ARGONZ AND DEL CASTILLO SYNDROME

(A Case Report)

by

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A syndrome with amenorrhoea and galactorrhoea has recently been described by Argonz and Del Castillo and Forbes and Associates, which is very similar to the Chiari-Frommei Syndrome but unrelated to pregnancy.

These patients had a lower than normal follicle-stimulating hormone excretion. Of particular interest was the finding of pituitary tumour in many of these cases. Forbes reported 15 such cases, 8 of which had evidence of tumour, and in 3 of these, operated upon, a chromophobe adenoma was found. Forbes believes that all these cases, with or without tumour, have an over-production of prolactin, so the fundamental mechanism of this syndrome and that of Chiari Frommel may be the same. The only distinguishing feature of the Chiari-Frommel Syndrome is that it occurs immediately following a pregnancy. Greenblat described 2 cases. Both had headaches and increased feeling of tiredness. In each case studies showed imbalance in pituitary activity, possibly due to a chromophobe adenoma that permits the production of an excessive amount of prolactin. When the syndrome appears soon after a pregnancy but in addition shows evidence of a pituitary tumour, it is difficult to classify the case. The following is a report of a case of secondary amenorrhoea associated with galactorrhoea unrelated to recent pregnancy and having a pituitary tumour and hence falling in the category of the Argonz and Del Castillo Syndrome.

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Case Report

A 27 years old female was admitted, on 9th November 1964, for secondary amenorrhoea of four years' duration.

Menarche was at age 12 years. Patient was married at the age of 13 years and had one full-term normal delivery at home at 15 years. The only complication during pregnancy was oedema of the feet. There is no history of post-partum haemorrhage or puerperal sepsis. The child was breast-fed for four years. Her periods were regular for sometime until the onset of amenorrhoea. The last two periods prior to amenorrhoea were scanty. Dimness of vision in the right eye occurred four months ago; at first distant vision was affected, later near vision and at present even moving fingers cannot be seen. Headache developed off and on and was worse on going out in the sun.

Her past menstrual history was normal. The cycles were regular lasting 4 to 5 days, the flow was moderate, there was no dysmenorrhoea. This woman had been treated elsewhere, withdrawal bleeding being induced by two injections of Estroprogyn every month for a year, but as soon

as the injections were stopped she had amenorrhoea. Last year a course of 32 injections of clinoestrol over a period of five months had been given producing only episodes of withdrawal bleeding.

On examination — The patient was well-nourished, of average build and average intellect. She answered questions coherently and was very co-operative. She seemed to have lost weight. Her weight 6 months ago was 132 lbs. and now 118 lbs.

There was no evidence of acromegaly or abnormal distribution of fat.

Her measurements were as follows:

Height — 62¾″; span — 65½″; bust — 36″; waist — 29″; hips — 36″.

There was a thin but normal growth of hair on the head without premature greying, axillary and pubic hair being scanty. The breasts were well developed and still secreting milk though her only child is over 10 years old and in spite of 32 injections of clinoestrol.

There was no evidence of gross anaemia and no enlargement of the thyroid gland. The pulse rate was 72. BP 115/70.

The central nervous system was normal except for right optic atrophy with partial concentric contraction of the visual field on the right side.

On pelvic examination external genitalia were small. The uterus was small in size and retroverted. The adnexa were not palpable. Cervix and vagina were normal.

The following investigations were done. R.B.C. 4,050,000 cu.mm. Haemoglobin — 10.6 gms.

Total W.B.C. — 7,200 per cu.mm., neutrophils — 50%, eosinophils — 6%, lymphocytes 43%, monocyte 1%.

Glucose tolerance curve —

	Blood sugar	Urine sugar
Fasting sample	105 mgm. %	Nil
1st sample ½ hour after ingestion of glucose	144 mgm. %	Nil
2nd sample	100 mgm. %	Nil
3rd sample	95 mgm. %	Nil
4th sample	84 mgm. %	Nil

Serum electrolytes —

Chlorides 560 mg./100 ml. Potassium — 20 mg./100 m./serum.

Sodium — 338 mg.100 ml. serum.

Routine examination of urine was normal.

Electro-cardiogram—within normal limits.

Fundoscopy — Right eye — disc pale, primary optic atrophy, vision, perception of light. Left eye — temporal pallor. Vision 6/18.

Perimetry — Right — partial concentric contraction suggestive of progressive (developing) optic atrophy. (Fig. 1).

Vaginal smear — showed moderate estrogen activity.

Endometrial biopsy — very scanty tissue, atrophic.

X-ray skull — Sella turcica very large with destruction of clinoid processes suggestive of increased intracranial tension due to intrasellar tumour. No evidence of abnormal extracranial calcification seen. (Fig. 2).

X-ray chest — minimal fibrotic Koch's lesion left infraclavicular region.

Adrenal-cortical function:—

24 hours urinary total neutral 17-Ketosteroids.

5.9 mgm. (24 hrs. sample).

Thorn test — There was no drop in eosinophils.

Thyroid Function —

Basal metabolic rate — + 11.5% after temperature correction.

Blood cholesterol — 215 mgm+.

Protein-bound serum iodine — 8.11 mcgm./100 ml.

