fluxes may provide important insight into the mechanism of hypertension.

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Increased incidence of menstrual abnormalities and hysterectomy preceding primary biliary cirrhosis

A J STELLON, ROGER WILLIAMS

Abstract

A study was performed to assess the incidence of previous hysterectomy and dilatation and curettage among women with primary biliary cirrhosis. In 87 patients with primary biliary cirrhosis hysterectomy or dilatation and curettage had been performed significantly more often than among 100 age matched normal controls and 80 age matched patients with chronic active hepatitis or alcoholic liver disease. Among the 47 patients with primary biliary cirrhosis who had undergone hysterectomy or dilatation and curettage operations had been performed at a mean of 10.7 years and 13.2 years, respectively, before the onset of disease. The main indication for hysterectomy among patients with primary biliary cirrhosis and controls was menorrhagia.

These menstrual disorders may be a consequence of high concentrations of oestrogens in patients with primary biliary cirrhosis.

Introduction

Both menorrhagia and amenorrhoea have been reported in association with chronic liver disease but not in women with primary biliary cirrhosis. In a study of patients with primary biliary cirrhosis we found an unexpectedly high proportion with menorrhagia, which had resulted in hysterectomy before the apparent onset of liver disease.

Patients and methods

Eighty seven consecutive patients with primary biliary cirrhosis, confirmed at biopsy, who were attending the outpatient department or being admitted for assessment were interviewed from January to December 1984. Patients' ages were in the range 35-70 years. A gynaecological and obstetric history was obtained from each patient, and when the patient had undergone any gynaecological procedure the appropriate hospital was contacted and the operative and pathological findings obtained. The control groups, who were similarly interviewed, consisted of 100 age matched, healthy hospital staff and 80 age matched women with either chronic active hepatitis (45 patients) or alcoholic liver disease (35).

Results

The table shows that there was a striking difference between the patients with primary biliary cirrhosis and the control groups with respect to the proportion who had undergone hysterectomy. Furthermore, among patients with primary biliary cirrhosis hysterectomy had been performed a mean of 10.7 years (range 1-30 years) before the diagnosis of liver disease in

Liver Unit, King's College School of Medicine and Dentistry, London SE5 8RX

A J STELLON, BSC, MRCP, clinical research fellow
ROGER WILLIAMS, MD, FRCP, director of liver unit

Correspondence to: Dr Williams.

Findings in patients with primary biliary cirrhosis compared with normal control subjects and patients with other liver diseases

	Normal controls (n=100)		Primary biliary cirrhosis (n=87)		Chronic active hepatitis (n=45)		Alcoholic liver disease (n=35)	
	Mean (SD)		Mean (SD)		Mean (SD)		Mean (SD)	
Age (years)	53.8 (9.6)		56.1 (9.3)		56.2 (9.5)		54.9 (8.6)	
Age at menopause	50.6 (2.9)		47.0 (5.7)*		50.9 (3.1)		46.8 (4.1)*	
Age at hysterectomy (years)	42.3 (8.2)		42.4 (4.8)		39.8 (4.7)		44 (6.1)	
No (%) of patients	Hysterectomy 16 (16)		Hysterectomy 29 (33)†		Hysterectomy 5 (11)		Hysterectomy 3 (9)	
No of patients with menorrhagia	11		24		3		2	
Postmenopausal and intermenstrual bleeding	3		2		0		1	
Dysmenorrhoea	1		1		1		0	
Abdominal mass	1		2		1		0	
Infertility	0		0		0		0	

*p<0.05 compared with normal controls (two tailed unpaired Student's *t* test).

†p<0.025 and ‡p<0.05 compared with normal controls (χ^2 analysis).

D and C=Dilatation and curettage.

26 (90%) of 29 patients. In patients with chronic active hepatitis or alcoholic liver disease hysterectomy had been performed a mean of 13 years (range 10-20 years) and 17.8 years (range 16-20 years), respectively, before the diagnosis of the liver disease.

The main clinical indication for hysterectomy in the patients with primary biliary cirrhosis was menorrhagia (83%); this was similar for the control groups (table). Findings at hysterectomy were compatible with such symptoms. For patients with primary biliary cirrhosis these comprised fibroids (51%), endometriosis (21%), pseudomucinous cystadenoma (10%), endometrial polyps (7%), and carcinoma of the cervix (3%). Patients in the control groups had similar findings. Of the 21 uteri removed from patients with primary biliary cirrhosis that were examined microscopically, endometrial hyperplasia was detected in five (24%).

