

Landmark Case Reports

POLYGLANDULAR SYNDROME CASE XLV (Surgical No. 27140.)

A syndrome of painful obesity, hypertrichosis, and amenorrhoea, with over-development of secondary sexual characteristics accompanying a low grade of hydrocephalus and increased cerebral tension. Pituitary, adrenal, pineal or ovary? Subtemporal exploration and decompression.

Dec. 29, 1910. Miss M. G., a Russian Jewess, single, aged 23, was referred to us by Dr. De Witt Stetten of New York. One of a numerous and healthy family, she was well until 16 years of age, having been free from the customary children's ailments.

The Present Malady. Her *menses*, which began at the age of 14, were regular for two years and then, 7 years ago, suddenly ceased, coincident with attacks of temporal headache, pain in the back and swelling of the feet.

Her *vision* began to fail at this time. There have since been periods of diplopia. Nausea with vomiting has occurred with the more severe headaches. She has had more or less intracranial discomfort ever since; often aching pains in the eyes. Dizziness and unsteadiness have been marked at times.

She has become stout, her *weight* increasing from 112 pounds two years ago to 137 pounds at present. *Other noteworthy symptoms* have been insomnia, tinnitus, extreme dryness of the skin, frequent sore throat, shortness of breath, palpitation, purpuric outbreaks, marked constipation, sudden attacks of dizziness with falling, a definite growth of hair and mustache during the past few years with marked falling out of the hair of the scalp. She feels chilly and cold all of the time and suffers from insomnia rather than from drowsiness. Muscular weakness is extreme and there is much complaint of backache and epigastric pains.

Physical Examination. A young woman 4 feet 9 inches in height, of extraordinary appearance. Her round face is dusky and cyanosed and covered with a fine growth of hair, which is particularly noticeable on forehead and upper lip (Fig. 281 Case XLV. Showing hirsuties of lip and forehead). Mucous membranes are of bright color despite her frequent bleedings.

Visceral (abdominal and thoracic) and *cardiovascular examinations* negative except for high tension of the pulse. *Neurological examination* reveals practically nothing other than the signs of intracranial pressure.

There is a definite tendency toward *hæmophilia*. The skin bruises easily and large spontaneous *ecchymoses* occur frequently. *Epistaxis* is almost a daily occurrence. She has bleeding haemorrhoids. Lumbar puncture, pricking of ear, etc., cause a wide subcutaneous extravasation.

Blood no abnormalities. RBC 5,300,000; WBC 12,000. Hgb. 85 per cent, Coagulation time 3 minutes. Wassermann negative; also for cerebrospinal fluid. *Blood pressure* high, averaging 185 mm. *Temperature and pulse* normal.

Analysis of Hypophyseal Manifestations. (a) *Neighborhood Symptoms:* The stereoscopic X ray shows what appears to be a somewhat thinned out sella of normal configuration but of small size, measuring only 1.0 cm. by 0.9 cm. in depth.

Eyes: Slight bilateral exophthalmos, greater on left than right. The optic nerves are congested and show a low grade of choked disc with no atrophic pallor. No present oculomotor palsies, though diplopia has occurred. *Fields* show constriction, particularly of temporal margins, with interlacing of colors (Fig. 282 Case XLV. Fields with constriction and color interlacing.). *Acuity:* Left and right 10/40.

Epistaxis has been frequent for years, often excessive, with daily nose bleeds. There has occasionally been a sudden discharge of clear fluid (rhinorrhoea?) in amounts sufficient to soak a handkerchief. Direct examination of pharynx negative.

(b) *General Pressure Symptoms.* Pressure headaches: a low grade of choked disc: color interlacing: nausea and vomiting: dizziness: pain in eyeballs: exophthalmos.

(c) *Glandular Symptoms. Skeletal:* A low stature (144 cm.) and delicate framework: extremities small, fingers tapering: nails long, well formed, no crescents. Her head squats on her high shoulders: she has the attitude and figure of a full term pregnancy (Fig. 283 Case XLV. Showing small stature, adiposity, cyanosis, purplish *linæ atrophicæ*).

The epiphyseal lines (radial and phalangeal) are still radiographically visible (Fig. 284 Case XLV. X ray of middle finger (unreduced) showing traces of epiphyseal lines. Fig. 285 Case XLV. X ray of wrist showing incomplete epiphyseal ossification). The *teeth* are widely spaced, notched, and suggest Hutchinsonian change.

Cutaneous. Skin during the past few years has become rough and dry and has a blue and dusky appearance. The body and extremities show an especial degree of cyanosis. There are a number of large subcutaneous ecchymoses over the lower extremities. The lineæ atrophicæ over the abdomen are of a deep brownish purple color (cf. Fig. 283). There is considerable *pigmentation*, particularly of eyelids, groins, pubes and areolæ. Mucous membranes clear.

