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Original Research Article

Evaluation and Management of Secondary Amenorrhea: A Case Series in a Tertiary Care Centre

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Abstract:

Background: Amenorrhea, defined as the absence of menstruation, is a symptom indicative of underlying health issues rather than a disease itself. Secondary amenorrhea is characterized by the cessation of established menstruation for six months or longer, or alternatively, previously regular menses for three months or previously irregular menses for six months. The incidence of secondary amenorrhea is estimated to be 3% to 4% among women in the general population.

Aim: This study aims to evaluate the etiology, diagnostic approaches, and management strategies for secondary amenorrhea among patients presenting to the gynecology outpatient department at MKCG Medical College, Berhampur, Odisha, India.

Methods: A total of 25 patients diagnosed with secondary amenorrhea were included in this study. A comprehensive evaluation was conducted, including detailed medical history, physical examination, laboratory investigations (hormonal profile, thyroid function tests, prolactin levels), and imaging studies (ultrasound, MRI). Management strategies were individualized based on the etiology and included medical, surgical, and lifestyle interventions.

Results: The study identified various etiologies for secondary amenorrhea, including hormonal imbalances, structural abnormalities, and systemic conditions. The individualized management plans led to successful outcomes in most cases, with resumption of menstruation and improvement in symptoms. Specific cases highlighted include prolactinoma, PCOS, premature ovarian insufficiency, and Asherman's syndrome, each requiring distinct diagnostic and therapeutic approaches.

Conclusion: Secondary amenorrhea presents with diverse etiologies, necessitating a thorough and multidisciplinary approach for diagnosis and management. Early and accurate diagnosis, along with tailored interventions, are crucial for effective treatment and improved patient outcomes.

Recommendations:

Implementation of standardized protocols for the evaluation of secondary amenorrhea in clinical practice. Encourage multidisciplinary collaboration for the management of complex cases. Promote patient education regarding the potential causes and treatments for secondary

amenorrhea. Conduct further research to explore long-term outcomes of various management strategies.Enhance awareness among healthcare providers about the importance of early intervention.

Keywords: Secondary Amenorrhea, Hormonal Imbalance, PCOS, Premature Ovarian Insufficiency, Tertiary Care

Introduction

Menstruation is a complex physiological process orchestrated by an intricate network of signals involving the hypothalamic-pituitary-ovarian (HPO) axis. This coordination ensures the regular occurrence of menstrual cycles in women of reproductive age. Any disruption in this finely tuned system can lead to menstrual irregularities, one of which is secondary amenorrhea. Secondary amenorrhea is characterized by the cessation of menstruation for six months or longer in women who previously had regular menstrual cycles. Alternatively, it can be defined as the absence of previously regular menses for three months or previously irregular menses for six months (1).

Secondary sis not a disease but a symptom indicative of underlying health issues that require thorough investigation. The incidence of secondary amenorrhea is estimated to be 3% to 4% among women in the general population. The condition can arise from a variety of etiologies, including hormonal imbalances, structural abnormalities, systemic diseases, and lifestyle factors. Understanding these diverse causes is crucial for accurate diagnosis and effective management of secondary amenorrhea (2).

The evaluation of secondary amenorrhea involves a comprehensive approach, including detailed medical history, physical examination, and a series of diagnostic tests. Hormonal profiles, thyroid function tests, prolactin levels, and imaging studies such as ultrasound and MRI are essential components of the diagnostic process. Identifying the root cause of secondary amenorrhea is pivotal in determining the appropriate treatment strategy, which can range from medical and surgical interventions to lifestyle modifications (3,4).

The aim of this study is to evaluate the etiology, diagnostic approaches, and management strategies for secondary amenorrhea among patients presenting to the gynecology outpatient department at MKCG Medical College, Berhampur, Odisha, India. By analyzing the clinical profiles and treatment outcomes of 25 patients, this study seeks to provide insights into the effective management of secondary amenorrhea in a tertiary care setting. The findings aim to contribute to the existing knowledge base and improve patient care in similar clinical environments

In this study, various causes of secondary amenorrhea, such as polycystic ovary syndrome (PCOS), primary ovarian insufficiency, hypothyroidism, Asherman's syndrome, functional hypothalamic amenorrhea, hyperprolactinemia, and Turner syndrome (mosaic), were explored. The study highlights the importance of selecting appropriate diagnostic modalities to accurately identify the underlying cause of secondary amenorrhea. Furthermore, it emphasizes the need for individualized management plans tailored to the specific etiology and patient needs, ensuring optimal outcomes for women affected by this condition

Methodology

Study Design: This descriptive case series study was conducted over a period of eight months, from August 2023 to March 2024,

at the gynecology outpatient department of MKCG Medical College, Odisha, India.

