Brunei International Medical Journal

OFFICIAL PUBLICATION OF
THE MINISTRY OF HEALTH
AND
UNIVERSITI BRUNEI DARUSSALAM

Volume 18 11 November 2022 (16 Rabiulakhir 1444H)

ENDOMETRIAL CARCINOMA IN A ADOLESCENT WITH DIABETES MELLITUS.

Nur Aiza IDRIS[1], Rosnani ZAKARIA[2], Azlina ISHAK[2], Siti Zarqah OMAR[3].

[1]Faculty of Medicine, Universiti Sultan Zainal Abidin, Terengganu, Malaysia.
[2]Department of Family Medicine, School of Medical Science, Universiti Sains Malaysia Health Campus, Kubang Kerian, Malaysia.
[3]Department of Pathology, Hospital Sultanah Nur Zahirah, Terengganu, Malaysia.

ABSTRACT

Abnormal uterine bleeding is one of the commonest presentation of adolescent gynaecology in health care setting, predominantly due to anovulatory cycles. However, chronic anovulation with other risk factors such as unopposed oestrogen and obesity could lead to endometrial hyperplasia and carcinoma even in young women. We report a case of an adolescent with history of obesity and diabetes mellitus type II, who had heavy bleeding for 4 years eventually diagnosed with endometrial carcinoma. We discuss the presentation, histological finding and also primary care doctor's role in identifying possible life-threatening cause of abnormal uterine bleeding in adolescents.

Keywords: Adolescent, Diabetes Mellitus, Endometrial carcinoma, Obesity, Menorrhagia.

Brunei Int Med J. *2022;18:171-174*

ISSN 1560 5876 Print
ISSN 2079 3146 Online

Online version of the journal is available at www.bimjonline.com

Brunei International Medical Journal (BIMJ)
Official Publication of
The Ministry of Health
and
Universiti Brunei Darussalam

ISSN 1560-5876 Print
ISSN 2079-3146 Online

Aim and Scope of Brunei International Medical Journal

The Brunei International Medical Journal (BIMJ) is a six monthly peer reviewed official publication of the Ministry of Health under the auspices of the Clinical Research Unit, Ministry of Health, Brunei Darussalam.

The BIMJ publishes articles ranging from original research papers, review articles, medical practice papers, special reports, audits, case reports, images of interest, education and technical/innovation papers, editorials, commentaries and letters to the Editor. Topics of interest include all subjects that relate to clinical practice and research in all branches of medicine, basic and clinical including topics related to allied health care fields. The BIMJ welcomes manuscripts from contributors, but usually solicits reviews articles and special reports. Proposals for review papers can be sent to the Managing Editor directly. Please refer to the contact information of the Editorial Office.

Instruction to authors
Manuscript submissions
All manuscripts should be sent to the Managing Editor, BIMJ, Ministry of Health, Brunei Darussalam; e-mail: editor-in-chief@bimjonline.com. Subsequent correspondence between the BIMJ and authors will, as far as possible via should be conducted via email quoting the reference number.

Conditions
Submission of an article for consideration for publication implies the transfer of the copyright from the authors to the BIMJ upon acceptance. The final decision of acceptance rests with the Editor-in-Chief. All accepted papers become the permanent property of the BIMJ and may not be published elsewhere without written permission from the BIMJ.

Ethics
Ethical considerations will be taken into account in the assessment of papers that have experimental investigations of human or animal subjects. Authors should state clearly in the Materials and Methods section of the manuscript that institutional review board has approved the project. Those investigators without such review boards should ensure that the principles outlined in the Declaration of Helsinki have been followed.

Manuscript categories
Original articles
These include controlled trials, interventional studies, studies of screening and diagnostic tests, outcome studies, cost-effectiveness analyses, and large-scale epidemiological studies. Manuscript should include the following; introduction, materials and methods, results and conclusion. The objective should be stated clearly in the introduction. The text should not exceed 2500 words and references not more than 30.

