CLINICAL REVIEW

Aetiology of postmenopausal bleeding

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Summary

A retrospective analysis has been made of 160 cases of postmenopausal bleeding. The women were at least 45 years old and the time lapse from the last menstruation was at least 2 years.

The cause was a malignant neoplasm in 23.75%. The incidence of malignancy showed a definite rise with advancing age and with increasing duration of bleeding. It was nearly twice as high in women who stopped menstruation after the age of 55 years. Malignancy also seemed to be more frequent in patients with profuse bleeding and in those who had amenorrhoea lasting for 20 years or more.

The most usual malignant lesions were endometrial and cervical carcinoma, the ratio of these two conditions being 1.6 : 1. Oestrogen administration was the most common cause in the non-malignant group: 12.5%. No cause for bleeding could be demonstrated in 8.8%.

The aetiology of postmenopausal bleeding is discussed.

Introduction

The general consensus of opinion is that genital bleeding occurring after the menopause must be considered as indicative of malignant disease, until it is proved to be otherwise. However, there is no universally accepted definition of postmenopausal bleeding. One year without bleeding at the appropriate time of life is the criterion for the menopause most often applied (Brewer & Miller, 1954; Sutherland & McBride, 1954; Cope, 1956; Lehto & Kinnunen, 1957; Woodruff, Prystowsky & Te Linde, 1958; Majewski & Fritsche, 1958; Patel, 1967; Procopé, 1971), although from an aetiological point of view a 2-year interval is to be preferred (Israel & Weber, 1956; Pacheco & Kempers, 1968). Nevertheless, some authors include all cases of bleeding after an interval of 6 months' amenorrhoea (Taylor & Millen, 1938; Payne, Wright & Fetterman, 1959; Hammouda, 1966; Benzie, 1967), or after the age of

50 or 53 years (Schwartz, 1943; Latour & Pelletier, 1961), while others do not state their criteria (McFadyen, 1952; Meier, 1960).

Although this inconsistent use of terminology, as well as differing geographical, racial and ethnic factors and the different character of hospitals, makes any comparison of the incidence of malignancy seen in various reports difficult to interpret, the contrast between the earlier and the more recent reports, from all over the world, is too obvious not to be recognized. Indeed, while most of the earlier work showed an incidence of malignancy in patients presenting with postmenopausal bleeding ranging from 53 to 90% (Zweifel, 1930; Taylor & Millen, 1938; Te Linde, 1940; Cheek & Davis, 1946), figures greater than 50% are seldom found in the more recent literature (Kraussold, 1962). In fact most of the recent series state incidences lower than 35% (McFadyen, 1952; Brzezinsky & Bromberg, 1953; Brewer & Miller, 1954; Sutherland & McBride, 1954; Israel & Weber, 1956; Cope, 1956; Lehto & Kinnunen, 1957; Woodruff *et al.*, 1958; Majewski & Fritsche, 1958; Payne *et al.*, 1959; Meier, 1960; Latour & Pelletier, 1961; Hammouda, 1966; Patel, 1967; Pacheco & Kempers, 1968; Laridon, 1971; Procopé, 1971).

Several reasons have been suggested for this apparent decrease in the incidence of malignant conditions as a cause of postmenopausal bleeding. The first is the widespread use of oestrogens, which some (Payne *et al.*, 1959; Hammouda, 1966; Jeffcoate, 1967; Copenhaver, 1968) regard as the most common cause of postmenopausal bleeding. It has been suggested too that this decline is largely a reflection of both an increased interest in, and facilities for, early diagnosis of malignant disease, especially cervical carcinoma, and an increased awareness of the serious implications of bleeding on the part of the laity and their medical attendants (Woodruff *et al.*, 1958; Novak, 1964; Pacheco & Kempers, 1968). More postmenopausal women than formerly are admitted to hospital for investigation of the cause of bleeding, resulting in a relative increase in the non-malignant causes.

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However, since most reports originate from large, usually academic, institutions, the present study was undertaken to establish whether or not cases seen in a general hospital reflected the same trend.

Materials and methods

Review of all patients seen for postmenopausal bleeding at the Sint-Michielskliniek, Brussels, between 1 July, 1968 and 30 June, 1971, was made. Postmenopausal bleeding during this period was invariably investigated by dilatation and curettage, exceptions to this practice being rare, e.g. in cases of advanced cervical carcinoma. The study was limited to women of 45 years or more, whose bleeding began at least 2 years after cessation of their menses, in order to eliminate from aetiological consideration as many physiological variations as possible.

There were 160 such patients, all of whom were included for study, irrespective of the amount of haemorrhage, and whether or not this was the primary complaint.