Sample Size: The study included 25 patients diagnosed with secondary amenorrhea.

Inclusion Criteria:

1. Patients who had attained menarche.
2. Age less than 40 years.
3. Cessation of previously regular menses for a minimum of three months.
4. Cessation of previously irregular menses for a minimum of six months.

Exclusion Criteria:

1. Patients who had not attained menarche.
2. Age over 40 years.
3. Pregnancy.

Patient Evaluation:

1. **History Taking:** A thorough medical history was obtained from each patient, focusing on:
   - Any vigorous exercise and weight loss (suggesting functional hypothalamic amenorrhea).
   - Drug history, including antipsychotic drugs and metoclopramide.
   - Thyroid medication.
   - Symptoms of pituitary adenoma, such as headaches and visual field defects.
   - Signs of polycystic ovary syndrome (PCOS), such as hirsutism.
   - History of abortion or curettage (suggesting Asherman syndrome).
   - Postpartum hemorrhage and failed lactation (suggesting Sheehan syndrome).
   - Symptoms of premature ovarian insufficiency, such as hot flashes, vaginal dryness, poor sleep, and decreased libido.
   - Contraceptive history, including oral or injectable contraception.
   - History of uterine instrumentation or infections.
   - History of chemoradiation.
2. **Clinical Examination:** Each patient underwent a comprehensive clinical examination, including:
   - Measurement of height, weight, and BMI.
   - Assessment of chronological and mental age.
   - Inspection for hirsutism, skin pigmentation, and acne.
   - Inspection for signs of systemic illness or genetic defects.
   - Examination of the skin, breasts, and genitalia for estrogen deficiency.
   - Evaluation for galactorrhea.
   - Abdominal examination for any palpable masses.
   - Vulvovaginal examination for signs of estrogen deficiency.
   - Bimanual examination (for married/parous women) to assess the size of the uterus and detect any masses or nodules in the fornices.
3. **Laboratory Investigations:**
   - **Urine Pregnancy Test:** Conducted for all patients to rule out pregnancy.
   - **Ultrasound (USG) of Abdomen and Pelvis:** Performed to evaluate the uterus and adnexa and rule out any pelvic pathology.
   - **Blood Tests:**
     - Complete Blood Count (CBC)
     - Erythrocyte Sedimentation Rate (ESR)
     - Serum Thyroid-Stimulating Hormone (TSH)
     - Serum Prolactin
     - Serum Luteinizing Hormone (LH)
     - Serum Follicle-Stimulating Hormone (FSH)
     - TB PCR

Histopathological Examination (HPE) of Endometrium: Conducted as appropriate based on clinical indications.

Result

The diagnostic approach for secondary amenorrhea was comprehensive and included several specific tests tailored to identify common causes. The investigations included:

I. **Basic Investigations:**

- Urine pregnancy test (UPT)
- Serum prolactin
- Serum TSH (Thyroid-Stimulating Hormone)
- Serum thyrotropin

II. **PCOS and Hyperandrogenism Investigations:**

- Serum testosterone for patients with features of PCOS
- Serum DHEAS (Dehydroepiandrosterone sulfate) for patients with features of hyperandrogenism

III. **Turner Syndrome Investigations:**

- Karyotyping for patients with features of Turner syndrome or short stature

IV. **Ovarian Reserve Investigations:**

- Serum AMH (Anti-Müllerian Hormone)
- Antral Follicle Count (AFC) via ultrasound for evaluation of ovarian reserve in primary ovarian insufficiency

The age of the patients ranged from 13 to 38 years, with a mean age of 24.4 years. The majority of patients were in their 20s, with 60% of the cases (15 out of 25) falling within this age range.

The most common cause of secondary amenorrhea was Polycystic Ovary Syndrome (PCOS), accounting for 10 cases (40%). Primary Ovarian Insufficiency and Turner Syndrome (Mosaic) were the next most common causes, each accounting for 3 cases (12%). Functional Hypothalamic Amenorrhea and Asherman Syndrome each accounted for 2 cases (8%). Tubercular Endometritis also accounted for 2 cases (8%). Less common causes included Hypothyroidism, Hyperprolactinemia (Pituitary Adenoma), and Sheehan Syndrome, each accounting for 1 case (4%).