Review articles

These are, in general, invited papers, but unsolicited reviews, if of good quality, may be considered. Reviews are systematic critical assessments of literature and data sources pertaining to clinical topics, emphasising factors such as cause, diagnosis, prognosis, therapy, or prevention. Reviews should be made relevant to our local setting and preferably supported by local data. The text should not exceed 3000 words and references not more than 40.

Special Reports

This section usually consist of invited reports that have significant impact on healthcare practice and usually cover disease outbreaks, management guidelines or policy statement paper.

Audits

Audits of relevant topics generally follow the same format as original article and the text should not exceed 1,500 words and references not more than 20.

Case reports

Case reports should highlight interesting rare cases or provide good learning points. The text should not exceed 1000 words; the number of tables, figures, or both should not be more than two, and references should not be more than 15.

Education section

This section includes papers (i.e. how to interpret ECG or chest radiography) with particular aim of broadening knowledge or serve as revision materials. Papers will usually be invited but well written paper on relevant topics may be accepted. The text should not exceed 1500 words and should include not more than 15 figures illustration and references

three relevant references should be included. Only images of high quality (at least 300dpi) will be acceptable.

Technical innovations

This section include papers looking at novel or new techniques that have been developed or introduced to the local setting. The text should not exceed 1000 words and should include not more than 10 figures illustration and references should not be more than 10.

Letters to the Editor

Letters discussing a recent article published in the BIMJ are welcome and should be sent to the Editorial Office by e-mail. The text should not exceed 250 words; have no more than one figure or table, and five references.

Criteria for manuscripts

Manuscripts submitted to the BIMJ should meet the following criteria: the content is original; the writing is clear; the study methods are appropriate; the data are valid; the conclusions are reasonable and supported by the data; the information is important; and the topic has general medical interest. Manuscripts will be accepted only if both their contents and style meet the standards required by the BIMJ.

Authorship information

Designate one corresponding author and provide a complete address, telephone and fax numbers, and e-mail address. The number of authors of each paper should not be more than twelve; a greater number requires justification. Authors may add a publishable footnote explaining order of authorship.

Group authorship

If authorship is attributed to a group (either solely or in addition to one or more individual authors), all members of the group must meet the full criteria and requirements for authorship described in the following paragraphs. One or more authors may take responsibility 'for' a group, in which case the other group members are not authors, but may be listed in an acknowledgement.

Authorship requirement

sign, and the analysis and interpretation of the data (where applicable); to have made substantial contributions to the writing or revision of the manuscript; and to have reviewed the final version of the submitted manuscript and approved it for publication. Authors will be asked to certify that their contribution represents valid work and that neither the manuscript nor one with substantially similar content under their authorship has been published or is being considered for publication elsewhere, except as described in an attachment. If requested, authors shall provide the data on which the manuscript is based for examination by the editors or their assignees.

Financial disclosure or conflict of interest

Any affiliation with or involvement in any organisation or entity with a direct financial interest in the subject matter or materials discussed in the manuscript should be disclosed in an attachment. Any financial or material support should be identified in the manuscript.

Copyright transfer

In consideration of the action of the BIMJ in reviewing and editing a submission, the author/s will transfer, assign, or otherwise convey all copyright ownership to the Clinical Research Unit, RIPAS Hospital, Ministry of Health in the event that such work is published by the BIMJ.

Acknowledgements

Only persons who have made substantial contributions but who do not fulfill the authorship criteria should be acknowledged.

Accepted manuscripts

Authors will be informed of acceptances and accepted manuscripts will be sent for copyediting. During copyediting, there may be some changes made to accommodate the style of journal format. Attempts will be made to ensure that the overall meaning of the texts are not altered. Authors will be informed by email of the estimated time of publication. Authors may be requested to provide raw data, especially those presented in graph such as bar charts or figures so that presentations can be constructed following the format and style of the journal. Proofs will be sent to authors to check for any mistakes made

ENDOMETRIAL CARCINOMA IN A ADOLESCENT WITH DIABETES MELLITUS.

