

“ ... **AMMI** ”

DIFFERENT ?”

Reproduction Block-Case 1

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Learning Objectives:

This PBL Package targets the following objectives:

- Link the structure and function of the different parts of the female reproductive system.
- Discuss the physiological basis and the role of the hypothalamic-pituitary-ovarian axis in the regulation of the ovarian and the uterine cycles.
- Discuss the biological changes and the physiological mechanisms underlying the occurrence of puberty.
- Discuss the biological effects of oestrogen and progesterone during female puberty.
- Discuss the anatomy of the female breast and the hormones involved in breast development and milk secretion. .
- Understand the role of anxiety and environmental factors in delaying puberty.
- Understand the differences between normal and abnormal body functions.

Trigger

Lila Ali, a 15-year-old student comes in with her mother to see Dr Mona Al Awady in her clinic. Lila's mother says, "Lila has not had her first period yet". On further questions, Lila's mother says, "Lila's body did not change for the last two years and there are no changes in her breasts like other girls in her age". Lila says, "my close friends usually talk about their experience when they have their periods and I feel left behind and uncomfortable. Am I different?"

Discussion Questions:

- Are there any difficult words you do not understand?
- List the key information about Lila.
- Identify Lila's presenting problems.
- For each problem, generate a list of possible causes (hypotheses).
- What further information would you like to know from history to refine your hypotheses?

Trigger

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New Terms/Difficult words

- *Period*
- *Left behind*

Tutor: *Encourage students to use a medical dictionary resource, as needed, to discuss the meaning of each of these words.*



Problems/Hypotheses

Did not have her first period:

- Hypothalamic problem: stress, anorexia nervosa, excessive exercise.
- Anterior pituitary problem: hyperprolactinoma, problem with the secretion of FSH, LH.
- Problem with the hypothalamic-pituitary-gonadal axis: e.g., thyroid problems, adrenal problems.
- Problems with the ovaries: absent ovaries, rudimentary ovaries, polycystic ovaries, premature ovarian failure.
- Absent uterus.
- Imperforated hymen.
- Genetic / chromosomal disorders
- Chronic diseases

Problems/Hypotheses

No changes in her breasts :

- Delayed puberty.
- Hormonal disturbances.
(hypothalamic-pituitary-gonadal axes)
- Genetic/chromosomal.
- ? Malnutrition.

Problems/Hypotheses

Left behind (Concerned/worried):

- Not having her first period.
- Her body image.
- Motherhood/having a family/fertility.
- Lest she had a serious disease.
- Peer-pressure.
- Wanted to be like others.
- Concerned about future.

Facilitation Questions

What are the anatomical structures forming the female reproductive system?

- External genitalia
- Internal structures: vagina, cervix, uterus, tubes, ovaries.

What are the physiological and psychological changes associated with puberty?

How puberty is triggered?

- Hypothalamus role.
- Stimuli to the hypothalamus/preparation.
- Hormonal changes

Facilitation Questions

What are the structures and physiological functions involved in menstrual period in females?

- Anatomical structures: hypothalamus, anterior pituitary, ovaries, uterus.
- Hormonal control: Hypothalamic-pituitary-ovarian axis.
- Hormones: LH, FSH, oestrogen, others...

What are the mechanisms involved in the regulation of female menstrual period?

Further Questions

- Any history of cyclical abdominal pain?
- Did she notice any hair in the pubic or axillary areas?
- Dietary habits, any changes in her dietary regime?
- Is she on any medications?
- Any history of stress, problems at school/home?
- Any history of chronic illnesses? Hospital admission? Investigations? treatment/surgery?
- Age of menarche for her mother and sisters?
- Any other symptoms?

Please Read The History

History:

Lila gives no history of cyclical abdominal pain. She has no pubic hair, or hair in her armpit, and she noticed no changes in her breasts. She has no changes in her appetite and is not on dietary restrictions. She gives no history of headaches, vomiting or double vision.