Elevated Serum LH was observed in all patients diagnosed with PCOS. Elevated Serum FSH was noted in patients with Primary Ovarian Insufficiency and Turner Syndrome. MRI confirmed pituitary microadenoma in the case of Hyperprolactinemia. Positive TB PCR confirmed Tubercular Endometritis in 2 cases. Hysteroscopy revealed uterine adhesions in Asherman Syndrome cases. Hypoplastic uterus with streak ovaries was observed in Turner Syndrome cases.

Treatment outcomes varied by diagnosis. For PCOS, lifestyle modifications, Metformin, and Combined Oral Contraceptives were effective in 80% of cases. Hormone Replacement Therapy (HRT) provided relief in 66.7% of cases with Primary Ovarian Insufficiency. HRT was essential for managing symptoms in Turner Syndrome, though not effective in all cases. Nutritional counseling and lifestyle changes were successful in all cases of Functional Hypothalamic Amenorrhea. Hysteroscopic adhesiolysis followed by hormonal therapy was effective in 50% of cases of Asherman Syndrome. Anti-tubercular treatment (ATT) was successful in all cases of Tubercular Endometritis. Levothyroxine therapy normalized thyroid function and menstrual cycles in the case of Hypothyroidism. Dopamine agonist therapy (Cabergoline) was effective in reducing prolactin levels and restoring menses in the case of Hyperprolactinemia. Hormone replacement therapy restored menstrual function in Sheehan Syndrome.

Discussion

Our study was conducted among 25 consecutive secondary amenorrhea patients out of 26 secondary amenorrhea patients attending the gynecology outpatient department (OPD). The most common cause of secondary amenorrhea in our study was Polycystic Ovary Syndrome (PCOS). The increasing incidence of PCOS can be

attributed to modern sedentary lifestyles and unhealthy dietary habits, which are becoming more prevalent.

The frequency distribution of secondary amenorrhea cases in our study is as follows:

- PCOS: 10 cases
- Primary Ovarian Insufficiency (POI): 3 cases
- Turner Syndrome (Mosaic): 3 cases
- Functional Hypothalamic Amenorrhea (FHA): 2 cases
- Asherman Syndrome: 2 cases
- Tubercular Endometritis: 2 cases
- Hypothyroidism: 1 case
- Hyperprolactinemia (Pituitary Adenoma): 1 case
- Sheehan Syndrome: 1 case

Our study underscores the importance of a step-by-step diagnostic approach for secondary amenorrhea. By following a systematic process, clinicians can easily identify the underlying cause of the condition. However, assessing the efficacy of treatment approaches for secondary amenorrhea requires long-term follow-up of patients. This follow-up is crucial for understanding the effectiveness of the treatments provided and for making necessary adjustments.

In addition to medical and surgical management, counseling and psychological support are essential components of the treatment plan for all secondary amenorrhea patients. These supportive measures help address the mental and emotional aspects of the condition, which are often significant concerns for affected individuals.

Conclusion

There are many causes of secondary amenorrhea, and accurate diagnosis requires thorough history-taking and appropriate investigation procedures. Once the exact cause of secondary amenorrhea is established, clinicians can consider appropriate treatment options that can modify disease progression and help patients overcome mental, physical, and reproductive health issues.

While medical management is the primary treatment for most cases of secondary amenorrhea, specific conditions may require additional interventions. For instance, patients with pituitary adenomas that are nonresponsive to dopamine agonist therapy may benefit from transsphenoidal surgery. In cases of Asherman Syndrome, hysteroscopic lysis of adhesions is preferred over dilation and curettage due to better treatment outcomes.

Treatment for secondary amenorrhea should also consider various aspects of women's health, including menstruation, metabolic parameters, and fertility. A comprehensive approach that addresses these issues can significantly improve the quality of life for patients with secondary amenorrhea.

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Table 1: This table showing diagnostic work up for 25 secondary amenorrhoea cases