Nur Aiza IDRIS[1], Rosnani ZAKARIA[2], Azlina ISHAK[2], Siti Zarqah OMAR[3].

[1]Faculty of Medicine, Universiti Sultan Zainal Abidin, Terengganu, Malaysia.
[2]Department of Family Medicine, School of Medical Science, Universiti Sains Malaysia Health Campus, Kubang Kerian, Malaysia.
[3]Department of Pathology, Hospital Sultanah Nur Zahirah, Terengganu, Malaysia.

ABSTRACT

Abnormal uterine bleeding is one of the commonest presentation of adolescent gynaecology in health care setting, predominantly due to anovulatory cycles. However, chronic anovulation with other risk factors such as unopposed oestrogen and obesity could lead to endometrial hyperplasia and carcinoma even in young women. We report a case of an adolescent with history of obesity and diabetes mellitus type II, who had heavy bleeding for 4 years eventually diagnosed with endometrial carcinoma. We discuss the presentation, histological finding and also primary care doctor's role in identifying possible life-threatening cause of abnormal uterine bleeding in adolescents.

Keywords: Adolescent, Diabetes Mellitus, Endometrial carcinoma, Obesity, Menorrhagia.

INTRODUCTION

Menstrual disorders are a common condition seen in primary care practice, with a prevalence of 10% to 30%.[1] The cause for abnormal uterine bleeding varies according to age. Anovulation is the most common cause in adolescents and structural lesion and malignancy in older women.[2, 3] The incidence of endometrial carcinoma in adolescents is extremely rare but increasing in trend, possible related to obesity that is currently more prevalent in young.[4, 5] We report a case of an 18-year-old obese girl with type II diabetes mellitus, who presented with symptomatic anemia secondary to menorrhagia and was eventually diagnosed with endometrial carcinoma. This case highlights that recognizing individual with risk factors would improve the management and outcomes of endometrial carcinoma diagnosed at a young age.

Corresponding author: Dr Rosnani binti Zakaria, MAFP (Malaysia), FRACGP (Australia), Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia.
Email:rosnani@usm.my, rosnaniz74@gmail.com;
Telephone number: +60-97676927

CASE REPORT

An 18-year-old girl presented with worsening dizziness and reduce effort tolerance. She was diagnosed with dysfunctional uterine bleeding of 4-year duration. She was prescribed cyclical oral progesterone and tranexamic acid to re-

duce the bleeding and hematinic for anemia. Her thyroid status, hormonal assay and coagulation profile were within normal range at the time of diagnosis and her initial ultrasonography showed thickened endometrium.

She attained menarche at the age of 10 years and her menstrual flow initially was oligo-menorrhea then became irregular cycle with menorrhagia after 4 years of menarche. She was also diagnosed with type II diabetes mellitus at the age of 16 years and was on oral anti-diabetic medication. She had a strong family history of diabetes but no family history of malignancy.

Physical examination revealed that the patient was pale but stable hemodynamically. Her height and weight were 137 cm and 65 kg, with body mass index of 34.6 kg/m^2. Acanthosis nigricans was presence over the posterior fold of her neck and axilla bilaterally. Transabdominal ultrasound revealed thickened endometrium of 16mm. She was referred for hospital admission and received one-pint pack cell transfusion and her haemoglobin increased from 6.8 g/dL to 8.5 g/dL post transfusion.

With history of chronic anovulation, being morbidly obese and history of diabetes, hysteroscopy and endometrial biopsy was performed under general anaesthesia to look for endometrial pathology. Hysteroscopy finding was fluffy endometrium with intrauterine polypoidal growth. Endometrial biopsy was taken and histologic examination reported presence of endometrial hyperplasia with atypia features. She was then prescribed regular oral progesterone (Provera® 20mg TDS) and planned for endometrial sampling for repeat biopsy after 3 months to look for any changes in the histological features.

