

# Advanced Vulvar Paget's Disease: Insight into a Rare Presentation

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**Abstract:-** Extra-mammary Paget's disease, a rare neoplasm, have variable rates of invasion. Vulva is the most common extra mammary site, others being perineal, perianal and scrotal region in a few cases. Presence of Paget's cells in tissue biopsy confirms the diagnosis, whereas invasion beyond basement to surrounding structure is associated with malignant nature of disease. It commonly occurs in postmenopausal, elderly females. This case reports told off a 71-year-old woman presented with an ulcerated lesion in vulva for 1-year duration which came out as invasive vulvar Paget's disease. Wide local excision followed by post-operative whole pelvic irradiation was given for radical cure. Unfortunately, patient had local recurrence within 1-year and was given metronomic chemotherapy with oral cyclophosphamide and capecitabine primarily. As disease was progressive in this regimen, she was shifted to metronomic chemotherapy with oral methotrexate and celecoxib. Patient had got symptomatic relief with current regimen and is continuing the regimen for last 3-years. This case report showed the high chance of recurrence in vulvar Paget's disease and partial response to oral methotrexate in such condition. More case reports and case series are needed for driving the definite conclusions on treatment protocol and role of oral metronomic chemotherapy for invasive vulvar Paget's disease.

**Keywords:-** Vulvar Paget's Disease; Wide Local Excision, Whole Pelvic Irradiation, Metronomic Chemotherapy.

## I. INTRODUCTION

Most common site of extra-mammary Paget's disease is vulvar region. It is a tenacious condition with higher prevalence of relapse and currently requires multi-modality management. Here, we present a case of recurrent, invasive vulvar Paget's disease in an old lady treated by multidisciplinary approach of surgery, radiation and chemotherapy.

## II. CASE SUMMARY

A 71-year-old woman presented with an ulcerated lesion in vulva for 1-year duration, which was insidious in onset, rapidly growing in size, painless but accompanied by pruritus. The pruritus was severe in intensity, off and on type, lasted locally in vulva for last 8-years, partially relieved by topical ointment application. She had no associated history of fever, weight loss, anorexia, headache, chest or abdominal discomfort. She was non-smoker, non-alcoholic and not having any chronic illness. Patient had no history of abnormal uterine bleeding and had attained menopause 20-years ago, menstrual cycles were uneventful. She had 2 children, delivered vaginally at government hospital. General physical and systemic examination was normal. Local examination revealed a 4.0 × 3.0 cm ulcerated, bright red, eczematous lesion in vulva and labia majora, more prominent on left side.

The patient's routine blood tests including complete hemogram and blood biochemistry profile, ultrasound of abdomen-pelvis region and chest radiograph were within normal limits. Patient underwent wide local excision of labial lesion with vulvar reconstruction. Histopathology of surgical specimen revealed Paget's cell in the lesion & surrounding epithelium and strong cytokeratin 7 (CK 7) positivity in tumor cell was noted by immunohistochemistry (IHC) staining. The histopathology and IHC appearance confirmed it as a case of vulvar Paget's disease with invasion into surrounding tissue.

To prevent local recurrence, patient was given post-operative whole pelvic irradiation in dose of 54 gray (Gy) in 30 fractions over 6 weeks. After that, she was on regular follow-up and remained asymptomatic for 14-months. Subsequently, the patient presented with red velvety ulcerated lesion with areas of necrosis in vulva and labia majora more on left side having a size of 4.0 × 6.5 cm implying disease recurrence (Figure 1).



Figure 1: Ulcerated, bright red, eczematous lesion in vulva and labia majora.

She was given oral metronomic chemotherapy with tablet cyclophosphamide (50 mg daily) and tablet capecitabine (500 mg twice daily) for 3-years. Despite having this treatment, the disease was still progressing and patient was given therapeutic trials of metronomic chemotherapy with oral methotrexate tablet (25 mg once weekly) and capsule celecoxib (20 mg twice daily). Patient had got symptomatic relief with current regimen and is continuing the regimen for last 3-years.

### III.DISCUSSION

Extra-mammary Paget's disease is an infrequent disorder with 6.5% frequentness and variable rates of invasion. [1] Vulva is the most frequent extra-mammary site, others being perineal, perianal and scrotal region in a few cases. It is often difficult to diagnose and is frequently present for many years before treatment begins. [2] It commonly occurs in females having old age after menopause. [3] Once diagnosed, it is being classified by Wilkinson and Brown system of classification into primary (cutaneous origin) and secondary (non-cutaneous origin). [4] The survival is not so poor with an 5-year overall survival is around 70%, however disease remain off and on in most of the surviving females. [5] The invasiveness contributed in 12% of diagnosed cases and have high relapse rate i.e. 12 to 61% with an average of 2 recurrences per patient. [6] In general, dermal invasion being key factor predicting recurrence, whereas role of pathologic features, R0 resectability, tumor cell aneuploidy, hormone receptor positivity, and cytogenetic abnormality in local recurrence is under research. [7]

The initial treatment of choice for lesion confined to vulva is surgical intervention which mainly consist of wide local excision (WLE) with local (inguino-femoral) lymph node dissection in majority of cases. The main challenge is of obtaining clear R0 surgical margin. In majority of cases, patients have post-operative local complications which are infection, hematomas and wound breakdown (incidence rates: 9–45%). [4] The post-surgery recurrence rates are also high (about 58%) with significant morbidity and these are similar to patient who didn't underwent surgery. [8]. Therefore, there is need for alternative treatment approach.

Radiation therapy (RT) is an option as definitive treatment for patients not eligible for surgery (medically unfit) or not willing for surgery. It can also be given in post-operative settings to prevent local recurrence and as second line treatment in patients having recurrence after surgery. Recommended dose range of radiation therapy is 55 Gy to 65 Gy by conventional fractionation for invasive vulvar Paget's disease. [9] Long-term follow-up in post radiotherapy patients showed less recurrence rates. [4]

A few numbers of chemotherapy related studies have been conducted till date, which limit the value of its significance. This includes clinical trials with FECOM (5-fluorouracil, epirubicin, carboplatin, vincristine, and mitomycin-C) regimen; FEC100 (fluorouracil, epirubicin, and cyclophosphamide) regimen followed by docetaxel; cyclophosphamide and capecitabine; methotrexate and celecoxib with variable outcome. [10-13] Regimen consisting of trastuzumab along with paclitaxel was also explored in a case report having lymph node metastatic Her-2-neu positive vulvar Paget disease, which showed partial response in terms of lymph node regression. [14]

In our case, patient was given post-operative adjuvant radiation therapy to prevent local recurrence within 1-month of surgical intervention. Later on, patient had reoccurrence after 14 months and then modality of treatment was changed to novel oral metronomic chemotherapy that is cyclophosphamide & capecitabine. 3-years later another novel regimen was explored in view of disease progression, which consisted of oral methotrexate. The patient has stable disease and is being on monthly follow up since last 3-years.

### IV.CONCLUSION

Invasive Paget's disease of vulva is an infrequent entity having aggressive clinical behavior. Majority of the cases do not resolve completely and have off and on recurrence pattern. Radical curative intent is the initial approach, but often palliation of symptoms becomes the goal of treatment. In our case, surgery followed by adjuvant radiotherapy was employed first for radical cure and metronomic chemotherapy was given while there was recurrence. However, the treatment yielded partial response and good subjective symptomatic relief. More case reports are needed for driving the definite conclusions on treatment protocol and role of oral metronomic chemotherapy for invasive vulvar Paget's disease.

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