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Secondary Amenorrhea: Causes, Management And Outcome Using Algorithmic Approach.

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Abstract: *Secondary amenorrhea in women of reproductive age may be an indication of an undiagnosed, chronic condition and appropriate treatment is dependent upon accurate diagnosis of the underlying etiology. A thorough clinical assessment and a few common laboratory tests can easily identify the most frequent causes of secondary amenorrhea. However. in these cases, misdiagnosis is unfortunately common and often the result of poor laboratory utilization in the form of a failure to employ indicated tests, the use of obsolete tests, or erroneous interpretation in the face of interfering factors or co-morbidities. Consequently, the algorithmic approach to laboratory evaluation in the context of secondary amenorrhea described in this review can minimize the risk of diagnostic error as well was decrease test volume, cost, and time to diagnosis.aim of the study is to evaluate the cause of secondary , management and outcome of secondary amenorrhea using an algorithmic approach in 100 cases patients of secondary amenorrhea who attended gynaecological OPD*
Key words: secondary amenorrhea , algorithmic approach

I. Introduction

Amenorrhea is the absence of menstrual bleeding. Secondary Amenorrhea is absence of menses in a normally menstruating Women for three cycles or six months or more.(1) In female of reproductive age, diagnosing amenorrhea is a matter of first determining whether pregnancy is the etiology. In the absence of pregnancy, the challenge is to determine the exact etiology of amenorrhea. The differential diagnosis of secondary amenorrhea is broad and can range from genetic abnormalities to endocrine disorders and psychological environmental and structural anomalies. To facilitate prompt and accurate diagnostic workup, obtaining a thorough history and performing detailed physical examination is essential. Then an algorithmic approach is followed to narrow the diagnostic possibilities. This kind of systemic approach avoids unnecessary and expensive diagnostic procedures. In this project an attempt has been made to evaluate the aetiopathology of secondary amenorrhea and their respective management and response of the patient to respective treatment.

II. Materials And Methods

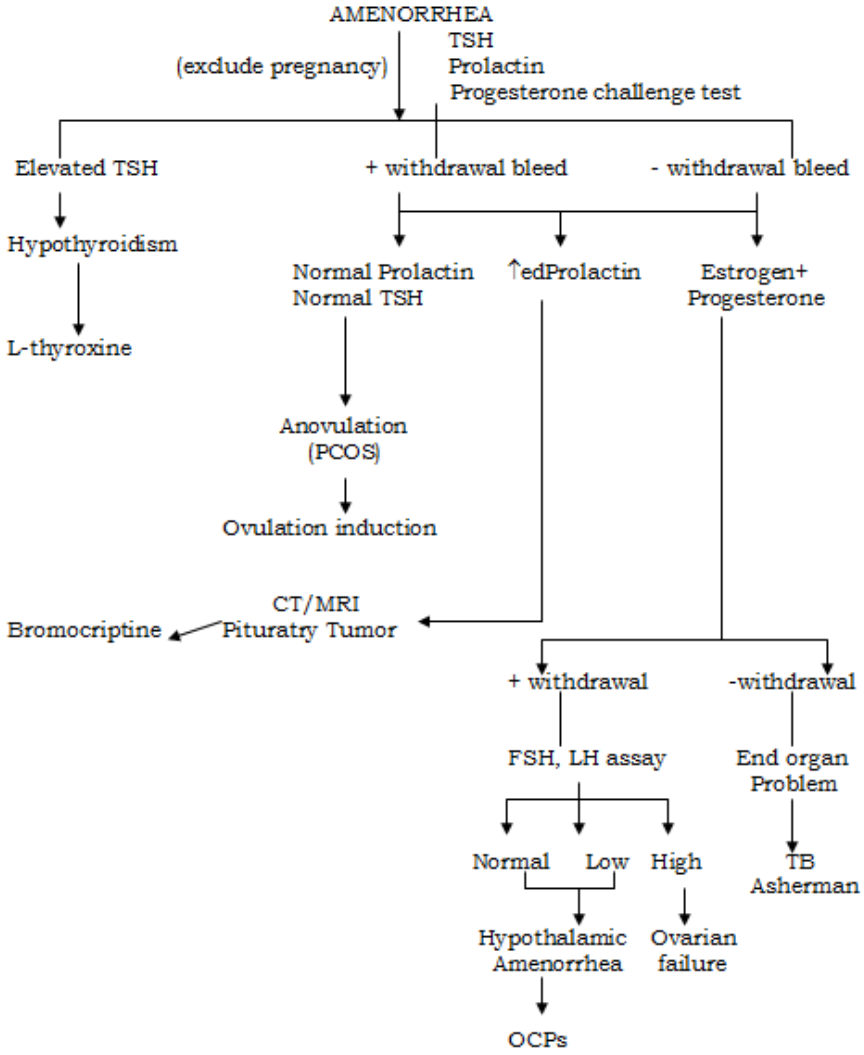
Hundred cases of secondary amenorrhea who attended Gynaecological OPD were the subjects of the present study.

