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Dr. Sudeshana Devi
Junior Resident, Department of
Obstetrics and Gynaecology,
Sapthagiri Institute of Medical
Sciences and Research Centre,
Bengaluru, Karnataka, India

Dr. Nandeeshha TD
Senior Resident, Department of
Obstetrics and Gynaecology,
Akash Institute of Medical Science
and Research Centre, Bengaluru,
Karnataka, India

Dr. Shamala BS
Junior Resident, Department of
Obstetrics and Gynaecology,
Sapthagiri Institute of Medical
Sciences and Research Centre,
Bengaluru, Karnataka, India

Corresponding Author:
Dr. Sudeshana Devi
Junior Resident, Department of
Obstetrics and Gynaecology,
Sapthagiri Institute of Medical
Sciences and Research Centre,
Bengaluru, Karnataka, India

Rare case of coagulative necrosis of uterine leiomyoma: Case report

Dr. Sudeshana Devi, Dr. Nandeeshha TD and Dr. Shamala BS

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Abstract

Coagulative tumor necrosis or tumor cell necrosis is a very rare type of fibroid degeneration, commonly occurs in 80% of leiomyosarcomas, but it is rare in benign uterine leiomyomas. Women with menorrhagia have increased levels of plasminogen activators in endometrium and use of anti-fibrinolytics can enhance the formation of thrombus in leiomyoma. Degeneration like red and hyaline in uterine leiomyomas may be associated with pregnancy and use of progestogen or OCP's but degeneration associated with use of anti-fibrinolytics can occur in any part of reproductive life.

Materials and Methods: We present the case of 28yr lady with heavy menstrual bleeding and severe dysmenorrhea since 2 years, diagnosed with fibroid uterus and was on anti-fibrinolytics (Tranexamic acid) on and off for 2years. Finally underwent a myomectomy, wherein we found a cheesy degenerative material with final histopathology report revealing as coagulative tumor necrosis without any atypical cells.

Conclusion: Coagulative necrosis is usually seen in malignant condition. Infarct type necrosis and thrombus was observed in benign leiomyoma, possibly secondary to prolonged, repetitive use of Tranexamic acid.

Keywords: Coagulative necrosis, leiomyoma, anti-fibrinolytics, Tranexamic acid

Introduction

Uterine leiomyomas is the most common gynecological cause for menorrhagia in reproductive age women [1]. There are many therapeutic options available for the condition including hormonal and non-hormonal. Tranexamic acid is a safe and effective non-hormonal medication that reduces menstrual blood loss by approximately 50% [3, 4]. It is now considered the first line therapy for the women with menorrhagia. Repetitive use of Tranexamic acid for long periods lead to inhibition of endometrial plasminogen activator and thus prevents fibrinolysis and break down of clot [5]. This leads to the formation of infarct type necrosis and thrombus of leiomyomas. Coagulative tumor necrosis or tumor cell necrosis occurs in 80% of leiomyosarcomas but it is very rare in benign uterine leiomyomas [6]; this type of necrosis is characterized by abrupt transition from viable to necrotic cells without intervening zone of reparative connective tissue reaction, similar features have been studied in uterine leiomyomas treated with arterial embolization [7]. When the overall gross and microscopic features of leiomyoma with coagulative tumor necrosis favours the benign lesion, the clinician should review the drug history. So that, this type of early and healing infarct necrosis is considered as underlining cause of apparent coagulative necrosis. This may otherwise result in diagnosis of smooth muscle tumor of uncertain malignant potential, leading to prolonged follow-up and unnecessary further surgical interventions.

Case report

A 28year old P₁L₁ presented with complaints of heavy menstrual bleeding since 2years with regular cycles with passage of large size clots and congestive dysmenorrhea, hence was diagnosed with fibroid uterus, managed conservatively with Tranexamic acid on and off for 2years.

On examination: Per vaginal: uterine size of 12-14 weeks which is uniformly enlarged with soft to firm in consistency, non-tender.

Radiology: Ultrasound showed solitary anterior wall sub serosal fibroid of 4.2 x 3.4x4.4cm with cystic changes; as she was symptomatic, underwent open myomectomy.

Intra op: Cut section of myoma showed cheesy caseous degenerative material oozing out from the center.



Fig 1: Cheesy caseous degenerative material from cut section of uterine fundus

Histo Pathology (HPE): Surgical pathological slides of this case were retrieved by two pathologists, specimen were processed in our lab using standardized procedures accredited by the college of American Pathologists. Specimen were fixed in 4% neutral buffered formalin and grossly examined, sectioned and blocks were selected and processed. We use the criteria for 1 block taken for each 1cm of the lesion. All slides were cut to 4 micrometers thick and stained with hematoxylin and eosin.

