CLINICAL CATEGORIZATION AND INVESTIGATIVE APPROACH TO SECONDARY AMENORRHOEA (STUDY OF 100 CASES)

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SUMMARY

In this study 100 cases of secondary amenorrhoea were studied clinically, endocrinologically and with laparoscopic guided ovarian biopsy. The most common cause of amenorrhoea found in this series was ovarian (54%). There were 27 cases of premature ovarian failure and 14 cases of polycystic ovarian disease. The scope of laparoscopy, ovarian biopsy is discussed. A single estimation of FSH and LH was found helpful in this study, rather than multiple estimation of hormone.

INTRODUCTION

The etiopathology of secondary amenorrhoea is diverse and can range from serious underlying disease like, pituitary tumour or it could just be a reflection of a psycosomatic disorder. Laparoscopy, ovarian biopsy and endocrine studies assist the work up of secondary amenorrhoea and help to localise the lesion. This communication presents the results of investigations of a hundred cases of secondary amenorrhoea and the value of laparoscopy, hormonal studies and ovarian biopsy is discussed.

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Accepted for Publication on 26/7/91

MATERIALS AND METHODS

One hundred women with secondary amenorrhoea attending the gynaecological department of Kasturba Medical College Hospital Manipal from January 1984 to December 1988 were included in the study. Analysis was based on clinical examination, evaluation by diagnostic laparoscopic findings, laparoscopic ovarian biopsy, radio-immuno assay of hormones and histopathological study of endometrium. Patients were examined for pituitary tumour or abnormalities of sella turcica by skull X-Ray, charting of visual fields and examination of fundus occuli, special investigation of computerised axial tomography (CAT Scan) was done when necessary.

The diagnostic classification of 100 cases of

TABLE I

Causes of Amenorrhoea

Local Causes :		
Genital tuberculosis	..	4
Asherman's syndrome	..	4
Cervical stenosis	..	3
Nonspecific endometritis	..	1
Ovarian Causes :		
Gonadal dysgenesis	..	11
Premature ovarian failure	..	27
Gonadotropin resistant ovary	..	2
Polycystic ovarian disease	..	14
Ovarian tumour	..	2
Hypothalamic Causes :		
Post pill amenorrhoea	..	4
Stress induced	..	2
Post meningitis	..	1
Hypothalamic dysfunction	..	1
Pituitary Causes :		
Chromophobe adenoma	..	2
Micro adenoma	..	2
Sheehan's syndrome	..	3
Acromegaly	..	1
** Hyperprolactinaemia	..	14
General systemic diseases	..	2
Total	..	100

** (Hyperprolactinaemia other than due to pituitary tumour)

secondary amenorrhoea as reached by extensive evaluation is shown in Table I.

Genital tuberculosis was seen in 4 out of 100 cases (4%) of secondary amenorrhoea. Cervical stenosis giving secondary amenorrhoea seen in 3 cases (3%) were mainly following post MTP infection. Ovarian cause contributed to the largest group of secondary amenorrhoea. 56 out of 100 patients (56%) had an ovarian pathology giving the problem of amenorrhoea. Gonadal dysgenesis was observed in 11 cases (11%) while premature ovarian failure accounted for 27 out of 100 cases (27%). We had two rare cases of gonadotrophin resistant ovary in our series. Two cases of ovarian tumour one being arrhenoblastoma and the other pseudomucinous cystadenoma of enormous size (15 kg), presented with secondary amenorrhoea. In hypothalamic causes (8 cases) 4 were due to post pill amenorrhoea. In twenty two patients who had pituitary problem as a basis for secondary amenorrhoea, three patients had chromophobe adenoma, two microadenoma of pituitary. Three patients had post partum pituitary necrosis (Sheehan's syndrome) while 17 cases had hyperprolactinaemia.

Laparoscopy and ovarian histopathology :

Table II gives the ovarian histopathology in our series of secondary amenorrhoea.

Ovaries were found to be streak in 11 cases and were small and corrugated were later proved to be cases of premature ovarian failure after hormonal evaluation. Serial sections of ovarian biopsy failed to show follicles in 31 cases and stromal fibrosis was seen in 5 cases. 13 out of 14 cases of PCO revealed microcystic ovaries. Patients with hypothalamo pituitary disorder had a normal looking ovary which contained follicles at different stages of development in some cases and few follicles in others. In two cases ovarian biopsy performed after laparotomy removal of tumour showed arrhenoblastoma and Pseudomucinous cystadenoma respectively.

Hormonal profile in secondary amenorrhoea

Radio-immunoassay of hormones was possible in 74 cases of secondary amenorrhoea. Eighteen cases showed hypergonadotrophic status. Most significant rise of gonadotrophins were found in cases of premature ovarian failure (POF). Eight cases of POF showed FSH range of 100-150 mIU/ml (mean FSH 110 mIU/ml). Two cases of raised FSH (mean 80 mIU/ml) with normal ovarian follicles were diagnosed to be rare cases of gonadotrophin resistant ovary.

Moderately elevated level of LH and normal FSH constituted the picture in 3 out of 10 cases of polycystic ovarian disease. Radio immuno assay of hormones gave a variable picture in group of patients who had hypothalamo - pituitary cause for amenorrhoea. Out of 30 cases in this group majority 19 (63.3%) were

TABLE II

Ovarian Histopathology

Primodial follicles absent	Primodial follicles present	Stromal fibrosis	Polycystic fibrosis thecosis	Tumour	Total
49	31	5	13	2	100

Eugonadotrophic 7 cases showed low gonadotrophin, (mean LH 3.5 mIU/ml) (mean FSH 4.6 mIU/ml), three cases showed high LH and 1 case had high FSH. These 4 cases with high gonadotrophin had hyperprolactinaemia as well.