- The age group of the cases was between 16-40 years .
- The duration of amenorrhea was atleast for 6 months or more in all the cases.
- The patients having secondary amenorrhea due to any obstetrical cause were excluded from the study.

Management Protocol:

Secondary amenorrhea presents the Gynaecologists and Endocrinoligists with a diagnostic challenge because of many disorders that can cause it. Thus its evaluation warrants a systemic approach to avoid unnecessary and expensive diagnostic procedures. An adequate history taking is essential. Besides the spontaneous history given by the patient, specific questioning was done to elicit relevant information to know the cause of amenorrhea. The clues to subsequent investigations was derived from history and physical examination.

FLOW CHART OF MANAGEMENT PROTOCOL



Observation

Table 1 : Age distribution of secondary amenorrhea cases.

Age	No of cases	Percentage
upto19	10	10
20-29	52	52
30-39	38	38
	100	

Table 2 : Duration of secondary amenorrhea

Duration	No of cases	Percentage
6 months- 1year	30	30
>1year -2 years	24	24
>2 Years	46	46
	100	

Table 3. Progesterone challenge test in secondary amenorrhea cases.

Progestational challenge test	No. of cases	Percentage
Withdrawal +	84	84
Withdrawal –	16	16
	100	

84 patient cases of secondary amenorrhea showed positive withdrawal response with Medroxy progesterone acetate (10 mg OD × 5 days) while rest 16 percent did not have any withdrawal bleeding with it.

Table 4. Estrogen and Progesterone Challenge Test.

Estrogen and Progesterone	No.of cases	Percentage
Withdrawal +	10	62.5
Withdrawal -	6	37.5
	16	

10 cases had positive withdrawal bleeding with estrogen and progesterone while 6 cases did not have any bleeding.

Table 5. Causes of secondary amenorrhea in study group.

Causes	No. of cases	Percentage
PCOS	30	30
Tuberculosis	30	30
Premature ovarian failure	10	10
Drug induced	9	9
Pituitary tumors	7	7
Hypothyroidism	7	7
Post D & C	3	3
Post myomectomy	1	1
Chronic debility (heart disease)	1	1
Sheehan's syndrome	1	1
No pathological factor	1	1

Table 6. Result of bromocriptine therapy on resumption of menstruation in hyperprolactinemic patients.

Time for resumption of menstruation	No. of cases	Percentage
3-6 weeks	24	82.80
7-10 weeks	4	13.80
> 11 weeks	-	-
No response	1	3.45
	29	

Table 7. Result of treatment for pelvic tuberculosis.

Resumption of menstruation (duration)	No. of cases	Percentage
3-6 months	15	50
7-9 months	9	30
> 9 months	5	16.67
No response	1	3.33

Table 8. Results of stopping drugs in drug induced amenorrhea (n=8).

Drug	Resumption of menstruation (duration)	No. of cases
OCPs	3-6 months	2
	6 month to 1 year	1
	> 1 year	1
Antiepileptics	1 month	2
Antipsychotics	1 month	2

Table 9. Results of treatment with levothyroxine in primary hypothyroidism (n=7).

Resumption of menstruation (duration)	No. of cases	Percentage
3-6 weeks	3	42.8
6-9 weeks	3	42.8
> 9 weeks	1	14.2
	7	

III. Discussion

The age distribution of secondary amenorrhea case is shown in Table 1. The majority of patients were in age group 20-29 yrs(52 percent) followed by patients in age group 30-39 yrs (38 percent) and minimum in age group upto19 yrs (10 percent). Similar results were observed by Baker ER et al. (1981) according to whom incidence of amenorrhea was higher in females less than 30 yrs of age(2)

Majority (46%) of patients had amenorrhea of more than 2 years duration (Table 3). This was because majority of patients presented very late and the maximum duration of secondary amenorrhea observed in this study was of 6 years. Hyperprolactinemia was present in 29% cases and galactorrhea in 18%. (table4). Kleinberg DL et al., 1977; Boyd AE III et al., 1977; Toles G et al 1974 have also confirmed the above findings in their respective studies on secondary amenorrhea(3,4)