Results

Aetiological groups

Malignant lesions were found in thirty-eight (23.75%) of the 160 patients (Table 1). There were twenty-one patients with endometrial and thirteen with cervical carcinoma, a ratio of 1.6 : 1. Twelve of the thirteen cervical carcinomas were of squamous-cell origin and all endometrial lesions were adenocarcinomas. In one patient two primary neoplasms, an adenocarcinoma of the endometrium and a squamous-cell carcinoma of the cervix, were found. There were two extra-uterine malignancies and one uterine sarcoma in the series.

Oestrogen administration was the most common benign cause accounting for the bleeding in twenty women (12.5%). Proliferative endometrium was noted in three, and hyperplasia in four cases without a history of oestrogen treatment. Atrophic endometrium was the only possible explanation for the bleeding in nineteen cases (11.9%). Endometrial polyps were responsible for six, and submucous fibroids in three cases. Pyometrium was found in one, and haematometrium in another patient without associated malignancy.

Ulceration of the cervix associated with uterine prolapse (7.5%) and cervical polyps (6.9%) were the most common cervical lesions. Fourteen patients (8.8%) suffered from clinically evident vaginitis: trichomonas, traumatic or senile in three, two and nine cases respectively. Two patients had benign ovarian lesions, though the relationship between these, a serous cyst and a pseudomucinous cystadenoma, and the bleeding was obscure.

Finally, in fourteen cases (8.8%) no cause for the bleeding could be found. In this group insufficient or no endometrium could be obtained on curettage.

TABLE 1. Causes of postmenopausal bleeding in 160 cases

Causes	Number of cases	%
Malignant:		
Adenocarcinoma of endometrium	21	13.1
Squamous cell carcinoma of cervix	12	7.5
Adenocarcinoma of cervix	1	0.6
Endometrial and cervical carcinoma	1	0.6
Sarcoma of uterus	1	0.6
Adenocarcinoma of ovary	1	0.6
Primary carcinoma of vagina	1	0.6
Total	38	23.75
Non-malignant:		
Oestrogen administration	20	12.5
Atrophic endometrium	19	11.9
Hypoplastic endometrium	4	2.5
Proliferative endometrium	3	1.9
Endometrial hyperplasia	4	2.5
Endometrial polyp	6	3.8
Submucous myoma	3	1.9
Pyometrium	1	0.6
Haematometrium	1	0.6
Ulceration of cervix associated with prolapse	12	7.5
Cervical polyp	11	6.9
Cervicitis with erosion	5	3.1
Senile vaginitis	9	5.6
Trichomonas vaginitis	3	1.9
Traumatic vaginitis	2	1.2
Vulval haemangioma	1	0.6
Urethral caruncle	2	1.2
Benign ovarian tumour	2	1.2
No cause found	14	8.8
Total	122	76.25
Grand total	160	100

Age groups

The ages on admission to hospital ranged from 45 to 83 years, with an average of 61.6 years. There was an increase in the incidence of malignancy with age (Table 2), and the average age for patients with malignant lesions was 64.0 years compared with 60.9 years for those with benign lesions.

The average age of the naturally occurring menopause was 49.9 years (malignant 50.6 years, non-malignant 49.5 years). 10% of all patients had not reached the menopause by 55 years of age. In this group the incidence of malignancy was 43.8%.

TABLE 2. Incidence of postmenopausal bleeding and malignancy in relation to age

Age groups	Number of cases	%	Incidence of malignancy (%)
45-54	28	17.5	14.3
55-64	81	50.6	23.5
65-74	37	23.1	27.0
≥ 75	14	8.8	35.7
Total	160	100	23.75

Duration of amenorrhoea

The average interval between the menopause and the onset of genital bleeding was 12.1 years (malignant 13.5 years, non-malignant 11.7 years). The longest interval was 33 years. Only 23.8% of women were less than 5 years postmenopausal when bleeding occurred and 22.6% had amenorrhoea lasting for 20 years or more. In the latter the incidence of malignancy was 30.5%. The mean interval was 8.3 years in patients with cervical malignancy compared with 15.8 years in those with endometrial carcinoma.

Bleeding

Although 25% of women sought advice for their symptoms within a week, 30.5% did so only after a delay of at least 3 months and 18.7% after 6 months or more. There was a marked difference in the incidence of malignancy in patients having a long or short history of bleeding, as is seen in Fig. 1.

FIG. 1. Ratio of malignant tumours in relation to the interval (in weeks (w) and months (m)) between the first appearance of postmenopausal bleeding and consultation at hospital.

Twenty-four patients (15%) experienced contact bleeding and in forty-seven (30%) only spotting occurred. In eighty-one cases (50%) frank genital bleeding was noted. Finally, in eight cases (5%) the character of the bleeding was not stated. In patients with frank bleeding the incidence of malignancy was 27.1%, compared with 20.8% in those with contact bleeding and 19.1% in those with spotting.