Hair of the head is thin and sparse. There is an abundant new growth of fine black hair over forehead, cheeks and upper lip. The hair of the eyebrows and temporal regions merges (Fig. 281). A fine hirsuties over back and hips.

The *subcutaneous tissues* feel boggy and tense. *Adiposity*, particularly limited to the abdomen, is marked and of recent origin. It is very painful and tender (*adiposis dolorosa*). No lipomata, but the fat is coarsely nodular.

Carbohydrate tolerance high. Assimilation limit for laevulose about 200 grams. Slight *thermic reaction* to anterior lobe injection of 0.2 gram hypodermically, with sensation of warmth and profuse perspiration.

Other Ductless Glands. *Pineal:* Possibly early Frühreife; hypertrophic genitalia; hypertrichosis; low grade of hydrocephalus. *Thyroid:* Right lobe somewhat enlarged; patient has noticed an increase in the size of her neck, which is partly from fat, however. *Adrenal:* Extreme pigmentation; asthenia; high blood pressure; tendency to bleeding; possibly the hypertrichosis. *Thymus* negative. *Ovaries* not palpable; infantile uterus; complete amenorrhoea.

There were no clear *therapeutic indications* except for the relief of intracranial pressure and in view of the tendency to bleeding a decompression was thought unjustifiably hazardous. She was discharged *Jan. 31, 1911*, and returned again for further study on *July 28th*, her condition largely unchanged, though the visual fields were even more constricted and vision was lowered to 15/70 left and 15/100 right.

Sept. 6, 1911. Operation. Right osteoplastic resection combined with subtemporal decompression; lumbar puncture; attempted exploration of interpeduncular region by overhanging brain method. Satisfactory view of space not obtained. Negative findings except for unusual thickness and vascularity of diploe, and tense and wet brain with low grade of hydrocephalus. Recovery was uncomplicated and an unexpected degree of relief was afforded by the decompression.

Subsequent Notes. A month later: no further headaches; subsidence of neuroretinal oedema; blood pressure low (130 140); sleeping better; a loss of 12 pounds in weight. Despite this improvement in the signs and symptoms of her intracranial disorder, she continued to complain of backache, of pain in the left side and swelling of the extremities. An exploration of the adrenals is under consideration.

COMMENT. The syndrome shown by this patient exemplifies the fact that terms such as Bartels' *dystrophia adiposo-genitalis* and Dercum's *adiposis dolorosa* may be made to include cases which neither of these writers intended to come within the scope of these designations. All of the cardinal symptoms of both of these maladies were shown skeletal undergrowth, adiposity and sexual dystrophy on the one hand, painful and tender adiposis with asthenia and psychic disturbances on the other.

The case is an instance of the combination of intracranial pressure symptoms with amenorrhoea, adiposity and low physical stature—a syndrome which might well be due to hypophyseal deficiency. But here, however, the similarity to the cases of hypopituitarism, which have been heretofore discussed, ends, and instead of the sexual infantilism of reversible type with which we have become familiar, the patient shows the secondary sexual development, mammary and genital, of a multipara, with unusual and recently acquired hirsuties.

A symptom complex of this type has been described with in association with certified *adrenal lesions*, which makes it appear that the adiposo genital syndrome may occur with derangements of other of the ductless glands than the hypophysis itself. The following case recently reported by Launois, Pinard and Gallais¹⁵⁴ will serve in illustration.

Their patient was a young woman of 19, with increasing weakness, lumbar pains and various nervous and mental disorders. The skin was harsh, dry, of a grayish brown tint, and covered with brush like, bluish scars from stretching by the excessive and rapidly acquired panniculus. She had grown a beard and mustache, and resembled a man of 25 more than a female of 19. There was a double choked disc. A tumor finally became palpable in the left hypochondrium, and at autopsy this proved to be *a malignant adenoma of the left suprarenal gland*.

Other cases with precisely the same syndrome have been recorded in the past by Linser (1903),¹⁶⁸ Bulloch and Sequeira (1905),³⁰ Guinon and Bijon (1906),^{105a} Bortz (1909),²³ and Bovin (1910).^{23a} In all of them adenomatous or hyperplastic adrenal tumors have been found and in some instances the constitutional transformation of the afflicted individual into an adipose and hirsute creature has been extraordinary. This has been particularly striking in some of the preadolescent patients who have shown a premature development

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of the sexual organs and accessory genital structures together with an astonishing hypertrichosis.

It will thus be seen that we may perchance be on the way toward the recognition of the consequences of *hyperadrenalism*. Heretofore the only recognizable clinical state associated with primary adrenal disease has been the syndrome of Addison, and the grouping of these cases may possibly add one more to the series of clinical conditions related to primary maladies of the ductless glands

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