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Emotional aspects of menstrual dysfunction

ABSTRACT: Psychological factors are the most common cause of menstrual dysfunction. Emotionally-induced disturbance at the hypothalamic level can lead to irregular cycles, dysfunctional uterine bleeding, or amenorrhea. Mild disturbances are usually associated with an ample amount of endometrial lining, and a period of withdrawal bleeding can usually be produced with progesterone. Where there is a deficiency of estrogen and consequently insufficient endometrial lining for withdrawal bleeding, organic pituitary and/or hypothalamic disease must be excluded. The psyche can also influence the uterus and ovary directly.

For years clinicians have been aware of the profound influence the psyche has on menstrual function. We are all familiar with instances in which couples who have been trying to conceive for years without success, do so soon after they have adopted a child and quit worrying about pregnancy. In most of these instances, the mental pressures of failing to conceive induced such anxiety that ovulation ceased; when worries about being childless ended, spontaneous ovulation and pregnancy followed.

Emotional factors may have a mild or major influence on ovulatory function. Mild anxieties may cause no appreciable change in the

menstrual cycle but may lead to infertility or habitual abortion by causing an inadequate development of the corpus luteum. This can be detected by noting that in the second half of the cycle (luteal phase) the basal body temperature is not staying up for 12 days or longer, or it may take several days after ovulation to reach the peak luteal phase temperatures (slow-rising chart). The rise in the basal body temperature after ovulation is a reflection of the thermogenic effect of the hormone progesterone. After ovulation, with the egg extruded from its follicle, hormone secretion shifts from the theca cell to the granulosa cell. For the first

time in the cycle progesterone is being secreted in significant quantities by this granulosa cell-dominated follicle, which is now called the corpus luteum.

The main function of the progesterone is to cause secretory changes in the endometrium in preparation for implantation of the fertilized egg about nine days after ovulation. Improper secretion of progesterone, which can occur if ovulation occurs before the follicle is properly "ripened," can result in infertility or abortion if the lining is insufficiently prepared. In addition to the temperature chart, late luteal phase vaginal hormonal cytology, serum progesterone, urinary pregnanediol, and endometrial biopsy are used to establish the diagnosis of an inadequate corpus luteum.

The same emotional factors causing an inadequate corpus luteum may result in anovulation. The patient may have irregular periods due to breakthrough bleeding (oligomenorrhea), or no period at all (amenorrhea). Some of the common environmental situations that may contribute to anovu-

lation include loss of a loved one, moving to a new environment, fear of pregnancy, marital strife, and change of job. Psychogenic factors are the most common cause of secondary amenorrhea, with weight loss as a close second cause.

Control mechanisms

While the fact that emotions can affect ovulatory function has long been apparent to clinicians, we are just beginning to learn how this is mediated. The basic control of the menstrual cycle is dependent on a very exact and delicate relationship between the hypothalamus, pituitary, and ovary. In the medial hypothalamus a decapeptide called the gonadotropin-releasing hormone (GnRH) is secreted. This hormone is necessary for both the synthesis and release of the luteinizing hormone (LH) and the follicle-stimulating hormone (FSH) of the pituitary. LH causes the synthesis of estrogen from theca cells in the ovary and both LH and FSH have a combined effect on the maturation of the follicle that leads to ovulation. The secreted estrogen exerts a negative feedback effect at the level of the pituitary for LH and FSH and also in the area of the ventromedial nucleus of the hypothalamus. This is the area responsible for constant secretion of the gonadotropins (LH and FSH). However, the dominant relation during the pre-ovulatory phase (follicular phase) of the menstrual cycle is a positive feedback to the cyclic center of the anterior hypothalamus, resulting in pulsatile release of GnRH, and thus causing pulsatile release of LH and to a lesser degree FSH. This eventually results in the mid-cycle surge of LH required for ovulation.

Mild dysfunction in the hypo-

thalamic-pituitary-ovarian axis may involve production of either slightly less estrogen than needed to cause the positive stimulation necessary for the mid-cycle LH surge or slightly too much estrogen, which exerts a negative feedback for FSH, thus preventing proper follicular maturation.