However, during her gynaecology follow-up (3 months after the first sampling), patient had no per vaginal bleeding since starting oral progesterone and, thus patient and her parents requested to withhold repeated endometrial sampling at that time. The team reluctantly agreed to the request and next follow-up was scheduled for another 3 months. Unfortunately, she experienced excessive PV bleeding again despite good compliance to the treatment and was counselled for a repeat endometrial sampling. The repeated endometrial biopsy under general anaesthesia was carried out and this time the histopathology examination revealed adenocarcinoma arising from the endometrial polyp. As her endometrial biopsy turned out to be cancerous lesion after trial of regular progesterone, patient and family was counselled for hysterectomy.

After patient's consent, total hysterectomy was done and full histopathology examination established the diagnosis of endometroid adenocarcinoma stage 1 based on FIGO criteria with myometrium invasion less than 50% of the myometrium thickness (Figure 1). Her lower uterine segment, cervix, bilateral fallopian tubes were not involved. She was given follow-up at gynaecology clinic for regular cancer surveillance with vault smear and pelvic ultrasound. A complete regime consisted of dietary modification and physical activity to reduce her weight was carefully supervised by a dietitian and her family physician. Her diabetes management was also intensified to reduce the risk of other malignancy. Future planning regarding marriage and possible child adoption was discussed briefly.

DISCUSSION

Endometrial or uterine carcinoma is the second most common gynaecology cancer worldwide in 2018.[6] Less than 10% of cases are diagnosed before the age of 45 years, therefore it is not considered as the first diagnosis in adolescent.[7] Most common presentation of endometrial carcinoma is abnormal

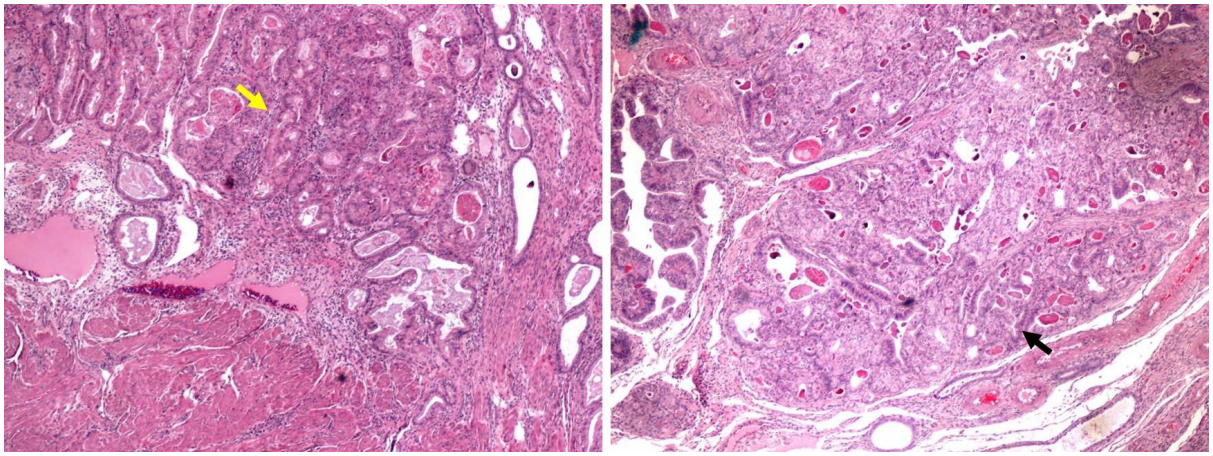

Figure 1: (a) The malignant endometrial glands (yellow arrow) are seen infiltrating into the myometrium (H&E 200x). (b) Malignant glands infiltration arranged in complex glandular pattern with cribriform formation (black arrow). Some of the glands are filled with intraluminal necrosis (H&E 100x). (Click image to enlarge a non annotated image.)

uterine bleeding such as in our case. [3] However, the commonest cause of abnormal menstrual bleeding in adolescents is anovulatory cycles, whereas endometrial carcinoma is extremely rare leading to misdiagnosis during early presentation.[2] Our patient presented with history of irregular menstrual cycle with menorrhagia for 4-year duration before the investigation for endometrial pathology was advised.