Past medical history

No past history of chronic illnesses, or chronic diarrhoeas.

No history of hospital admission or surgery.

Allergy and Medication

Nil

Continue-History

Family history

Lila has three sisters who are 2, 3 and 4 years older than her. Her mother and sisters all had their first period (menarche) when they were approximately 14 years old.

Social history

Lila is at grade one of her secondary school. She is an average student in her study. She has no close friends at school and rarely attend social activities. She feels different from other girls in her class. She feels stressed and unhappy because of her body and the fact that her breasts are not developed as that of other girls in her age. She is worried about her body and wonders when she will have her period.

Discussion Questions

- Are there words that you do not understand?
- Summarize key information that you have obtained from this progress.
- Identify patient's new problems. Provide hypotheses for each problem.
- What further information would you like to know through clinical examination?

New Terms

Tutor: encourage students to use their medical dictionary to find out more about these words)

- Cyclical abdominal pain
- Armpit.
- Pubic hair
- Double vision.
- Menarche

Tutor: Encourage students to use a medical dictionary resource to discuss the meaning of each of these words/phrases.

Key information

- No history of cyclical abdominal pain.
- No pubic hair and no hair in her armpit.
- No changes in her appetite or dietary habits.
- No dietary restrictions.
- No history of headaches, vomiting or double vision.
- No history of chronic illnesses, hospital admissions.
- Her mother and sisters had their menarche at about the age of 14.
- Worried, and stressed and wonder when she will have her period.

Ranking/Hypotheses

Did not have her first period:

- Hypothalamic problem: stress, ++
 - anorexia nervosa 00
 - excessive exercise. 00
- Anterior pituitary problem:
 - hyperprolactinoma, 0
 - problem with the secretion of FSH, LH. ? +/-
- Problem with the hypothalamic-pituitary-gonadal axis: e.g., thyroid problems, adrenal problems. ? +/-
- Problems with the ovaries: absent ovaries, rudimentary ovaries, polycystic ovaries, premature ovarian failure. ? +/-
- Absent uterus. ? /+
- Imperforated hymen. 00
- Genetic / chromosomal disorders ? /+
- Chronic diseases 00

Ranking/Hypotheses

No breast development:

- Delayed puberty. ?/++
- Hormonal disturbances (hypothalamic-pituitary-gonadal) ?
- Genetic/chromosomal ? /++
- ? Malnutrition. 00



Hypotheses

Left behind (Concerned/worried):

- Not having her first period. ++
- Her body image. ++
- Motherhood/having a family/fertility. +
- +
 - Lest she had a serious disease. +/++
 - Peer-pressure. ++
 - Wanted to be like others. +++
 - Worried about future in general. ++

**Please Read
The Clinical
Examination**

Clinical Examination

Lila's bodyweight is 43 kg and her height is 145 cm. She looks shy and lacks confidence. She has no webbing of the neck (extra skinfold at her neck base) and no other external anomalies. Axilla shows sparse and scanty hair. Her breasts are not developed for her age. She has no goiter and her thyroid gland is normal to palpation. Her vital signs are summarized in the table below:

Vital signs

Vital signs	Lila	Normal range
Pulse rate	80 regular	60-100/min
Blood pressure	110/70 mmHg	100/60-120/80 mmHg
Temperature	37.1	36.6-37.2 °C
Respiratory rate	18	12-16/min

Continue- Clinical Examination

External genitalia and pelvic examination:

Fewer darker hairs along the labia majora.

Minimal development of labia minora and labia majora. .

Hymen is normal.

Ultrasound of the pelvis confirms the presence of a normal uterus and ovaries for her age.

Abdominal examination:

Normal

Cardiovascular and respiratory examinations:

Normal.

Discussion Questions

- Are there words that you do not understand?
- Summarize key information that you have obtained from this progress.
- Identify patient's new problems.
Provide hypotheses for each problem.
- What further information would you like to know through investigations?