Biogenic amines

The hypothalamus is not the highest center of control; the cerebral cortex and limbic system seem to be able to influence hypothalamic control. Biogenic amines from higher centers influence hypothalamic function, and it is through this mechanism that emotions alter ovulatory function. The main CNS biogenic amines are dopamine, norepinephrine, and serotonin. They influence all hypothalamic-releasing hormones. At present, there is evidence that dopamine suppresses LH.^{1,2}

Dopamine and prolactin

Another hormone involved in control of the menstrual cycle is prolactin. Elevation of serum prolactin causes reciprocal lowering of the gonadotropins, especially FSH, resulting in amenorrhea and sometimes galactorrhea.³ Good evidence has been found that dopamine is the prolactin-inhibitory factor that normally keeps the prolactin-producing cells in a suppressed state.⁴ Psychological stress can result in an increase in prolactin, which in itself can alter the menstrual cycle by the inhibitory effect that it has on LH.⁵

Stress may alter ovulatory function through its effect on still another pituitary hormone, adrenocorticotrophic hormone (ACTH). ACTH stimulates secretion of glucocorticoids from the zona fascicu-

lata and androgens from the zona reticularis of the adrenal gland. There seem to be two areas of the hypothalamus producing the corticotropin-releasing factor (CRF), which is responsible for ACTH secretion. The lower area is considered the center responsible for the daily normal diurnal type of secretion of cortisol; the higher hypothalamic center causes greater increases of ACTH under stress conditions, resulting in greater cortisol secretion necessary during fight or flight. An increase in either cortisol or androgens can inhibit the gonadotropins. This adrenal stress syndrome can be associated with hirsutism but this is not specific for this condition since the other anovulatory conditions may result in polycystic ovaries, which are also associated with hirsutism.

Anorexia nervosa

Two of the classic psychological disturbances affecting ovulation are anorexia nervosa and pseudocycosis. In anorexia nervosa, the individuals (90% females) develop weight loss, amenorrhea, dry skin, marked constipation, abdominal pain, and marked cold intolerance. Their physical examination is characterized by bradycardia, delayed relaxation of the Achilles reflex, and occasional edema. The clinical and metabolic features of anorexia nervosa have been nicely summarized by Warren and Van de Wiele.⁶

We are just beginning to understand the mechanisms responsible for the signs and symptoms of anorexia nervosa. Most of them can be accounted for by the weight loss itself. Some of the symptoms and signs, such as cold intolerance, constipation, and bradycardia, may be related to a decrease in the func-

tional thyroid hormone triiodothyronine (T_3) and an increase in the inert hormone reverse T_3 .^{7,8} The amenorrhea and estrogen deficiency can also be explained by weight loss. There is an area in the hypothalamus, called the gonadostat, that is responsible for control of the gonadotropins. This area is "turned on" at puberty when the individual attains a critical weight. Prior to this time the hypothalamus is inhibited by very low levels of sex steroids; but this negative inhibition is considerably diminished

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and, in fact, positive stimulation for LH occurs with low estrogen levels when this critical weight is achieved.⁹ Loss of 15% of body weight is usually sufficient to interfere with the delicate balance between the hypothalamus, pituitary, and ovary to cause anovulation, whereas loss of greater than 25% usually turns off most stimulation to the ovary, resulting in estrogen deficiency.^{10,11}

Thus in anorexia nervosa there is a return to a prepubertal type of gonadostat. Though we do not know the exact psychological cause for this aversion to food, those who feel that these individuals fear their developing sexuality argue that weight loss represents a reversion to a more secure prepubertal state. But the psychological disturbance leading to the anorexia can alter gonadal function even without significant weight loss. Amenorrhea

frequently precedes the weight loss or continues when the patient has regained or even surpassed her original weight. In this situation the amenorrhea is related to a functional disturbance of the hypothalamic-pituitary-ovarian axis. A menstrual flow can be induced by progesterone withdrawal, and ovulation can be induced by giving clomiphene citrate.

