Spectacular Response of a Locally Advanced Vulvar Carcinoma in a Relatively Young Patient: Successful Multimodal Strategy Using Induction Chemotherapy and Concurrent Chemoradiotherapy.

Abstract

Introduction :

Vulvarcarcinomais a rare malignancy, and locallyadvancedinoperable T4 tumorsrepresent a major therapeutic challenge, particularly in relativelyyoung patients. HPV-associatedtumors, often p16-positive, are characterized by rapid and aggressive local invasion.

Case Presentation:

We report the case of a 51-year-old womanwith HPV 16 and p16-positive T4N1 inoperablevulvarcarcinoma. Shereceivedweekly induction chemotherapyconsisting of paclitaxel and carboplatin for 12 cycles, followed by concurrent chemoradiotherapyusing IMRT and cisplatin. The patient experienced a **spectaculartumorregression**, bothclinically and radiologically, withcompletedisappearance of inguinal lymphadenopathy and near-completeregression of vaginal and perineal extensions. Treatmenttolerancewas excellent.

Discussion:

This case highlights the effectiveness of a multimodal strategy in a relativelyyoung patient withinoperable T4 vulvarcarcinoma. Induction chemotherapyallowssignificanttumordownstagingprior to chemoradiotherapy, whilemaintaining an appropriateintervalenhancestolerance and recovery. A multidisciplinary and individualizedapproachis essential to maximizeresponse, optimize the chance of cure, and preservequality of life.

Conclusion:

The combination of induction chemotherapyfollowed by concurrent chemoradiotherapyrepresents a safe and effective therapeutic option for patients withlocallyadvanced, inoperablevulvarcarcinoma, includingrelativelyyoungwomen.

Keywords:

Vulvarcarcinoma, Vulvar cancer, HPV 16, p16, Induction chemotherapy, Concurrent chemoradiotherapy, Locallyadvancedtumor, Tumorresponse, Multimodal treatment.

Abbreviations

- **VIN:** VulvarIntraepithelialNeoplasia
- **HPV:** Human Papillomavirus
- **RCP:** MultidisciplinaryTumorBoardMeeting
- **ECOG:** EasternCooperativeOncology Group
- **IRM:** Magnetic Resonance Imaging (MRI)
- **TEP-TDM:** Positron EmissionTomography – ComputedTomography (PET-CT)
- **SUV:** StandardizedUptake Value
- **IMRT:** Intensity-Modulated Radiation Therapy
- **OS:** Overall Survival
- **PFS:** Progression-Free Survival
- **LVSI:** LymphovascularSpace Invasion

Introduction

Vulvar cancer is rare, accounting for lessthan 5% of all gynecologicmalignancies [1,2], and primarily affects olderwomen, mostcommonlythose over 70 years of age [3]. HPV-associatedtumors, oftenp16-positive, occur at a youngerage and display rapid and extensive local invasion [4,5]. Locallyadvanced T4 tumorsthat are not amenable to surgeryrequire a multimodal approachcombining induction chemotherapy and chemoradiotherapy to improve local control and overallprognosis [6,7].

We report the case of a relativelyyoung patient with HPV 16/p16-positive T4N1 vulvarcarcinomawhodemonstrated a spectacularresponse to a multimodal therapeuticstrategy, underscoring the importance of personalized, multidisciplinary management.

ClinicalPresentation

The patient was a 51-year-old woman, menopausalsinceage 42, an active chronicsmoker (20 pack-years), G3P3 with vaginal deliveries, and with no significantmedical, surgical, or familyhistory. Shehadneverundergone HPV screening or regulargynecologic surveillance.

Clinicalsymptomsbegan 18 monthsbeforepresentationwith the onset of an ulcerated, pruriticclitorallesion, initiallypainless but progressivelybecomingpainfulduringwalking and sexual

intercourse. The lesiongraduallyincreased in size and becamecomplicated by persistent pruritus and occasional minimal bleeding. Worsening pain, functionaldiscomfort, and aestheticconcernultimatelymotivatedhergynecologic consultation.

Initial ClinicalExamination

- Vulvarinspection: infiltratingulcerated–exophyticlesion on the inner surface of the leftlabia minora, measuringapproximately 5–6 cm, witherythematous areas and necroticcrusts, associatedwithinflammatorydeformation of the clitoris.
- Vaginal examination: cervix and vaginal wallsmacroscopically normal.
- Digital vaginal examination: localized induration at the upperanterolateralleft vaginal wall.
- Inguinal areas: no palpable lymphadenopathybilaterally.