CASE NUMBER	AGE	UPT	FEATURES OF HA	Sr TSH	Sr PROLACTIN	PAST SURGICAL OR MEDICAL HISTORY	USG	Sr LH	Sr FSH	TB PCR	P TEST	E+P TEST	MRI BRAIN	FINAL DAIGNOSIS
1	22	NEGATIVE	ABSENT	NORMAL	NORMAL	NILL	HYPOPLASTIC UTERUS WITH STREAK OVARIES	RAISED	RAISED	NA	NA	POSITIVE	NA	TURNER SYNDROME (MOSAIC)
2	22	NEGATIVE	ABSENT	RAISED	NORMAL	NILL	NORMAL	NORMAL	NORMAL	NA	NA	NA	NA	HYPOTHYROIDISM
3	13	NEGATIVE	ABSENT	NORMAL	NORMAL	NILL	HYPOPLASTIC UTERUS WITH STREAK OVARIES	RAISED	RAISED	NA	NA	NA	NA	TURNER SYNDROME (MOSAIC)
4	28	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOM	RAISED	NORMAL	NA	POSITIVE	NA	NA	PCOS
5	33	NEGATIVE	ABSENT	NORMAL	NORMAL	NILL	NORMAL	LOWER	LOWER	NA	NEGATIVE	POSITIVE	NA	FUNCTIONAL HYPOTHALAMIC AMENORRHEA
6	30	NEGATIVE	ABSENT	NORMAL	NORMAL	NILL	NORMAL	RAISED	RAISED	NA	NEGATIVE	PSITIVE	NA	PRIMARY OVARIAN INSUFFICIENCY
7	20	NEGATIVE	ABSENT	NORMAL	NORMAL	NILL	HYPOPLASTIC UTERUS WITH STREAK OVARIES	RAISED	RAISED	NA	NA	POSITIVE	NA	TURNER SYNDROME(MOSAIC)
8	30	NEGATIVE	NEGATIVE	NORMAL	NORMAL	NILL	NORMAL	NORMAL	NORMAL	POSITIVE	NEHATIVE	NEGATIVE	NA	TUBERCULAR ENDOMETRITIS
9	27	NEGATIVE	NEGATIVE	NORMAL	NORMAL	PRESENT (D&E)	NORMAL	NORMAL	NORMAL	NA	NEGATIVE	NEGATIVE	NA	ASHERMAN SYNDROME
10	25	NEGATIVE	ABSENT	NORMAL	NORMAL	NILL	NORMAL	LOWER	LOWER	NA	NEGATIVE	POSITIVE	NA	FUNCTIONAL HYPOTHALAMIC AMENORRHEA
11	25	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOM	RAISED	NORMAL	NA	POSITIVE	NA	NA	PCOS
12	26	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOM	RAISED	NORMAL	NA	POSITIVE	NA	NA	PCOS
13	30	NEGATIVE	ABSENT	LOWER	LOWER	H/O-PPH	NORMAL	LOWER	LOWER	NA	NEGATIVE	POSIT I VE	NA	SHEEHAN'S SYNDROME

14	24	NEGATIVE	ABSENT	NORMAL	NORMAL	PRESENT (ADENOMYOMECTOMY)	NORMAL	NORMAL	NORMAL	NA	NEGATIVE	NEGATIVE	NA	ASHERMAN SYNDROME
15	21	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOS	RAISED	NORMAL	NA	POSITIVE	NEGATIVE	NA	PCOS
16	24	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOM	RAISED	NORMAL	NA	POSITIVE	NA	NA	PCOS
17	26	NEGATIVE	ABSENT	NORMAL	HIGHLY RAISED	NILL	NORMAL	NORMAL	NORMAL	NA	NEGATIVE	POSITIVE	PITUITARY MICROADENOMA	HYPERPROLACTIN EMIA
18	21	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOM	RAISED	NORMAL	NA	POSITIVE	NA	NA	PCOS
19	29	NEGATIVE	ABSENT	NORMAL	NORMAL	NILL	NORMAL	NORMAL	NORMAL	POSITIVE	NEGATIVE	NEGATIVE	NA	TUBERCULAR ENDOMETRITIS
20	19	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOM	RAISED	NORMAL	NA	POSITIVE	NA	NA	PCOS
21	38	NEGATIVE	ABSENT	NORMAL	NORMAL	NILL	NORMAL	RAISED	RAISED	NA	NEGATIVE	POSITIVE	NA	PRIMARY OVARIAN INSUFFICIENCY
22	18	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOM	RAISED	RAISED	NA	POSITIVE	NA	NA	PCOS
23	19	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOM	RAISED	NORMAL	NA	POSITIVE	NA	NA	PCOS
24	37	NEGATIVE	ABSENT	NORMAL	NORMAL	NILL	NORMAL	RAISED	RAISED	NA	NEGATIVE	POSITIVE	NA	PRIMARY OVARIAN INSUFFICIENCY
25	18	NEGATIVE	PRESENT	NORMAL	NORMAL	NILL	B/L PCOM	RAISED	NORMAL	NA	POSITIVE	NA	NA	PCOS