Thyroid status of the patients was assessed by serum TSH levels as TSH measurement provides the best single screen for thyroid dysfunction and can accurately predict thyroid hormone dysfunction in about 80% cases (5). In this study 5% cases had overt hypothyroidism and 2% had subclinical hypothyroidism (Table 5). Prelepskaia V et al. (1990) in their study of secondary amenorrhea caused by hypothyroidism have also given nearly the same incidence (4.8%).(6)

After a negative pregnancy test all the 100 cases of secondary amenorrhea were subjected to progesterone challenge test; 84% cases had withdrawal bleeding while 16% did not bleed at all. The patients who were withdrawal negative were subjected to estrogen and progesterone test. 10 out of 16 cases had withdrawal bleeding while 6 patients did not bleed.All 10 cases of premature ovarian failure had withdrawal bleeding with estrogen and progesterone.Those who were withdrawal negative had either Asherman's syndrome due to previous deep D & C (3 cases) or postmyomectomy 1 case). 2 Cases of extensive endometrial tuberculosis with fibrosis were also withdrawal negative. Literature also confirms that if there is extensive endometrial damage, the subject may not have withdrawal bleeding on progesterone challenge test (7)

Table 5 shows that 55% cause of secondary amenorrhea was due to hypothalamic-pituitary dysfunction. Our findings are in accordance with Vigerky RA et al. (1989) who have reported this to be the most responsible cause of secondary amenorrhea (54.7%)(8). This group includes the cases of PCOS (30%), drug induced (9%), pituitary tumors (7%), hypothyroidism (7%), Sheehan's syndrome (1%) and hypothalamic amenorrhea (1%). In a study conducted by Reindollar et al, (1986) PCOS was responsible for 28% of secondary amenorrhea cases(9)). Genital tuberculosis was responsible for 30% cases of secondary amenorrhea. These high figures causing systemic or genital tuberculosis are because tuberculosis is an extremely common infection in this part of country;. According to Behide AG et al. (1987), one third cases of genital tuberculosis exist in India(10). According to Ashok Kumar et al. also, tuberculosis of genital tract is of common occurrence, which causes secondary amenorrhea due to endometrial fibrosis(7).

Majority (82.8%) cases resumed their periods between 3-6 weeks of initiation of bromocriptine therapy (Table 6). Our findings are in agreement with those of Cuellar F.G. (1980) whose 80% patients resumed their perods in 5.7 weeks of therapy.(11)

All the 30 cases of tuberculosis either pulmonary or genital who had secondary amenorrhea were given anti-tubercular drugs for a period of 9 moths (or for 12 months where the response was not adequate). It was observed that 5% had resumption of menstruation between 3-6 months of therapy, 30% menstruated between 7-9 months of therapy; 16.67% responded after 9 months and 3.33% did not show any response to the treatment even after 1 year of therapy (Table 7). The last case had extensive endometrial damage.

Nine patients had secondary amenorrhea due to drug intake Four cases who developed amenorrhea due to prolonged use of OCPs were asked to discontinue the pills in order to resume their periods. It was observed that 2 cases resumed their periods within 3-6 months of stopping pills, 1 case between 6 month- 1 year and the remaining 1 after 1 year of stopping the pill intake. Two cases that were on antiepileptic started menstruating 1month after stopping the drug therapy(those who had completed the treatment) Another 2 cases who were on antipsychotic also started menstruating after 1 month of cessation of treatment (Table 8). Sheeram also olds the same view that post pill amenorrhea may take years to correct itself after stopping OCP's(12)

The withdrawal of antiepileptic and antipsychotic leads to immediate resumption of menstruation.

7 cases of primary hypothyroidism when treated with L-thyroxine showed satisfactory results. 42.8% cases resumed their periods within 3-6 weeks of therapy. Another 42.8% responded within 6-9 months and the rest 14.2% after 9 weeks (Table 9). Our findings are in accordance with those of Hershlag and Petrson (1966)(13)

IV. Conclusion

Many a times unnecessary costly investigations are carried out to know the cause of secondary amenorrhea. A careful history taking and through physical examination are mandatory before advising any investigation. By systematically investigating the patient (as outlined in the flow chart) unnecessary investigations can be avoided. Thus making a management cost-effective and more appropriate. The conditions which are not amendable to treatment should be explained to the subjects. Appropriate support and counseling are necessary to promote healthy attitudes and healthy behaviours.

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