There were no atypical cells demonstrated and there was no mitotic activity within the tumor cells. Mitotic figures in 40 eye power fields (HPF = 0.57mm², Nikon eclipse E600 microscope x 40 objective). The only evidence of thrombosis and organization of thrombus within the vessels were recorded. Multiple small, delicate papillary structures projecting into vascular spaces. This were lined by single layer of endothelial cells, surrounding collagenized course. The endothelial cells showed no significant atypical or mitotic figures. Fusion of papillae with the formation of anastomosing network of blood vessels was focally seen. The infarct in each of these slides showed apoptotic cellular debris and inflammatory cells and interface between viable and necrotic tissue. The zone of granulation tissue and hyaline fibrosis was patchy and not well formed. On this basis, the appearance of necrotic cells, diagnosis of coagulative tumor necrosis was made.

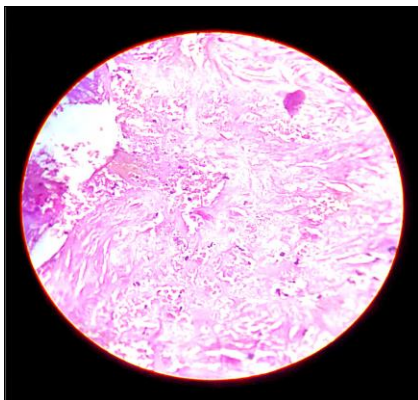


Fig 2: The infarct in this slide showed apoptotic cellular debris and inflammatory cells and interface between viable and necrotic tissue

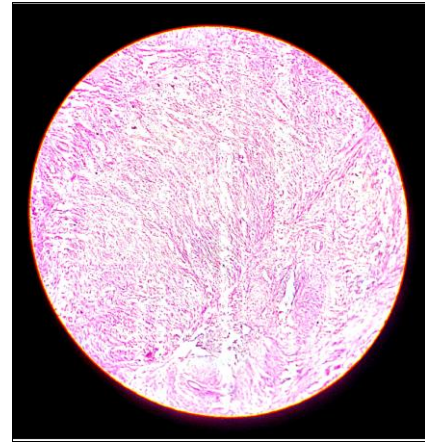


Fig 3: Slide shows zone of granulation tissue and hyaline fibrosis without significant atypical or mitotic figures

Discussion

This is a clinicopathological case report of Tranexamic acid and its association with necrosis and thrombosis in uterine leiomyomas [8]. Tranexamic acid is a synthetic derivative of amino acid lysine. It exerts its antifibrinolytic effect through the reversible blockade of lysine-binding sites on plasminogen molecules [9]. It inhibits endometrial plasminogen activator and thus prevents fibrinolysis and the breakdown of the clot [10]. Although tranexamic acid is commonly prescribed to women with menorrhagia worldwide, the clinical and histologic association with thrombosis and necrosis of leiomyomas, to our knowledge, has not been investigated. Our study shows that infarct-type necrosis and thrombosis of leiomyomas is more commonly observed in patients treated with tranexamic acid. Necrosis in uterine smooth muscle tumor has received much attention in the medical literature. A large number of authors are emphasized the prognostic importance of tumor cell necrosis. In assessing the behavior of uterine smooth muscle tumors, the presence or absence of coagulative tumor necrosis is of paramount importance under most circumstances [11], affects the interpretation and final diagnosis. Necrosis in leiomyomas may be infarct type or true coagulative tumor necrosis. The zone of necrosis is usually separated from viable tumor via zone of reparative connective tissue (granulation tissue and hyaline fibrosis) and there is usually associated hemorrhage [12]. Symptoms related to necrosis of leiomyomas would presumably be similar to those described for treatment with arterial embolization, this includes pelvic pain, nausea, generalized malaise and low-grade fever [13, 14]. Even though the drug may reduce the heavy bleeding associated with leiomyomas, clinician should be aware of theoretical symptoms associated with tranexamic acid induced necrosis. Although it is difficult to establish a relationship between the pain and the commencement of administration of tranexamic acid [15], it may be advisable for the prescribing clinician to warn the patient of these possible complications or this may otherwise result in diagnosis of smooth muscle tumor of uncertain malignant potential, leading to prolonged follow-up and unnecessary further surgical intervention.

Conclusion

Infarct type necrosis and thrombosis of uterine leiomyomas is a rare clinical condition but can be commonly observed in patient exposed to tranexamic acid [16]. Drug induced necrosis of uterine leiomyomas can be differentiated from other types of necrosis as early and the reparative connective tissue reaction between the

viable and necrotic tissue [17]. When the overall gross and microscopic features of leiomyoma with necrosis favour a benign lesion, the clinical and the drug history should be reviewed so that, this type of early and healing infarct type necrosis is considered as possible underlining cause of apparent coagulative necrosis [18, 19]. Symptoms related to necrosis of leiomyoma may include pelvic pain and low grade fever and the clinician should be alert to them when treating patient with tranexamic acid.

Conflict of Interest

Not available

Financial Support

Not available

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