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A CASE OF SPONTANEOUS LACTATION ASSOCIATED WITH MENSTRUAL IRREGULARITY AND STERILITY

P. HEBERDEN, M.B., B.CH. (RAND)

and

W. COOPER, M.B., B.CH. (RAND), M.R.C.P. (EDIN.)

From the Coronation Hospital and the University of the Witwatersrand, Johannesburg

Spontaneous and persistent lactation not associated with pregnancy or acromegaly appears to be a relatively uncommon condition. We report a case where galactorrhoea was the presenting symptom of an obese nulliparous patient.

CASE REPORT

A 35-year-old married woman was admitted to hospital in January 1957 for investigation of a spontaneously occurring galactorrhoea. The patient was an obese Coloured woman who complained of fullness of the breasts and a milky discharge, especially from the left nipple. This condition had been present for 18 months and during this time the discharge had fluctuated in intensity, being most active in the premenstrual cycle. The secretion had ceased spontaneously for a week or two on several occasions, but during the past 3 months the discomfort had increased and the milky discharge became more profuse. Sterility and menstrual irregularity were prominent features of the history. Menstruation had commenced at the age of 11 years, lasted 6-7 days, and pursued a regular 30-day cycle. In recent years, however, the flow had diminished, the cycle become irregular, with frequent episodes of amenorrhoea, and 7 years of married life had failed to result in a pregnancy.

The patient was found to be an obese Coloured woman who weighed 209 lb. and measured 59½ inches in height. Clinically she exhibited none of the features of acromegaly, and on examination the possibility of pregnancy was excluded. Oiliness of the facial skin was associated with a mild form of seborrhoeic dermatitis. Striae and hirsutism were absent. The breasts were pendulous but of normal consistency, and yielded a milky secretion on gentle pressure. Although not profuse, pressure always produced this secretion, varying in amount from a few drops to a thin stream on each occasion. Pelvic examination combined with an endometrial biopsy was performed at a later date, under general anaesthesia, and no gross abnormality of the genital organs was detected. The blood pressure was 150/90 mm. Hg, and examination of the nervous system including fundoscopy and examination of the visual fields, revealed nothing abnormal.

The following investigations were carried out:

X-ray of chest and skull: No abnormality noted.

Coned views of pituitary fossa: No abnormality noted.

Urinalysis on repeated examination showed nothing of note.

Urinary 17-ketosteroids: 8.8 mg. in 24 hours and 5.2 mg. in 24 hours (estimated as dehydroisoandrosterone).
Urinary FSH: 6-12 mouse units in 24 hours (on 3 occasions).
Xenopus frog test: negative.
Full blood-count: Within normal limits.
Blood Urea: 27 mg. per 100 ml.
Serum sodium: 130 mEq. per litre.
Serum potassium: 4.6 mEq. per litre.
Serum chloride (as Na Cl): 100 mEq. per litre.
Serum protein—bound iodine: 6.6 µg. per 100 ml. and 3.7 µg. per 100 ml.
Serum cholesterol: 300 mg. per 100 ml.
Serum inorganic phosphorus: 3.2 mg. per 100 ml.
Serum calcium: 5.1 mEq. per litre.
Blood serological test: Negative modified Ide.
Blood sugar: 68 mg. per 100 ml. (fasting).
Glucose tolerance test: A normal curve.
Insulin sensitivity test: No evidence of 'hypoglycaemia unresponsiveness'.
Basal metabolic rate: +1.
Endometrial biopsy: This was performed on the 1st day of the menstrual cycle and the minute pieces of endometrium submitted for study showed nothing of significance.

DISCUSSION

A detailed account of current opinion regarding the complex endocrine control of mammary growth and lactation is beyond the scope of this report, but certain views call for mention. The development of the breast is controlled by oestrogen, which leads to growth and branching of the mammary duct system, while progesterone leads to glandular development. During pregnancy the placenta forms both oestrogen and progesterone, thus stimulating duct proliferation and the glandular cells. An anterior pituitary gonadotrophin, prolactin, is thought to be responsible for the stimulus to the alveolar epithelium to synthesize milk. Prolactin is probably formed by the eosinophil cells of the anterior pituitary gland, and acts only on breasts that have been previously conditioned by oestrogen-progesterone