The percentage of patients with primary biliary cirrhosis who had previously undergone dilatation and curettage was significantly higher than that for the control subjects (table). Dilatation and curettage had been performed a mean of 13.2 years before the diagnosis of liver disease in 22 (85%) patients with primary biliary cirrhosis, the clinical indication in most cases being menorrhagia or irregular menstrual bleeding (table). The age at menopause in the patients who had not undergone a hysterectomy was significantly lower in patients with primary biliary cirrhosis or alcoholic liver disease than in age matched normal subjects (table).

Comment

The significantly higher incidence of hysterectomy or dilatation and curettage, the indications in both instances being menorrhagia, in patients with primary biliary cirrhosis than in normal subjects and patients with other chronic liver diseases has not been reported previously. Coagulation abnormalities and myxoedema, both of which may occur in association with primary biliary cirrhosis, were excluded as possible causes of menorrhagia.

The underlying pathological abnormalities found in the specimens obtained at hysterectomy—namely, fibroids, polyps, endometrial hyperplasia, and endometriosis—are all believed to be caused by, or exacerbated by, high oestrogen states.¹ In a recent study of postmenopausal women with chronic liver disease high free oestrogen concentrations and higher free oestrogen to androgen ratios were found than in age matched controls.² Although the abnormalities were no greater in patients with primary biliary cirrhosis than in the other liver disease group (alcoholic cirrhosis), the functional disturbance in primary biliary cirrhosis may have been present for longer. The existence of a prolonged asymptomatic phase of primary biliary cirrhosis is now well documented,³ and it is possible that when the hysterectomies were carried out the disease was already present in an asymptomatic phase.

Dysfunctional uterine bleeding as a cause of the menorrhagia also needs to be considered. This occurs as a result of excessive proliferation of the endometrium caused by unopposed oestrogen action consequent on anovulatory cycles,⁴ and the latter are occasionally associated with follicular cyst formation of the ovaries. Interestingly, five of the 21 uteri examined and five of 14 curettings obtained showed endometrial hyperplasia, and in six patients follicular cysts of the ovary were noted at the time of hysterectomy.

A postmortem study of women with cirrhosis has found pathological evidence of hyperoestrogenism,⁵ and this lends support to the presence of an absolute or relative excess of oestrogen as the cause of the menorrhagia in primary biliary cirrhosis.

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100 YEARS AGO

The East London Waterworks Company deserve at least some commiseration, for, as the results of an accident, they are now involved in a difficulty from which it will require all their energy and ingenuity to free themselves. Some years ago one of their filter-beds gave way, and "some eels of very minute size" found their way into the Company's mains. Since then these creatures have grown, and rapidly increased in numbers, and periodically, in the warmer months, they have manifested their presence in certain localities, despite all the efforts of the Company's staff to get rid of them. Occasionally a communication-pipe becomes blocked, and examination discloses a dead eel to be the cause. In several cases the water from the pipe has been noticed to be bad, and those who have drunk of it have suffered from more or less severe illness. The cause has been found to be a putrid eel. Quite recently a case of typhoid fever in the West Ham district has been investigated, and one of the causes alleged is the presence in the water of a dead eel. However this may be, it is not pleasant to have any doubts raised as to the purity and wholesomeness of the water from the household tap. The puzzling part of the whole matter is that eels are able to exist in the mains in spite of the enormous pressure of water, which varies from 30 lbs. to 100 lbs. to the square inch. And further, upon what do the creatures live, since the water is presumably pure? Is the water as free from organic impurity as it professes to be; or is there something in it which serves the eels for food, and which, apart from the eels, might of itself, under favouring circumstances, prove injurious to the drinkers of the water? There is one way by which the consumers of this water can protect themselves, and that is by boiling it before use. This course is habitually adopted by many prudent housekeepers in districts where eels are not known to exist, and we commend its adoption in the present case. It is a pity the process of boiling cannot be applied to the eels in the mains. They could scarcely be expected to resist that "pressure," and their dead bodies could no doubt then be finally flushed out. (*British Medical Journal* 1886;ii:729.)