Discussion and conclusion

Although the incidence of postmenopausal bleeding due to malignancy is now only half that of 30 years ago, it remains sufficiently high to require thorough investigation. In fact, at least one out of every five women consulting a gynaecologist for postmenopausal bleeding has a malignant tumour. Analysis of our data shows that while overall malignancy was found in 23.75%, this was higher among certain groups of patients. It was nearly twice as high (43.8%) in women who stopped men-

struation after the age of 55 years. The incidence of malignancy showed, furthermore, a definite rise with increasing duration of bleeding (Fig. 1) and also the previously reported observation that the incidence of malignancy rises with increasing age (Cheek & Davis, 1946; Lehto & Kinnunen, 1957; Laridon, 1971; Procopé, 1971) was confirmed (Table 2). Malignancy also seemed more frequent in patients with profuse bleeding (27.1%) and in those who were 20 years or more postmenopausal when bleeding occurred (30.5%).

The commonest malignant causes were endometrial and cervical carcinoma. The 1.6:1 ratio between these two conditions in this series is higher than the ratio in most series. This seems to corroborate the statement that more thorough use of cervical smears has lowered the incidence of advanced cancer of the cervix as a cause of postmenopausal bleeding, though we probably would have noted a larger number of cervical malignancies had we begun our study less than 2 years after the menopause. It is well known that cervical cancer develops at an earlier age than endometrial cancer, and also the average interval between the menopause and bleeding, which was 8.3 years in patients with cervical and 15.8 years in those with endometrial cancer bears this out.

A non-malignant condition was involved in 76.25% of the cases. Both the average age and interval after the menopause were lower than in the malignant group. The cases showing a hormonal effect in the endometrium constitute an interesting group. Such an effect was usually due to oestrogen administration, which was the most common benign cause of bleeding (12.5%). This is higher than in most reports. Nonetheless, a malignant process may underlie a bleeding presumed to be due to an oestrogen effect, as was the case in one of the patients with endometrial carcinoma. Hence, the need for careful investigation of these cases. If no oestrogens have been given, the possible involvement of a pathological ovarian process should be borne in mind, but the possibility of other sources should also be considered (Sutherland & McBride, 1954; Novak, 1964; Procopé, 1971).

Atrophic endometrium was the second most common finding in the non-malignant group. It was diagnosed in 11.9% of the cases, which is in agreement with previous observations usually varying between 5.1 (Sutherland & McBride, 1954) and 23% (McFadyen, 1952). Although some authors (Brewer & Miller, 1954; Woodruff *et al.*, 1958) are reluctant to ascribe the bleeding specifically to the atrophic endometrium, interestingly curettage is usually curative in these cases, and the postmenopausal bleeding ceases thereafter. It was striking, however, that neither the average age nor the average interval

after the menopause was any higher in this group than in the whole series.

Polyps from either endometrial or endocervical origin were found in 11.7%. All endocervical and all but one of the endometrial polyps presented at the external cervical os, and they showed considerable surface ulceration or necrosis. Cervicitis with erosion was less common than in some other series (Sutherland & McBride, 1961; Payne *et al.*, 1959; Latour & Pelletier, 1961; Pacheco & Kempers, 1968; Procopé, 1971) as was ulceration of the cervix associated with uterine prolapse, though the latter accounted for 7.5% of the cases. These patients usually had a severe degree of prolapse for many years, but merely sought advice once bleeding was noticed. They also had the highest average age (67.3 years) and interval after the menopause (18.9 years).

Fourteen patients (8.8%) suffered from clinically evident vaginitis, but the principle that even the slightest degree of bleeding demands a diagnostic curettage was adhered to in this group. It should be noted that senile vaginitis was a common concomitant finding also in the malignant group. The incidence of other benign conditions was low, while in 8.8% of the cases no cause for the bleeding could be demonstrated despite thorough investigation. This is in agreement with most reports showing an incidence between 3.2% (Majewski & Fritsche, 1958) and 20% (Benzie, 1967).

Although both the ratio endometrial/cervical carcinoma and the incidence of oestrogen-induced bleeding are higher in this series than in most reports, this still seems to be insufficient to account for the divergences from earlier reports stating percentages of malignancy more than twice or three times as high as that studied. In recent years, there have been increasing facilities for treatment of malignant disease. Skilful surgery and radiotherapy have become available to the smaller medical centres, which previously referred patients to larger institutions. Since most reports originate from the latter, this may well be an important factor accounting for the high incidence of malignancy in the early reports and for the generally quoted decrease in the incidence of malignancy in postmenopausal bleeding. As for the increased awareness of the importance of postmenopausal bleeding, it was disconcerting to see that its effect was not as high as one would like. Indeed, 30% of the patients had been bleeding for at least 3 months before being seen, and nearly as many as 20% merely sought advice after a delay of 6 months or more. While most of these delays were due to the patient's indifference or ignorance, in a few instances they were still attributed to cautious observation by the physician. Therefore, the need for careful evaluation of every case of postmenopausal bleeding can not be overemphasized.

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