res (such as the Italian culture) women are conditioned at an early age to behave « like ladies » and not be sexually active (Gillan 1987).

The reported frequency of extravaginal coital activity was 30.18% in the three groups of women interviewed and it was significantly higher in parity 2 and $\geqslant 3$ women. In comparison, the Redbook Study in 1974 showed that some 90% of the American wives have engaged in oral sexual intercours, and some 43% in anal intercourse (Tavris et Sados, 1974). It is possible that this data is undervalued due to the reticence of the patients.

In conclusion sexual behavior did not greatly vary in relation to the women's parity, although parity $\geqslant 3$ women reported a lower frequency of « very frequent » coitus, a higher frequency of extracoital sexual activity, and their partners more frequently took the first initiative in sexual activity. The most likely explanation for the lack of evident difference of sexual behavior in these three groups of women is that all were in fertile age and shared many common characteristics, i.e., average age, religious faith, level of education, type of work and sexual experience.

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A CLINICAL AND EPIDEMIOLOGICAL STUDY OF 245 POSTMENOPAUSAL METRORRHAGIA PATIENTS

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Précis: Endometrial adenocarcinoma or atypical hyperplasia was found in 24.4% of the cases with postmenopausal bleeding; associated conditions at risk were obesity, nulliparity, and age over 60 years.

Summary: The Authors report the incidence of endometrial adenocarcinoma and atypical hyperplasia in 245 women who had undergone uterine curettage for post-menopausal bleeding.

In 4 cases a stenosis of the cervix precluded the curettage.

Of the remaining 241 patients, 71.3% had negative histology; in 24.4% histology was compatible with adenocarcinoma or atypical endometrial hyperplasia; in a third group of 10 patients a different type of gynecological neoplasia was diagnosed.

Obese, nulliparous women resulted significantly more affected by endometrial adenocarcinoma. The highest inicdence was noted among women over 60 years of age.

The Authors describe some epidemiological and clinical characteristics of the population under study.

Key words: postmenopausal bleeding; endometrial adenocarcinoma.

INTRODUCTION

The term postmenopausal metrorrhagia (or postmenopausal bleeding) defines the occurrence of bleeding from the genital tract in women over 45, one year after the cessation of menses ([1, 2]).

This symptom alarms the patient and, although in most cases it is not associated with a tumor, it does increase the risk of developing uterine cancer ([1]).

As a matter of fact 80% of endometrial adenocarcinomas occur in the postmenopausal period ([3]) and this is the most common tumor at this point in life. In patients with postmenopausal bleeding, notably, adenocarcinoma is reported to occur in 1.5% ([4]) to 28% ([5]) of cases, depending on the Author, although much higher incidence rates (up to 53% or even 90%) have been reported in literature in past years ([6, 7]).

In an earlier study ([8]) we identified posmenopausal metrorrhagia ascribable to adenocarcinoma in 24% of our patients. This rate rose to 28% with the inclusion of cases of atypical hyperplasia and 29% with the inclusion of all genital malignant tumors (Table 1) ([9, 10, 11, 12]).

The case histories of adenocarcinoma patients moreover are known to show occasional postmenopausal bleeding in 75% of cases ([1]).

The early appearance of these symptoms and the relatively easy performance of endometrial histology generally permit an early diagnosis of this tumor. The most suitable surgical intervention can consequently be timely performed and is successful – as is well known – in a large majority of cases (85%) when this neoplasia in treated in FIGO stage I (International Federation of Gynecology and Obstetrics). The success rate approaches 100% when the tumor is well differentioted (G1) and non-invasive (M0-M1) ([13]).

Furthermore, this disease has some rather characteristic epidemiological features which make it easier to detect groups of patients at risk.

Endometrial carcinoma has been shown to occur more frequently in patients who undergo oestrogenic treatment in climateric ([14]) and in obese women ([13]). Diabetes, arterial hypertension, early menarche, late menopause, nulliparity and late primiparity are other frequently associated factors ([15]).