The Metapiron test to determine the function of the anterior lobe of the pituitary could not be done as metapiron was not available.

The patient was advised to undergo an operation for removal of the tumour but she refused to take the risk as the only disability she had was amenorrhoea and dimness of vision in one eye only.

Discussion

Secondary amenorrhoea is sometimes due to a pituitary tumour as in this case. Hypopituitarism is seen

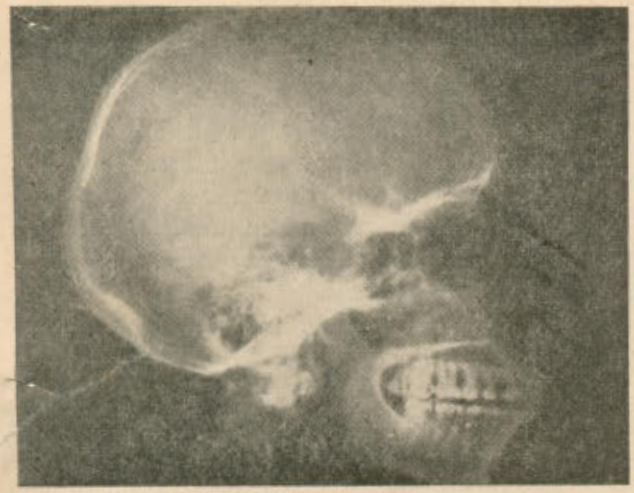

Fig. 1
Perimetry showing partial concentric contraction of the right side suggestive of progressive (developing) optic atrophy.

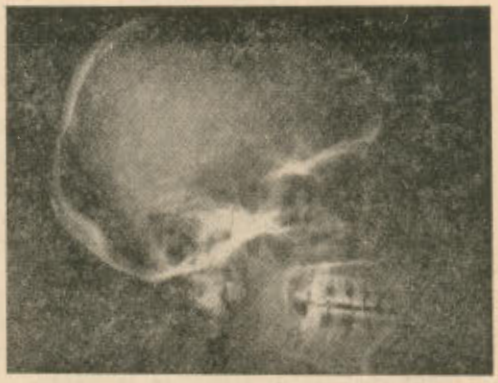

Fig. 2
X-ray film of the skull showing enlargement of the Sella Turcica with destruction of the clinoid processes.

with chromophobe adenomas of the anterior lobe. These tumours erode or balloon out the sella turcica, the enlargement being evident on ordinary skull roentgenograms as in this case. Gonadal function showed earliest impairment with progressive anterior lobe damage, amenorrhoea being present in all women at the time of operation in the Neurosurgical clinic of the University in Cologne. The incidence of recurrence in the purely chromophobe adenomas was 8.9% and recurrence was manifested by severe headache and visual disturbances. Henderson states that the incidence of pituitary tumours in Dr. Cushing's clinic is 17.8%. A normal sella may be found in 2 to 8 per cent of the patients with chromophobe adenoma. Since films of the sella generally give no information as to an extrasellar extension additional examination such as lumbar encephalography and carotid angiography should be done.

Lumbar encephalography allows a selective filling of the ventricular system and of the suprasellar cisterns which permits a diagnosis of even a very small suprasellar extension. Carotid angiography will demonstrate the lateral displacement of the intracavernous portion of the carotid artery by a growing adenoma. Six cell categories can be distinguished in the anterior lobe of the hypophysis, each of which appears to be associated with a particular hormone. The distinguishing staining reactions of the various cells are due not to the cytoplasm but to the secretory granules in the cytoplasm. Acidophilic cells in pituitary adenomas are of 2 varieties, one of which is erythrosinophilic and secretes prolactin, the other being "Orangeophilic" is involved in acromegaly. Both

the typical adenoma and the mixed adenoma, which often look like the chromophobe type contain these secretory (alpha) particles; adenomas not associated with endocrine symptoms appear to be devoid of secretory granules.

One of the interesting features of this case is the visual disturbance which is unilateral. The secondary constitutional disturbances of pituitary insufficiency, due to compression of normal glandular tissue, are so inconstant and unimportant that the disorder is not likely to be recognised until the tumour is large enough to compress the optic nerves, chiasma or tracts. In cases with an early clinical syndrome the growth protrudes just sufficiently above the level of the sella to produce optic or chiasmal compression. Its rounded dome is covered by the stretched diaphragma sellae and the only serious symptom is impaired vision. As the tumour grows it bursts through the dural capsule in one or more directions.

Only one eye is affected when there is involvement of one optic nerve, either by lateral extension of the adenoma beneath the diaphragma or by a nodule of tumour which has penetrated through the diaphragma, thereby causing as its only manifestation a unilateral field defect bearing no resemblance to the usual temporal hemianopia. The sella sometimes is normal in size but the corresponding anterior clinoid process is eroded. In some cases the diaphragma sellae has been found intact, but a unilateral bulge or lateral protrusion of the tumour underneath it may be sufficiently localised to affect seriously one optic nerve, especially when the chiasma is post-fixed, without causing any functional disturbance of the other nerve.

Treatment is a problem that must be evaluated chiefly by its effect on restoring vision. The intrasellar portion of a large adenoma has no capsule other than that made by the compressed remains of the pituitary body, which may be flattened into a thin shell.

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