Histopathological findings of the endometrium in patients with dysfunctional uterine bleeding

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Summary: The histopathological examination of the endometrium in cases of abnormal functional uterine bleeding frequently reveals the type of functional disturbance and assists correct treatment. On this basis, 7,000 endometrial curettages from patients with abnormal uterine bleeding were studied. The 1,282 cases with no endometrium in phase, organic changes, or systemic disorders were defined as dysfunctional uterine bleeding; the endometrial lesions were then classified and the histological findings correlated with the patients' ages. The endometrial curettages revealed an anovulatory cycle in 984 (77%) of the patients, and an ovulatory cycle in 298 (23%). Of the cases with an anovulatory cycle, 446 patients (47.5%) showed endometrial hyperplasia, 412 (41.86%) showed abnormal endometrial proliferation due to prolonged persistence of a follicle, while 106 (10.77%) showed deficient endometrial proliferation. Three hundred and thirty four cases (71.67%) of endometrial hyperplasia were (simple) cystic hyperplasias, 124 (26.60%) were (complex) adenomatous hyperplasia, and 8 (1.71%) were atypical hyperplasia. Of the cases with an ovulatory cycle, 252 (84.56%) showed deficient endometrial secretion due to a prolonged proliferative phase, while the other 46 (15.43%) showed deficient secretion due to luteal phase defect. Seven hundred and thirty six patients with an anovulatory cycle and 212 with an ovulatory cycle – i.e. 948 (74%) of the 1282 patients studied – were at the climacteric. The conclusions may be summarised as follows. *i*) Dysfunctional abnormal uterine bleeding was found more often at the climacteric and chiefly in the form of an anovulatory endometrium; *ii*) 88.14% of cases (1130 patients) presented histological signs of oestrogen influence in the form of either an anovulatory endometrium or an ovulatory endometrium; *iii*) Cystic (simple) hyperplasia was the most common form of endometrial hyperplasia.

Key words: Endometrium; Functional disturbances; Abnormal uterine bleeding; Histopathology.

INTRODUCTION

Abnormal uterine bleeding is one of the most frequent clinical manifestations of gynaecological disease ([1, 2, 3]). It is caused by lesions in the uterus or, more rarely, by systemic diseases ([1, 4, 5, 6]). Uterine lesions involve *i*) organic disorders, and *ii*) functional disturbances ([7]).

Abnormal uterine bleeding due to functional disturbances is termed dysfunctional uterine bleeding (DUB) ([1, 8, 9, 10, 11, 12]). It is thought to result from an imbalance among the sex steroid hormones. The disturbance is endogenous and results from the functions of the hypothalamus-pituitary-ovary axis ([1, 13, 14, 15, 16]). Any change in the ovarian hormones causes irregularities in the maturation of the endome-

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trium, which is these hormones target organ ([1, 5]). Although clinicopathological conditions of the spectrum of morphological changes associated with DUB are not known, there are certain histological characteristics of the endometrium which find quite a good indication of the sex steroid hormone abnormalities ([11]).

On this basis, a study was conducted of the histological findings in endometrial curettages from women presenting abnormal uterine bleeding, with a view to classifying the endometrial abnormalities and correlating the frequency of each type with the patients' ages.

MATERIALS AND METHODS

The study was retrospective and the examination of 7,000 endometrial curettages from women with a history of abnormal uterine bleeding. The patients were divided by age into three categories: *i*) reproductive age; *ii*) climateric; and *iii*) menopause.

In all cases, the H+E sections in the laboratory's records were examined and new sections of the paraffin blocks stained with the H+E, Van Gieson, PAS, and Gomori methods were made only when it seemed advisable.

In the first part of the study, curettages showing evidence of organic changes, inflammation, polyp, pregnancy, or neoplasm were excluded. The 1282 remaining cases could be described, according to clinical and histopathological criteria, as cases of DUB.

RESULTS

The 1282 cases that could be described as DUB were divided into two categories according to the form of the cycle: *i*) anovulatory, and *ii*) ovulatory ([1, 5, 11]). Histological findings revealed characteristics of an anovulatory cycle in 984 cases (77%) and those of an ovulatory cycle in 298 cases (23%). Of the 984 cases of an anovulatory cycle, 178 concerned patients of reproductive age, 736 patients at climacteric, and 70 patients at menopause. The histological abnormalities of the endometrium in the cases of anovulatory abnormal uterine bleeding were divided into three groups ([15, 17, 18]): 106 cases (10.77%) involved deficient endometrial proliferation; 412 cases (41.86%) involved disordered endometrial proliferation and persistent proliferative phase; and 466 cases (47.35%) involved hyperplasia of the endometrium.