Patients with postmenopausal bleeding who present histoligic findings of adenomatous hyperplasia should be given specific attention, as the glandular changes underlying this kind of hyperplasia have a proven worsening evolution and – if un-

Table 1. – *Incidence of neoplastic pathology in pazients with postmenopausal bleeding.*

Author	Year	Total patients	Frequency of pathology
Procope	1971	1085	28 %
Ganbrell	1974	363	3 %
Mantalenakis	1977	1038	22.7%
Isaacs	1978	143	23 %
Miyazaw	1983	138	8 %
Lidor	1986	226	7 %
Alberico	1987	158	29 %

Table 2. – *Postmenopausal bleeding*: frequency of atypical hyperplasia, endometrial adenocarcinoma and other genital neoplasias.*

No. cases per year	1981	1982	1983	1984	1985	1986	1987	1988	Total
	18	16	25	30	33	37	60	26	245
Endometrial adenocarcinoma	6	7	8	7	7	11	4	3	52
Atypical hyperplasia	1	–	1	2	–	2	1	–	7
Ovarian carcinoma	–	–	–	–	–	–	–	3	3
Cervical carcinoma	–	–	–	–	1	1	–	–	2
Twofold-morphology carcinoma	–	–	–	–	–	–	2	–	2
Leiomyosarcoma	–	1	–	–	–	–	–	–	1
Carcinosarcoma	–	–	–	–	–	–	1	–	1
Metastasis from vaginal carcinoma	–	–	–	1	–	–	–	–	1
							Total pathological cases		69

* N = 245

treated – turn into carcinoma in 28% to 38% of cases ([16]). A study by Hathcock ([17]) reported the presence of atypical or adenomatous hyperplasia before adenocarcinoma was diagnosed in 52% of 235 patients who had undergone histological tests in the previous decade.

The incidence of endometrial adenocarcinoma has significantly increased over the last ten years ([18]).

10.5 out of 100,000 is the figure for the Province of Trieste ([19]).

The same statistical source also indicates that this tumor increasingly occurs in younger age groups.

In view of all this we believe that a diagnostic protocol should be implemented for cases with postmenopausal bleeding in order to detect the disease as early as possible.

To this end several investigation techniques have been suggested which permit taking both cytologic and histologic specimens from the uterine cavity without hospitalization.

While recognizing the usefulness of these techniques in screening patients relatively at risk for this carcinoma, we nevertheless share the view of other Authors that cases with postmenopausal bleeding require the taking of histologic specimens with dilatation and curettage (D&C) under general anaesthesia ([1, 2, 15, 20, 21]).

The frequency of endometrial adenocarcinoma in patients with postmenopausal bleeding is retrospectively analyzed in this work and some clinical and epidemiological features of this neoplasia are assessed.

MATERIAL AND METHODS

We have collected data on 245 patients hospitalized in the Department of Obstetrics and Gynaecology of Trieste Children's Hospital (Istituto per l'Infanzia) in whom postmenopausal metrorrhagia had been diagnosed. All patients underwent fractional curettage of the uterine cavity under general anaesthesia in Day-hospital regime. The histological findings were analyzed at the Institute of Histology ad Pathological Anatomy of Trieste University.

The data taken from the clinical files were filed and processed with an Olivetti M28 computer.

The statistical significance of the results was assessed using the χ^2 method.

RESULTS

Table 2 shows the number of patients included in the study, with a yearly breakdown, totalling 245 curettages performed

Table 3. – *Distribution of population based on age and histological findings* *.

Age	Negative histology N = 172 ** No.	%	Positive histology N = 59 *** No.	%	χ^2	Other general neoplasias N = 10 No.	%
<45	1	0.6	–	0		–	0
45 - 50	14	8.1	3	5.1	p <0.01	–	0
51 - 55	68	39.5	15	25.4	p <0.01	–	0
56 - 60	53	30.8	13	22.0	p <0.01	3	30
61 - 65	13	7.6	7	11.9	p >0.01	5	50
66 - 70	11	6.4	9	15.2	p >0.01	–	0
71 - 75	10	5.8	10	16.9		1	10
76 - 80	2	1.2	2	3.5		1	10
					p <0.02		

* N = 245
** No histological evidence of neoplastic disease
*** Histological evidence of endometrial adenocarcinoma / atypical hyperplasia

on patients with postmenopausal bleeding. The ordinate axis reports the histological diagnosis made in patients with neoplasias .We have also included patients with atypical endometrial hyperplasias as this histological finding is similar to endometrial adenocarcinoma in some clinical features and in the natural history of the lesion. We have subdivided our series into three groups: *a*) no histological evidence of neoplastic disease; *b*) histological evidence of endometrial adenocarcinoma/ atypical hyperplasia; *c*) histological evidence of other genital neoplasias.