stimulation, and is itself luteotrophic, stimulating the release of progesterone from the corpus luteum of the ovary. There is evidence that prolactin secretion is stimulated by suckling, probably *via* a nervous pathway to the hypothalamus and finally controlled by circulating blood-hormone levels. Recent work by Bensen *et al.* (1957) suggests that oxytocin, a posterior pituitary hormone stimulates the release of prolactin. Lactation does not occur simply as a function of prolactin but apparently requires the synergistic action of both prolactin and the adrenal cortex (Gomez and Turner, 1937, Nelson, and Gaunt, 1937). A complex relationship exists between the pituitary and the ovary and it is known that oestrogen has a profound influence upon pituitary activity. After castration there occurs a marked increase in the gonadotrophic activity of the pituitary, and Zondek (1932) observed an increase in the urinary excretion of FSH in both sexes after castration; at the menopause a similar increase is found. Nelson (1936) believes that the reason why lactation does not occur during the last months of pregnancy is the inhibiting effect of large quantities of oestrogen on the pituitary gonadotrophin, prolactin; the decrease in systemic oestrogen which follows parturition permits the pituitary to release prolactin and stimulate lactation. There is thus sufficient evidence to show that the gonadotrophic activity of the anterior pituitary is sensitive to the circulating ovarian hormones, especially oestrogen, and under certain conditions this balance may be disturbed.

Numerous cases of spontaneously occurring lactation, or alteration in mammary activity, have been recorded in both sexes. Mechanical stimulation of the nipple is cited as a common cause, and Knott (1907) records 3 cases of spontaneous lactation in unmarried nursemaids who repeatedly suckled their charges. Other causes mentioned are pineal tumours (Oestreich and Slawyk, 1899), disease of the ovary, testis and suprarenal cortex (Krestin, 1932), post-encephalitic parkinsonism (Riese, 1928) and acromegaly (Davidoff, 1926); galactorrhoea may also be a symptom of the menopause. Chiari *et al.* (1855) and Frommel (1882) described a condition of utero-ovarian atrophy associated with persistent lactation and amenorrhoea. This condition, however, appears after childbirth and is directly related to parturition, and further descriptions of the Chiari-Frommel syndrome have recently appeared in the literature (Gilbert, 1941, and Mendel, 1946). Persistent lactation not associated with pregnancy is a less common entity. Krestin (1932) describes 2 cases of spontaneous lactation associated with enlargement of the pituitary in non-pregnant, non-acromegalic women.

An interesting syndrome of spontaneous galactorrhoea, amenorrhoea and low urinary FSH excretion has been described by Forbes *et al.* (1954) and by Argonz and del Castillo (1953). Forbes *et al.* investigated 15 non-acromegalic women who presented with this syndrome. Of these 15 patients, 9 had never been pregnant, some had irregular periods, but the majority experienced amenorrhoea. Nearly all had some degree of obesity, hirsutism and seborrhoea and all but one exhibited a low urinary FSH excretion. Failure

to menstruate following the administration and withdrawal of progesterone demonstrated a lack of endogenous oestrogen in the majority of cases. A striking feature of the series was the high incidence of pituitary tumour. In 8 of these 15 patients there was evidence of a tumour, and in 3 it was proved by biopsy to be a chromophobe adenoma of the anterior pituitary gland. These authors further studied lactation in nursing mothers and concluded that normal lactation was not due to the absence of FSH, which occurred in their group of nursing mothers in slightly higher amounts than in a group of non-lactating mothers. Nor did they feel that it was due to lack of oestrogen alone, because some nursing mothers have regular periods, and they maintain that neither the menopause nor castration cause lactation. These authors quote Cushing (1932-33), who postulated that the cells in the chromophobe adenomata are always pre-eosinophilic in type and, since lactation occurs in acromegaly, they feel that the syndrome is due to pituitary dysfunction whereby a specific hormone is produced in excessive amounts. Argonz and del Castillo (1953) express the view that spontaneous galactorrhoea is pituitary or hypothalamo-pituitary in origin, resulting in eosinophilic hyperfunction of the anterior pituitary. They feel that the condition is not primarily gonadal since, at the menopause and after castration, the urinary FSH is increased. The oestrogen insufficiency therefore resulted from lack of pituitary stimulation. They were, however, unable to detect any upset in the hypothalamus, nor were they able to demonstrate any evidence of a pituitary tumour in these cases, and substitution therapy did not influence the galactorrhoea.

SUMMARY

A case is recorded of a married woman aged 35 years who presented with the features of obesity, galactorrhoea, menstrual irregularity and sterility, not related to pregnancy or acromegaly. The literature bearing on the differential diagnosis is reviewed. The mechanism of this condition is not known but current views on this aspect of endocrine dysfunction are discussed.

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Red Cross War Memorial Children's Hospital, Rondebosch, Cape. The next meeting in the Postgraduate Seminar Series of lectures under the auspices of the University of Cape Town Department of Child Health will be held in the lecture theatre of this Hospital

on Wednesday 2 April at 5 p.m. Speaker, Dr. A. B. Murray; subject, 'Normal and abnormal formation of red blood cells in childhood'. All medical practitioners are welcome.

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