PREMATURE OVARIAN FAILURE - AN OVERVIEW

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SUMMARY

Premature ovarian failure (POF) was looked for when there was cessation of ovarian function before the age of 40 years. Serum FSH level more than 40 mIU/ml in association with hypo-oestrinism and secondary amenorrhoea of more than one year are the criteria to diagnose POF. 24 cases were reviewed with special reference to the study of etiological factor. There were 10 controls. 10 of the 24 patients had associated auto-immune disorders. 14 patients had serum Ig measured of which 10 had no significant associated diseases but their serum Ig values were elevated suggesting an auto-immune process. In the teenage girls and in patients with primary amenorrhoea (but having at least one ovary), chromosomal aberrations were predominant. Inheritance was found in 2 women.

INTRODUCTION

Premature Ovarian Failure (POF) is generally accepted when there is cessation of ovarian functioning before the age of 40 years (Coulam et al., 1983). Shaw et al. (1992) mentioned it to be relatively common affecting one percent of women under 40 years. Ruchsen et al (1972) included both cases of primary and secondary amenorrhoea in their study.

POF is not an immediate life-threatening state but it has got substantial impact on the women's physical and mental health. It is associated with all the complications of menopause occuring at a much earlier or younger age and thus having a longer time to produce the deleterious effects on the affected women. Where POF occurs at an earlier age, infertility is an added problem. An insight is necessary into this dreaded morbidity as to why there should be premature

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structural and functional derangement of ovaries.

The etiology of POF has been the subject of several speculations and studies. Jacob et al (1959) suggested chromosomal aberration as a factor which was not confirmed by many others (Boczcowski et al, 1969). Coulam et al (1983) provided evidence for a genetic cause of POF which occured in generations. Coulam et al (1979) earlier observed that almost 20% of patients with POF with normal Karyotype have associated auto-immune disease. Vallotton and Forbes (1986) suggested an auto-immune mechanism as a possible etiology in some cases. In the present study, a critical analysis of women with POF was made to detect any etiological/epidemiological factor.

PATIENTS AND METHODS

24 patients attending the Gynaecology OPD of I.P.G.M.E. & R. & S.S.K.M. Medical Hospital Calcutta, were studied during the period March 1990 to July 1993. The upper age limit for POF was fixed at 40 years. Cases presenting with both primary and secondary amenorrhoea were included. Pregnancy was excluded. The cases were considered for study when they fulfilled the following criteria:

1. Secondary amenorrhoea more than one year and primary amenorrhoea at 16 years age.
2. Serum FSH level more than 40 mIU/ml.
3. Hypo-oestrinism and deficiency features.

There were 10 control cases - 5 fertile, healthy, menstruating women of age range 20 to 40 cases (except one hypothyroid) and 5 healthy women who had natural menopause of 2 to 7 years duration.

The following was the study protocol :

A. A thorough history taking and clinical examination.
B. Routine blood, urine and stool examination, X-ray chest.
C. Serum hormones : FSH, LH, Estradiol, Prolactin and TSH estimation.
D. Endometrial biopsy.
E. Vaginal cyto-hormonal study.
F. U.S.G./laparoscopy/ovarian biopsy in selected cases.
G. Karyotyping in all 4 cases of primary amenorrhoea and in 3 of the 5 cases of secondary amenorrhoea at their teenage.
H. Serum IgG and IgM determination in 14 cases in study group and 10 control cases measured by single radial immuno-diffusion technique using Tripartigen plates (Non-partigen - Behring).

Study facilities for circulating ovarian-antibodies were not available and as such IgG and IgM values determined, elevated level of which might significantly be a pointer to auto-immune disorder (Ananthanarayan and Panikar, 1990).

RESULTS

Table I, II and III show the profile of patients. Serum FSH in the study group ranged from 44 to 110 mIU/ml and LH from 13.1 to 65 mIU/ml. Serum estradiol values varied between 10 to 40 pg/ml in 22 patients, and above 40 pg/ml. in the rest. Serum Prolactin levels were within normal limits in all patients

Table I

Profile of Patients with Primary Amenorrhoea

Case No.	Name Age (Yrs.)	Significant associated disease	Karyotype	Antibodies (g/lit.)		Laparoscopy	Ovarian biopsies
				IgG (8.02-17.6)	IgM (0.65-2.80)		
1.	1B (27)	VH at 10 yrs. DM at 12 yrs	46 XX	-	-	OV(R) - Normal sized. OV(L) - Absent	Few atretic follicles
2.	JC (19)	-	46 XX/ 46 XX p.del in few	19.0	4.25	OV(R) - Streak OV(L) - Normal sized.	Few atretic follicles
3.	NK (23)	HT at 19 yrs.	46 XX	-	-	OV(R) - Normal sized OV(L) - Absent	Scant active follicles
4.	UK 17	-	45 x 0	> 37.7	4.37	OV (both) - Streak	*

* Developed bilateral highly anaplastic dysgerminoma during the study period.

Abbreviations : OV - ovary; R-right; L-Left; VH-viral hepatitis; DM-diabetes mellitus; HT-hypothyroid.

Table II

Profile of patients with secondary amenorrhoea and associated autommune disorder

Case No.	Name Age (yr.)	Age at last menses	Age at menarche (years)	Significant illness or associated auto-immune disorder	IgG (g/lit) Normal 8.02-17.6	IgM (g/lit) Normaly 0.650-2.80	USG/Laparoscopy/ ovarian biopsy in few
5.	DG 36	35	12	Ovariotomy (R) at 28 yrs. Rheumatoid arthritis 15 30 yrs.	-	-	OV (L) biopsy-active follicles.
6.	GC 37	35	15	Rheumatic fever and carditis at 10 yrs.	26.5	> 4.83	USG - ovaries appear
7.	SG 26	21	14	HT at 22 yrs.	7.0	.0320	USG - ovaries appear normal.
8.	AR 38	35	10	HT at 30 yrs.	-	-	"
9.	SD 33	31	13	Typhoid at 13 yrs. HT at 30 yrs.	-	-	"
10.	SD 19	17	11	HT at 17 yrs.	-	-	"
11.	NN 22	15	15	Mumps and chicken pox in childhood Aplastic anaemia	19.0	2.90	"
12.	AS 38	37	12	HT at 36 yrs.	15.6	4.48	"

Abbreviations : Ov. - ovary; R - right ; L - left; HT - hypothyroid.

Table III

Profile of patients with secondary amenorrhoea without any associated autoimmune disorder

Case No.	Name Age (yr.)	Age at last menses	Age at menarche (years)	Significant illness or associated auto-immune disorder	IgG (g/lit) Normal 8.02-17.6	IgM (g/lit) Normaly 0.650-2.80	USG/Laparoscopy/ovarian biopsy in few
13.	RS 26	26	15	TB endometritis at at 19 yrs.	-	-	USG/lap: Extensive adhesions, ov. not seen.
14.	HB 25	23	13	-	26.5	3.92	USG - ovaries appear normal
15.	GK 32	28	12	-	26.1	3.8	
16.	RD 19	18	15	Premature menopause in mother & sisters	22.5	2.52	Ov. biopsy- no active follicles stromal hyperplasia.
17.	AM 35	34	12	Premature menopause in mother and sister	-	-	USG - ovaries appear normal.
18.	LS 32	27	17	Pulmonary TB (treated) at 17 yrs. D/C (1991) : scanty non-sec. endomet., no TB	-	-	USG/lap : OV (R) - multiple follicles on surface. OV (L) - T.O. mass
19.	LM 17	16	13	-	12.5	4.48	USG - ovaries appear normal.