Endometria presenting histological characteristics of hyperplasia were divided into three types. The classification proposed by the WHO ([19]) was used, and the hyperplasias were distinguished as simple, complex, and atypical. There were 334 cases of simple hyperplasia (71.67%), 124 cases of complex (adenomatous hyperplasia (26.60%), and 8 cases of atypical hyperplasia (1.71%).

Of the 8 cases of atypical endometrial hyperplasia, 1 presented histological characteristics compatible with carcinoma of the endometrium. It was classified as hyperplasia, however, because of the patient's youth ([20]).

The 298 cases of DUB with an ovulatory cycle were divided into two categories. Of these, 252 (84.56%) were due to relatively insufficient progesterone resulting from prolonged oestrogen influence; and 46 (15.43%) to luteal phase defect.

Seventy-six endometrial curettages showed histopathological abnormalities characteristic of exogenous use of hormonal preparations.

DISCUSSION

Histopathological examination of the endometrium is a diagnostic means for determining the aetiology of DUB. It is essential in all cases of abnormal uterine bleeding, except for those involving patients at puberty ([15]).

The histopathological findings in DUB are classified in two groups: those involving an anovulatory cycle and those involving an ovulatory cycle ([11]). The di-

stinction is important because these two forms present different pathogeneses and require different types of treatment [2, 5]. It is generally accepted and most studies have found that DUB usually accompanies an anovulatory cycle [1, 10, 14, 18, 21], the percentages quoted varying between 80% and 90% [10, 11]. Very few studies have found DUB predominantly accompanying an ovulatory cycle [22]. In our study, 77% of the cases involved an anovulatory cycle. Abnormal uterine bleeding accompanied by an anovulatory cycle is more frequently encountered at climacteric [23]. Fifty per cent of patients presenting this form of abnormal uterine bleeding are over 45 years of age; 20% are at puberty, and 30% are of reproductive age [10]. In our study, 75% of cases with an anovulatory cycle were patients at climacteric, a proportion which accords with Scommegna's findings (his study also included patients at puberty) [10].

Endometria with an anovulatory cycle present the histological characteristics of inadequate oestrogen stimulation. Deficient endometrial proliferation (due to inadequate oestrogen stimulus) is observed in a small number of patients with DUB. At climacteric such endometria do not present abnormal bleeding because they are at a normal stage of adaptation to reduced oestrogen levels [5]. The final stage of this deficient type of endometrial maturation is atrophy, resulting from total absence of sex steroid hormones [1, 24]. Abnormal uterine bleeding is usually a feature of endometria presenting signs of oestrogen influence in the form of disordered endometrial proliferation of endometrial hyperplasia [1, 5, 10]. In our study, approximately 77% of patients with DUB accompanied by an anovulatory cycle presented a proliferative endometrium with signs of disordered maturation (41.86%) or endometrial hyperplasia (47.35%). In either case, the endometrium was under persistent oestrogen influence. Pathogenetically and histologically, abnormal endometrial proliferation is the first stage of the transition to endometrial hyperplasia if the oestrogen is not arrested [5, 18].

The most common type of endometrial hyperplasia is the simple or cystic hyperplasia [1]. In our study, evidence of simple hyperplasia was found in two thirds of the endometrial curettages from patients with DUB. The other third showed complex or adenomatous hyperplasia, though only 8 cases had signs of atypical hyperplasia. The frequency of atypical endometrial hyperplasia varies considerably. This is probably due to the fact that the histological characteristics of atypical endometrial hyperplasia are often very similar to the histological picture of well differentiated adenocarcinoma confined to the endometrium [5, 25, 26, 27].

Abnormalities in endometrial maturation with abnormal secretory phase patterns are more often a cause of sterility than of abnormal bleeding [15]. Consequently, abnormal uterine bleeding with an ovulatory cycle makes up a small percentage of cases of DUB. In our study, cases of abnormal uterine bleeding with the histological characteristics of an ovulatory cycle made up 23% of the cases of DUB; and of these 84.56% showed evidence of a prolonged previous phase.

Similar to cases of DUB caused by endogenous factors are the cases where hormonal preparations have been used. The histopathological changes vary considerably [28], depending on the type of preparation used, the proportion of oestrogen and progestogen, the duration of use, and the patient's previous hormonal condition [1, 5, 29]. The typical histological findings in these cases that is they do not resemble any of the normal or known endogenous histopathological changes in the endometrium [5]. In our study the number of cases of abnormal uterine

bleeding with a history of use of hormonal preparations was too small to allow us to draw conclusions about the various histological changes in the endometrium typical of each preparation.

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