Table 3 reports the age distribution of patients with postmenopausal bleeding, with the relative histological findings. Negative histological finding are more frequent in the 51-60 years age group while positive histological findings are more fre-

Table 4. – *Epidemiological features: population distribution based on histological findings* *.

	Negative histology N = 172 ** No.	%	Positive histology N = 59 *** No.	%	χ^2	Other general neoplasias N = 10 No.	%
Arterial hypertension	62	36.1	21	35.6	p <0.01	2	20
Obesity	36	20.9	14	23.7	p <0.01	1	10
Liver diseases	21	12.2	9	15.2	p >0.01	1	10
Diabetes	20	11.6	5	8.5	p <0.01	1	10
Nulliparity	20	11.6	13	22.0	p <0.01	3	30
Late menopause (>55 yrs.)	6	3.5	5	8.5		–	0
Early menarche (<10 yrs.)	1	0.6	4	6.7		–	0
					p <0.1		

* N = 241
** No histological evidence of neoplastic disease
*** Histological evidence of endometrial adenocarcinoma / atypical hyperplasia

Table 5. – *Severy of bleeding: population distribution based on histological findings* *.

	Negative hystology N = 172 **		Positive histology N = 59 ***		χ^2	Other general neoplasias N = 10	
	No.	%	No.	%		No.	%
Mild	106	61.6	31	52.5	$p < 0.01$	8	80
Moderate	43	25.0	25	43.4	$p > 0.01$	–	20
Severe	19	11.1	3	5.1	$p < 0.01$	–	0
Not specified	4	2.3	–	0		–	0
					$p < 0.01$		

* N = 241

** No histological evidence of neoplastic disease

*** Histological evidence of endometrial adenocarcinoma / atypical hyperplasia

quent in older age groups (61-65 years and 66-70 years). The X2 Test has shown a significant distribution of these data only in the 45-50, 51-5 and 56-60 year groups. Taken altogether – conversely – these data failed to show significant correlation ($p < 0.02$).

Table 4 shows a list of epidemiologic characteristics drawn from these patients' case histories. In this case too the group with positive histological finding has been compared to the group with negative histological findings.

Patients with histological evidence of adenocarcinoma or atypical hyperplasia had more frequently a record of obesity, liver disease, nulliparity, late menopause or early menarche.

Only obesity and nulliparity were statistically significant.

Nulliparous and obese patients were more frequent in the group with positive findings.

In collecting clinical and case-history data we divided our patients into three groups according to the severity of bleeding: *a*) mild when the patient reported more or less continuing dripping; *b*) moderate when the patient reported menstruation-like bleeding; *c*) severe when metrorrhagia was so severe as to require urgent curettage. The comparison of the two groups (positive/negative histological finding) did not show significant percent age differences in the severity of bleeding ($p < 0.01$) (Table 5).

During this study we identified cases with abnormal gynaecological findings (Table 6). Interestingly enough about one third of our patients (belonging to either group) had uterine myomatosis.

We then analyzed the hysterometric data comparing the frequency of figures exceeding 8 cm (Table 7) which were 42.4% in patients with positive histological findings and 37.8% in patients with negative findings. The same table

Table 6. – *Finding on gynaecologic examination: population distribution based on histological findings* *.

	Negative histology N = 172 **		Positive histology N = 59 ***		Other genital neoplasias N = 10	
	No.	%	No.	%	No.	%
Normal	93	54.1	28	47.4	2	20
Myomatosis	48	27.9	18	30.5	2	20
Atrophy	24	13.9	11	18.6	1	10
Adnexal pathology	13	7.5	4	6.8	4	40

* N = 241

** No histological evidence of neoplastic disease

*** Histological evidence of endometrial adenocarcinoma / atypical hyperplasia

Table 7. – *Hysterometry: population distributlon based on histological findings* *.

	Negative histology N = 172 **		Positive histology N = 59 ***		χ^2	Other general neoplasias N = 10	
	No.	%	No.	%		No.	%
⩽7 cm	99	57.5	24	40.7	p >0.2	3	30
⩾8 cm	65	37.8	25	42.4		4	40
No assessment	7	4.1	9	15.2		3	30
No curettage	1	0.6	1	1.7		–	0

* N = 241

** No histological evidence of neoplastic disease

*** Histological evidence of endometrial adenocarcinoma / atypical hyperplasia

reports those cases in which this feature was not assessed, and two cases in which curettage was not possible because of severe cervical stenosis. One of these two patients had negative endometrial histological findings with "Endoscann" curettage and – in the absence of other clinical symptoms – followed an out-patient programme of checks that were always negative. The second one had further severe episodes of bleeding and – as curettage was not possible – underwent total hysterectomy. The histological test showed an endometrial adenocarcinoma.