Pseudocyesis

Another condition illustrating the effect of the psyche on menstrual function is pseudocyesis. In this condition, the woman falsely believes that she is pregnant. She usually develops hypomenorrhea or amenorrhea, the abdomen gradually enlarges, the breasts enlarge and the areolae become hyperpigmented; frequently there is galactorrhea. The clinical characteristics have been reviewed by Fried and associates.¹²

Many of these women are found to have an elevated prolactin, which can explain the galactorrhea.^{13,14} LH, FSH, urinary estrogens, and pregnanediol are usually lower than normal.¹⁵ Pseudocyesis thus illustrates a condition in which the psyche can elevate prolactin and this in turn can alter gonadotropin function. Other evidence also exists that stress can increase prolactin levels.¹⁶

Workup

Thus the psyche can cause certain somatic manifestations that are difficult to discern from organically caused disease. In most instances, the psychological disturbance interferes only with ovulation, and the ovary continues to produce estrogen, allowing the endometrial lining to build up. If the patient demonstrates withdrawal bleeding

as a reaction to progesterone and/or a good estrogen effect on vaginal hormonal cytology, and if there is also a reasonable psychological explanation for the menstrual dysfunction, such as moving to a new environment, no further workup is usually necessary. The patient would simply be continued on progesterone therapy, such as medroxyprogesterone acetate, 10 mg for eight days, every 4 to 6 weeks. If pregnancy is desired, ovulation may be induced by giving the patient a fertility medication, such as clomiphene citrate.

Differential diagnosis

Occasionally the endocrine disturbance is more severe, and even though there may be obvious psychological problems the clinician cannot be sure whether these psychological factors are causing or result from the endocrinopathy. Anorexia nervosa can easily be confused with panhypopituitarism, especially since patients with anorexia nervosa frequently lie and claim to have decreased appetites, as may be seen in adrenal insufficiency. Clinically the two conditions can be distinguished by demonstrating much more energy, preservation of sexual hair, and usually much more profound weight loss in patients who have anorexia nervosa.

One of the first hormones to become deficient because of a pituitary tumor is growth hormone, and reserve for this hormone is measured by stimulation tests (e.g., insulin hypoglycemia). In anorexia nervosa, growth hormone is normal or increased. Though 17-ketosteroids and hydroxycorticosteroids are frequently decreased in anorexia nervosa, the serum cortisols are frequently increased or show a

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reversed diurnal variation; this, of course, is different from the case with pituitary lesions.

Other tests helpful in distinguishing hypogonadotropic hypogonadism on a psychological versus organic pituitary basis include the level of elevation of serum prolactin (chromophobe adenomas secrete the hormone, and levels greater than 100 ng/100 ml should make one very suspicious of a pituitary lesion); a gonadotropin-releasing hormone (GnRH) stimulation test, where a greater than normal response would be indicative of a functional hypothalamic disturbance; skull x-ray studies with tomograms of the sella turcica; and visual field evaluation.

Other problems

Irregular cycles or amenorrhea are not the only effects that psychological factors can have on the menstrual cycle. Anovulation from any cause can lead to dysfunctional uterine bleeding. However, depression can occasionally cause dysfunctional uterine bleeding that is extremely resistant to hormonal therapy. Thus, the psyche appears also to have a direct effect in some

instances on the endometrial lining. This endometrial factor can also be responsible for amenorrhea. An occasional individual will show ample estrogen on the vaginal hormonal smear or on estrogen assays, but very little tissue on endometrial biopsy. This type of amenorrhea can be very resistant to hormonal therapy even with high doses of estrogen and progesterone.¹⁶ For some reason, this condition occurs frequently following automobile accidents. Its etiology has not yet been explained.

The psyche also appears to influence the ovary directly. We have seen several cases of women who, shortly after their husbands died, developed amenorrhea, hot flashes, and other symptoms of menopause, along with elevated gonadotropins as in menopause. When these women began dating, their symptoms frequently abated, with return of menstrual function and normal levels of LH and FSH. □

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