Initial laboratory tests showed:

- Normal CBC, slightlyelevated CRP (18 mg/L)
- Normal renal and liverfunction
- Negativeserologies for HIV, syphilis, and hepatitis B/C

PathologyResultsfrom Biopsies

- Multiple biopsies of the leftlabiaminora: VIN3 in several areas.
- Deep biopsy:moderatelydifferentiated non-keratinizinginfiltratingsquamouscellcarcinoma, p16 positive.
- Cervical biopsy:acanthoticmucosawithoutatypia.

Initial Imaging

- PelvicMRI: lesioncentered on the leftlabia minora and clitoris, measuring 7.7 × 5 × 1.85 cm, withmoderate extension to the lower vaginal walls, early infiltration of the leftlevatorani muscle, partial involvement of the puborectal and iliococcygeal bundles, contact with the ischiopubicramus, and limited infiltration of the ischiorectalfossa. Partial invasion of the leftanterolateral anal canal wall (1.2 cm).
- Right inguinal lymphnodes: up to 1.4 cm.
- PET-CT: SUVmax 17, no othersuspiciousfoci.

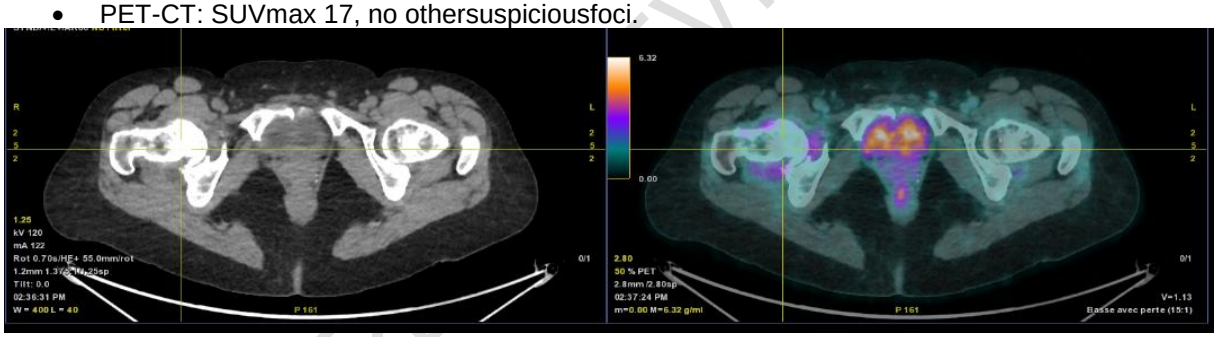

Image 01: *PET-CT findingsshowing the initial involvement of the vulva (axial view).*

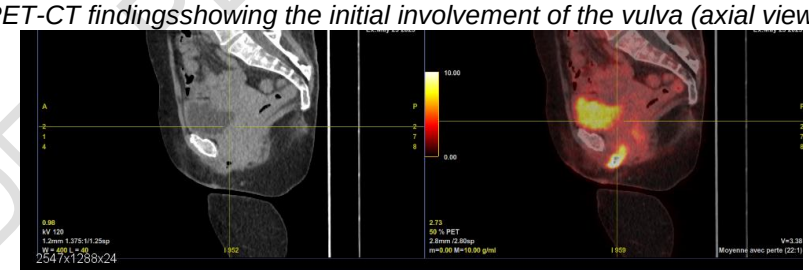

Image 02: *PET-CT findingsshowing the initial involvement of the vulva (sagittal view).*

Initial RCPDecision

Radical total vulvectomywithbilaterallymphnodeassessment.

The patient refusedtreatment and waslost to follow-up for six months.

ClinicalEvolutionAfter 6 Months

- Ulceratednecrotic mass >15 cm, verypainful
- Decline in general condition, 6 kg weightloss, anemia 10.8 g/dL
- Dysuria and tenesmus
- No significantlymphedema
- Inguinal lymphnodeslikelyinflammatory

RepeatMRI: extensive leftpelvicinvolvement, large infiltration of the levatorani, abscessed areas, contact with the ischiopubicramus.

PET-CT: major local progression and evolvinglymphnodeinvolvement.

Final staging: T4N1M0, inoperable.

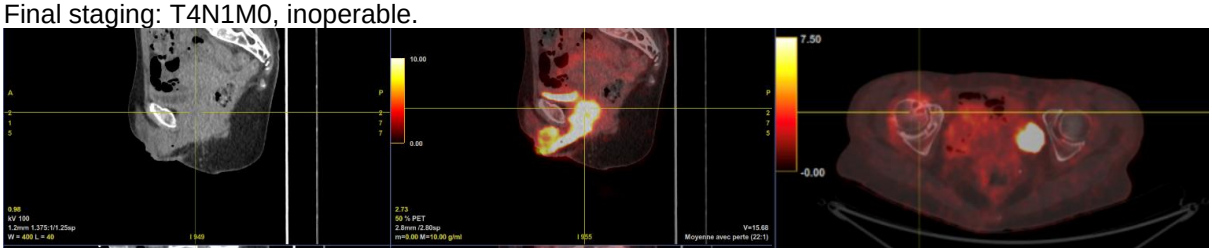

Image 03: *PET-CT findingsshowinginvolvement of the vulvafollowing progression to a T4N1M0 lesion (sagittal and axial views).*