Table 8 lists the histological findings from patients' curettage; endometrial adenocarcinoma was detected in 20.9% of cases. This figure rises to 23.8% with the inclusion of cases of atypical hyperplasia. Altogether, 69 patients showed positive evidence of genital neoplasia (28.16% - see table 2 for comparison).

The data reported in Tables 8 and 2 show a slight discrepancy with regard to the total number of patients: 245 as against 240. This is so because in 4 cases of menopausal bleeding the presence of severe cervical stenosis made endometrial biopsy impossible. As no objective symptoms were detected in follow-up we decided not to make further attempts at endometrial biopsy. In the fifth case, who presented persistent bleeding, curettage of the uterine cavity was repeatedly attempted but always failed. After clinical examination, total hysterectomy was performed. Histological examination of the surgical specimen showed a well differentiated endometrial adenocarcinoma.

Finally, neoplastic pathologies were detected in two patients with no histological evidence of disease. The first one was a twofold-morphology cervical carcinoma diagnosed thanks to biopsy of the cervix and portio. In the second one the curettage gave a histologic finding of "glandu-

Table 8. – *Outcome of histological tests following fractional curettage: N = 240* *.

	No.	%
Proliferative endometrium	60	25.0
Null product	55	22.9
Endometrial carcinoma	50	20.9
Cystic-adenomatous hyperplasia	35	14.6
Cystic-adenomatous polyp	11	4.6
Senile atrophy	8	3.4
Atypical hyperplasia	7	2.9
Dysfunctional endometrium	6	2.5
Necrobiosis	2	0.8
Cervical carcinoma	2	0.8
Leiomyosarcoma	1	0.4
Carcinosarcoma	1	0.4
Twofold-morphology carcinoma	1	0.4
Metastasis from vaginal carcinoma	1	0.4

* 5 patients with cervical stenosis.

Table 9. – *Interval between menopause and onset of bleeding (in years)* *.

Years	Negative histology N = 172 ** No.	%	Positive histology N = 59 *** No.	%	χ^2	Other genital neoplasias N = 10 No.	%
⩽1	87	50.6	28	47.4	p <0.01	2	20
2	30	17.5	20	33.9	p <0.01	2	20
3	14	8.1	3	5.1		–	0
4	2	1.2	–	0		–	0
5	8	4.7	–	0		–	0
6	3	1.7	–	0		–	0
7	3	1.7	2	3.4		–	0
⩾8	25	14.5	6	10.2	p <0.01	–	60

* N = 241

** No histological evidence of neoplastic disease

*** Histological evidence of endometrial adenocarcinoma / atypical hyperplasia

Table 10. – *Interval between onset of bleeding and hospitalization (in weeks)* *.

Weeks	Negative histology N = 172 ** No.	%	Positive histology N = 59 *** No.	%	Other genital neoplasias N = 10 No.	%
⩽1	108	62.8	25	42.4	4	20
2	24	14.0	8	13.6	2	20
3	15	8.7	7	11.8	1	10
4	5	2.9	3	5.1	1	10
5	8	4.6	5	8.5	1	10
⩾6	12	7.0	11	18.6	1	10

* N = 241

** No histological evidence of neoplastic disease

*** Histological evidence of endometrial adenocarcinoma / atypical hyperplasia

lar polyp of the uterine cavity"; total hysterectomy for uterine myomatosis was performed and the histological section of the surgical specimen detected a circumscribed focus of endometrial adenocarcinoma.

This was therefore our only false positive.

The period of time elapsing between menopause and occurrence of metrorrhagia with consequent performance of curettage was also considered (Table 9). The comparison of the two groups (positive/negative histological findings) showed no significant difference.

The lapse of time (expressed in weeks) between the onset of symptomatology and hospitalization was finally analyzed. Interestingly enough, considering that these cases were admitted to our Center as emergencies, 19.18% of our patients had turned to the gynaecologist as late as one month after the appearence of these symptoms (Table 10).