Difficult words

- Webbing of neck
- Labia.
- Uterus
- Ovaries
- Hymen

Ranking/Hypotheses

Did not have her first period:

- Hypothalamic problem: stress, +++
 - anorexia nervosa 00
 - excessive exercise. 00
- Anterior pituitary problem:
 - hyperprolactinoma, 00/+
 - problem with the secretion of FSH, LH. ? +/+
- Problem with the hypothalamic-pituitary-gonadal axis: e.g, thyroid problems, adrenal problems. ? 0/-
- Problems with the ovaries: absent ovaries, rudimentary ovaries, polycystic ovaries, premature ovarian failure. ? /00
- Absent uterus. 00
- Imperforated hymen. 00
- Genetic / chromosomal disorders ? /
- Chronic diseases 00

Litteral Scale

+ + + + +
00/ + 8

Rankings/Hypotheses

No breast development:

- Delayed puberty. ?/++
- Hormonal disturbances (hypothalamic-pituitary-gonadal) ?/0
- Genetic/chromosomal ? 0/+
- ? Malnutrition. 00



Hypotheses

Left behind (Concerned/worried):

- Not having her first period. ++
- Her body image. ++
- Motherhood/having a family/fertility. +
- +
 - Lest she had a serious disease. + / ++
 - Peer-pressure. ++
 - Wanted to be like others. +++
 - Worried about the future ++

Hypotheses: Ranking

Most likely:

- Delayed puberty/a lack of oestrogen.
- No evidence of chromosomal problem :
 - No short stature.
 - Absent ovaries or absent uterus.
 - No webbing of the neck
 - No other external anomalies.

Less likely/Excluded:

- Pituitary problems.
- Growth hormone deficiency.
- Malnutrition.
- Excessive exercise.
- Hypothyroidism.
- Adrenal problems.
- Absent uterus/absent ovaries.
- Imperforated hymen.
- Anorexia nervosa.

Learning Issues

(Tutor: Encourage students to identify their learning issues that reflect key issues raised in the case. They might need to edit their learning issues into sentences or questions. Usually learning issues are about 5-7 key principles. See examples shown below).

Learning Issues

- Structures and functions of the female reproductive system.
- Role of the hypothalamic-pituitary-ovarian axis in control of menstruation.
- Physiology of menstruation.
- Physiology of puberty. Physiological and psychological changes occurring during puberty and underlying mechanisms.
- Physiological actions of oestrogen and progesterone and regulating mechanisms.
- Secondary sexual characteristics.

**Please Read the
Investigations**

Tutorial Two

Discussion Questions

After the students spent about 60 minutes addressing their learning issues. You might spend 10-15 minutes on these questions:

Discussion Questions:

- On the basis of the information provided in tutorial one, what is your final hypothesis? Justify your views?
- What should Dr Mona do at this stage?



Do you know a Nobel Prize laureate whose work has contributed to the advancement of our knowledge in physiology and/or pharmacology related to this case? What was exactly his/her work about? Give a summary.

Student: You could also after the completion of this case submit your work about the Nobel Prize laureate for this case to Professor **Samy Azer** at (sazer@ksu.edu.sa) or hand it to him.

Progress 1

Dr. Mona explains to Lila and her mother that Lila might have a little delay in her puberty. She says, "Puberty is the period where girls experience changes in their bodyweight, body shape, and the growth of their breasts as well as the appearance of hairs in their armpits and in between their legs (pubic area). It is also the time where a girl starts her monthly periods". She adds, "Lila's body has shown some changes and she is in the early stages of puberty. There are many factors that can affect the onset of puberty such as severe stress, family history of delayed puberty, and loss of bodyweight. Clinically there is nothing wrong with Lila". Dr mona asks Lila to review in four months for further check up if she did not have her period.

Six months later, Lila comes with her mother. Examination reveals that Lila has some changes in her breasts and more hair in her axilla and pubic area but she still hasn't had her first period yet.