Endometrial carcinoma has been subdivided into two types. Type I is associated with unopposed oestrogen exposure and often preceded by endometrial hyperplasia with atypia and had goood prognosis.[5,8] Type II is oestrogen-independent, with high prevalence among elderly and carries a poor outcome.[8] Our young patient had type I endometrial cancer with underlying diabetes and obesity which carries good prognosis. Her strongest risk factor for developing endometrial carcinoma was obesity. Obesity had been identified as a strong risk factor for development of endometrial carcinoma in women younger than 25 years old.[4, 9] Therefore, weight reduction would be beneficial for cancer prevention as it is one of the modifiable risk factor.

When young women present with abnormal uterine bleeding, especially those with risk factors such as obesity, diabetes or chronic anovulation, a pelvic ultrasound and endometrial sampling is advisable.[3-5,7] A high index of suspicion of endometrial pathology should be sought and early referral to gynaecologist for hysteroscopy and biopsy should be made.

Treatment of endometrial carcinoma in adolescents is challenging as preserving fertility would be a concern in addition to complete remission of the disease.[10] Identifying endometrial carcinoma in its precancerous or early stage of the disease could prevent invasive treatment such as hysterectomy. Conservative treatment with progesterone was reported to be feasible and safe in endometrial hyperplasia and early stages of cancer without myometrium invasion.[5, 10] However, for our case, total hysterectomy was a final decision after her biopsy confirmed cancerous lesion despite regular progesterone for 6 months.

CONCLUSION

Recognising the possibility of a serious cause for a common complaint and proceed with further evaluation and early referral can improve prognosis of a terrible disease. Primary care doctors play a major role in identifying individuals with symptoms and risk of cancer

particularly among low prevalence age group.

ACKNOWLEDGEMENT

We thank our Gynaecology team in Hospital Sultanah Nur Zahirah, for their expertise in co-management of the patient.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1: Liu Z, Doan QV, Blumenthal P, Dubois RW. A systematic review evaluating health-related quality of life, work impairment, and healthcare costs and utilization in abnormal uterine bleeding. Value Health. 2007;10(3):183-94. [PDF]. [Accessed on 31st January 2021].

2: Yüce O, Yüce T, Orhun Ç. Overview of abnormal uterine bleeding in adolescents: Diagnosis and management. IJWHR. 2017;5:158-63. [PDF]. [Accessed on 31st January 2021].

3: Wouk N, Helton M. Abnormal uterine bleeding in premenopausal women. Am Fam Physician. 2019;99(7):435-43. [FullText]. [Accessed on 1st February 2021].

4: Rosen MW, Tasset J, Kobernik EK, Smith YR, Johnston C, Quint EH. Risk factors for endometrial cancer or hyperplasia in adolescents and women 25 years old or younger. J Pediatr Adolesc Gynecol. 2019;32(5):546-9.

5: Galczynski K, Nowakowski L, Rechberger T, Semczuk A. Should we be more aware of endometrial cancer in adolescents? Dev Period Med. 2016;20(3):169-73.

6: Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. [FullText]. [Accessed on 31st January 2021].

7: Pellerin GP, Finan MA. Endometrial cancer in women 45 years of age or younger: a clinicopathological analysis. Am J Obstet Gynecol. 2005;193(5):1640-4. [PDF]. [Accessed on 31st January 2021].

8: Setiawan VW, Yang HP, Pike MC, McCann SE, Yu H, Xiang YB, et al. Type I and II endometrial cancers: have they different risk factors? J Clin Oncol. 2013;31(20):2607-18. [PDF]. [Accessed on 31st January 2021].

9: Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, et al. Obesity and endometrial hyperplasia and cancer in premenopausal women: A systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17.

10: Kalogera E, Dowdy SC, Bakkum-Gamez JN. Preserving fertility in young patients with endometrial cancer: Current perspective. Int J Womens Health. 2014;6(1):691-701. [PDF]. [Accessed on 1st February 2021].