DISCUSSION

In our experience 24% of patients with postmenopausal bleeding were diagnosed adenocarcinoma or atypical hyperplasia. This figure increased to 43.7% if the series was confined to patients over 60 years of age. Bleeding in menopause and age over 60 are therefore closely correlated with this pathology.

The other factors of risk for endometrial adenocarcinoma, though in some cases confirming their frequent association with this disease, often failed to show statistically significant correlations in our study.

This may be partly due to the fact that our data have been collected retrospectively with all the consequent limitations. However, while a cost-benefit analysis does not justify a screening programme in the population relatively at risk for adenocarcinoma, the onset of objective symptoms like postmenopausal bleeding does demand curettage under general anaesthesia.

This investigation is to be carried out regardless of the severity of bleeding. 52.5% of our histologically positive patients, as a matter of fact, reported only occasional blood dripping. The lapse of

time between menopause and the onset of postmenopausal bleeding should not influence this diagnostic approach either. Curettage is therefore unavoidable in these cases, though admittedly not fully risk-free nor accurate in 100% of uterine tumors and sometimes has to be repeated ([22]).

Our case series recorded only one false negative and only in 2% of patients did the curette fail to reach into the uterine cavity. In these cases, in the absence of objective symptoms, the patient was closely followed-up by taking cytologic and/or bioptic endometrial specimens in an outpatient regime with "Perna" or "Endoscann" curettes.

Interestingly, in 22% of cases the curettage specimen was not sufficient for the histologic preparation; in some cases, this may be due to endometrial atrophy which is rather frequent in elderly patients.

Examination of the cavity was always performed by experienced clinicians and no tumor has so far been detected in the follow-up of these patients (varying between 1 and 6 years).

The incidence of endometrial adenocarcinoma is significantly increasing throughout the world. However, thanks to the characteristics which have been mentioned earlier on (early onset of objective symptoms, relatively slow growth, high differentiation and consequent low malignancy potential in a large number of cases, relatively easy access to the uterine cavity) this disease should be detected in an early stage.

Surgical therapy, successful progestinic hormonal treatments and the satisfactory response of this tumor to radiotherapy should concur in lowering the mortality rate of this carcinoma significantly.

Unfortunately, these conditions are not always present and the diagnosis is still often made rather late as compared to the onset of the symptoms. A study carried out in Milan on 173 cases of endometrial adenocarcinoma has shown that the disease was diagnosed six months after the onset of the symptoms in over 50% of cases, and two years after or later in 20% of cases ([23]).

In our experience too, the diagnosis was made more than six months after the first postmenopausal bleeding in about 20% of cases.

This is partly due to underestimation of the importance of postmenopausal bleeding on the part of the patient, but may also be partly due to mismanagement of the cases by general pratictioners ([23]). This delay is detrimental to the patient since the evolution of this tumor – slow as it may be according to its natural history – worsens the prognosis.

We therefore believe that a targeted screening and early diagnosis protocol should be implemented for this section of the population – elderly women – often neglected by information and mass screening campaigns.

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PRENATAL DIAGNOSIS OF CYSTIC ADENOMATOID MALFORMATION OF THE LUNG

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Summary: Two cases of congenital cystic adenomatoid malformation of the lung (CCAML) are described. In the light of recent literature the prenatal diagnosis and management are discussed.

Key words: Prenatal diagnosis; Obstetrical management; Adenomatoid malformation.

INTRODUCTION

Congenital cystic adenomatoid malformation (CCAML) is a rare disease of the lung ([1, 2, 3]). The majority of about 200 cases, that have been described up to now, were diagnosed after birth, prenatal ultrasonographic diagnosis being reported in only 20 cases ([1, 4, 5]).

Based on the size of the cysts, the lesion is classified into three types with different prognosis, which is also influenced by other possible associated defects ([6, 7, 8]). The perinatal outcome is characterized by intrauterine death in 14% of the cases; premature delivery is common in the presence of fetal hydrops and hydramnios; severe respiratory distress in 70-80% of the cases require surgical therapy immediately after birth ([9–14]). The newborn with less extensive lesions show mild episodes of cyanosis and recurrent pulmonary infections during the first year of life ([11, 14–17]).

In the present report two cases of CCAML that were prenatally diagnosed in the Department of Obstetrics and Gynecology of Ferrara University are reported.