Prolactin was normal in 60 cases and increased in 16 cases. The various causes of hyperprolactinaemia are given in Table III.

In all 17 cases showed hyperprolactinaemia

TABLE III

Hyperprolactingaemia causes

Drug induced	3
Primary hypothyroidism	1
Pituitary tumour	3
Idiopathic	10
Total	17

(serum prolactin 70-250 ng/ml.) 3 cases with pituitary tumour, two microadenoma and one chromophobe adenoma showed hyperprolactinaemia. 3 cases of hyperprolactinaemia, presented as post pill amenorrhoea. Out of 17 cases 7 patients had galactorrhoea.

Serum testesterone was found high in 3 cases of P.C.O. One case of arrhenoblastoma showed serum testesterone of 6.3 ng/ml. TSH was low in 10 cases and normal in 64 cases. T3 and T4 estimation was normal in all 74 cases (TSH <.1 mIU/ml). Normal (.1-.9 mIU/ml).

DISCUSSION

Secondary amenorrhoea is a common symptom with variety of different causes. Investigations like laparoscopy, ovarian biopsy and radioimmuno assay of hormones help to localise the cause. The value of laparoscopy in diagnosis of genital tuberculosis is undoubted, secondary amenorrhoea due to tuberculosis endometritis was found in 4 out of 100 cases (4%). This incidence is considerably less as compared to 42% reported by Devi P.K. in 1962 and 24% by Mehrotra in 1971. The remarkable reduction in last 2 decades implies better health care system and public awareness of disease entity.

Use of laparoscopic guided ovarian biopsy has opened a new door in diagnosis, prognosis and management of a case of secondary amenorrhoea (Black and Govan 1972). In 11 out of 100 cases Streak gonads were observed with laparoscope and ovarian biopsy revealed no follicles in these group. These cases of gonadal dysgenesis presenting as premature ovarian failure is due to Mosaicism of sex chromosomes. The secondary sexual characters and menarche with few periods are due to few follicles which underwent atresia later in life.

Premature ovarian failure was dianosed in 27 cases of secondary amenorrhoea. All showed absent primodial follicles, increased gonadotrophins and low serum oestradiol. In 22 out of 27 cases (81.48%) ovaries were small and corrugated but in 5 cases ovaries appeared normal but showed no follicles on histopathology. High serum gonadotrophin values clinched the diagnosis of POF in these cases. Two of our cases showed high serum gonadotrophins. (mean FSH 80.8 mIU.ml) normal primodial follicles and no progression. These were rare cases of gonadotrophin resistant ovary as described by Jones and Demore Ruchseh (1969).

In cases of secondary amenorrhoea due to H.P. dysfunction a good number of follicles seen on ovarian biopsy indicates a better prognosis. Skyes and Ginsberg (1972) have reported return of menstruation or pregnancy after therapy in patients who had a good folliclar stock. Few cases of pregnancy in POF after oestrogen therapy have been reported. The efficiency of estrogens according to Manet et al is due to induction of FSH receptors in residual follicles by estrogens, while Richard et al suggested that estrogens increased LH receptors as well as ovarian sensitivity to FSH.

After estrogen progesteron cyclical therapy in 17 cases of POF one pregnancy is reported by

Shoichi et al (1988).

With the Herald of radio immuno assay of hormones in the gynaecological endocrinology the diagnosis of two clinical conditions which are almost alike in all respects changes dramatically as seen in gonadal dysgenesis and H.P. dysfunction, axis shows tern variation besides cyclic fluctuation with monthly periodicity (Friedman 1972). It is therefore proposed that multiple daily estimation of hormones have to be done in secondary amenorrhoea (Friedman 1972). However we found that in order to establish to which diagnostic group patients with amenorrhoea belongs it is only necessary to administer progesteron therapy and then perform either a single LH or FSH estimation. Measuring LH is helpful in establishing the diagnosis in patients who had withdrawal bleeding following progesteron. It is important to measure FSH in patients who do not have withdrawal bleeding after progesteron to determine whether they have ovarian or H.P. failure. A diagnosis of ovarian failure may be made in patients with an elevated FSH. Thus a single estimation of FSH and LH was found helpful in our study which is in conformity with Kletzkyoi et al (1975).

Serum gonadotrophin estimations however cannot differentiate between H.P. dysfunction and H.P. failure. This differentiation is best possible by pituitary gonadotrophin reserve test using synthetic LHRH (Bohnet et al 1976).

Summary and Conclusion :

100 cases of secondary amenorrhoea investigated by methodical evaluation using laparoscopy ovarian biopsy and radio-immuno assay of hormones are analysed.

Diagnostic classification included 4 cases of genital T.B., 27 cases of premature ovarian failure. Gonadal dysgenesis causing secondary amenorrhoea was seen in 11 cases. This is attributed to the fact that in the process of follicular atrosia some of the follicles could have survived upto age of puberty and thus patient would have had few normal periods.

The most important advantage of radio immuno assay is the convenience with which it is possible to study a wide range of materials using a single common technique.

A single estimation of FSH and LH was found helpful in this study rather than multiple estimation of hormones.

Case reports of estrogen-progesteron cyclical therapy giving rise to ovulation and even pregnancy is a welcome news for the patients with premature ovarian failure.

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