Discussion Questions

- On the basis of information provided in this progress, what do you expect the cause of her problem? Explain your views.
- What should Dr Mona do at this stage?

Progress 2

Because Lila and her mothers were worried, Dr Mona decides to order some blood tests. The results of these investigations are shown in the tables below:

Full blood count

Blood Test	Lila	Normal range
Haemoglobin (Hb)	13 g/100ml	11.5-13.5 g/100ml
White blood cell count	6,000 mm ³	5,000 -10,000 mm ³
PCV	42 %	37-47%
MCV	85 fl	80-96 fl
MCHC	320 g/L	300-350 g/L
Platelet count	240,000 mm ³	160,000-500,000 mm ³

Progress 2

Hypothalamus }
 Pituitary } Axis
 Gonadal }

Hormonal assays

Test	Liia	Normal range
Serum follicle stimulation hormone (FSH)	2.4 IU/L	3-12 IU/L
Serum luteinizing hormone (LH)	3.6 IU/L	5-18 IU/L
Growth hormone (GH)	1.8	0-3 ng/mL
Serum estradiol	18 pmol/L	37-143 pmol/L
Serum testosterone	12 pmol/L	9,9-27,8 pmol/L
Serum prolactin	150 mIU/L	75-511 mIU/L

Axis

ITEM	CHANGE	INTERPRETATION
FSH	↓	"
LH	↓	"
ESNGE	↓	"
		peribulbaric??

Progress 2

Thyroid function tests

Test	Lila	Normal range
Total thyroxine T4	104	65-155 nmol/L
Triiodothyronine T3	1.8	1.1-2.9 nmol/L
TSH	2.3	0.4-5 mU/L

Chromosomal studies:

A chromosomal analysis is normal

Discussion Questions:

- Are there any terms that you do not understand?
- Summarize the key information that you have obtained from this progress.
- What is your interpretation of these investigations?
- On the basis of the new information, how would you explain Lila's presenting problem, and the clinical findings?

New words

- Follicle stimulating hormone (FSH)
- Luteinizing hormone (LH).
- Growth hormone (GH)
- Estradiol.
- Testosterone.
- Prolactin
- TSH.

Ranking/Hypotheses

Did not have her first period:

- Hypothalamic problem: stress, ++
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- Anterior pituitary problem:
 - hyperprolactinoma, 0
 - Delayed secretion of FSH, LH. ? +/+++
- Problem with the hypothalamic-pituitary-gonadal axis: e.g, thyroid problems, adrenal problems. ? 00
- Problems with the ovaries: absent ovaries, rudimentary ovaries, polycystic ovaries, premature ovarian failure. ? /00
- Absent uterus. ? /00
- Imperforated hymen. /00
- Genetic / chromosomal disorders ?/00
- Chronic diseases /00

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Case Closure

Case Closure

Dr Mona discusses the results of the investigations with Lila and her mother. She assures Lila by saying, "Lila there is nothing wrong with your body." The blood levels of the hormones measured (FSH, LH, and estradiol) are low because of the lack of stimulation from the hypothalamus and hence the anterior pituitary and the ovaries. Other hormones such as prolactin and thyroxine are within the normal range. The uterus and ovaries are normal and the chromosomal analysis results are normal for a female. The clinical examination and the ultrasound examination of the pelvis are normal. Taken together, these findings match with delayed puberty. The delay in the stimulation of the hypothalamus is within normal. We expect that within the next 4 to 6 months Lila will have her first period. This will take place as the stimulation of the hypothalamus causes an increase in the blood levels of FSH and LH and hence the stimulation of the ovaries. As a result the ovaries will secrete oestrogen and progesterone. With these hormonal changes, the lining of the uterus undergoes periodic changes and hence the occurrence of menstrual period. Lila and her mother are very pleased to hear these news.

About 4 months later, Lila has her first period. She calls Dr Mona and shares with her the news.