written three additional cases have been observed making a total of ten patients to date.