Therapeutic Management (RCPDecision)

Induction Chemotherapy

- Paclitaxel 80 mg/m² weekly
- Carboplatin AUC 2 weekly
- 12 cycles
- Premedicationwithcorticosteroids and antihistamines

Clinicalevolution:

Progressive improvement in pain, disappearance of bleeding, improvedappetite and sleep, bettermobility, ECOG 1, and completeresolution of inguinal lymphadenopathy.

Post-chemotherapyMRI: major regression, near-completedisappearance of the clitoral component, and significantreduction in vaginal, perineal, and levatorani extension.

Image 04: *Magnetic resonanceimaging (MRI) performedafter induction chemotherapy.*

Intervalbeforechemoradiotherapy: a 3-week delaywasrespectedafter the final induction chemotherapy cycle to allowhematologic and generalrecovery, according to currentrecommendations [8,9].

Concurrent Chemoradiotherapy :

- Initiated 3 weeksaftercompletion of induction chemotherapy
- IMRT radiotherapy:
  - Pelvis 46 Gy (2 Gy/fraction, 23 fractions)
  - Vulvartumor boost 20 Gy (2 Gy/fraction, 10 fractions)
  - Total dose: 66 Gy
- Cisplatin 40 mg/m² weekly × 5 cycles
- Observedtoxicity: Grade 2 radiodermatitis, wellmanagedwith local care

Post-TreatmentEvaluation

- Nearly normal vulvaranatomy
- No residual induration
- Sphincter tonepreserved

PET-CT at 3 months post-treatment: normalization of vulvar and nodal hypermetabolism, minimal diffuse vaginal uptake.

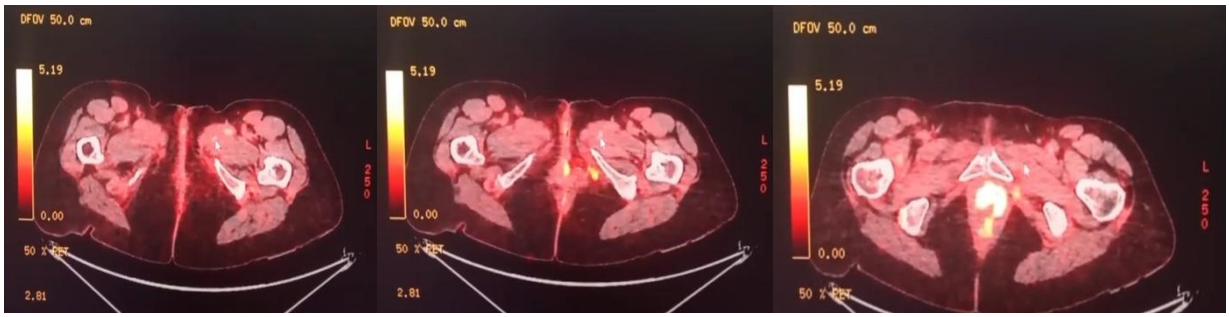

Image 05: *Follow-up PET-CT scan performedthreemonthsaftercompletion of induction chemotherapy and concurrent chemoradiotherapy.*

Follow-Up

- At 3 months post-chemoradiotherapy: ECOG 0, no pain, no lymphedema, full return to normal dailyactivities, no clinical or radiologicrecurrence, and significantimprovement in quality of life.

Discussion

Vulvar cancer is a rare entity, accounting for approximately 0.3 to 1% of all female cancers, with a lower incidence in younger patients [1,2]. The majority of vulvarcarcinomasoccurafter the age of 70, but HPV-associatedforms (often p16 positive) affect younger patients and exhibit a more rapid invasive potential [3,4].

Rarity and relevance of the case

Our patient, aged 51 and HPV 16/p16 positive, represents an unusual profile for advanced T4N1 vulvar cancer. The combination of relativelyyoungage and a large initial tumorburdenmakesthis case clinicallyinteresting and scientificallysignificant [5,6].

Diagnosis and initial management

Precancerouslesions (VIN3) wereidentified on multiple biopsies, with a deep area showinginfiltrating, moderatelydifferentiated non-keratinizingsquamouscellcarcinoma, p16 positive. The detection of VIN3 and p16 positivity highlights the major role of HPV in vulvarcarcinogenesis and allowsdifferentiationbetweentwo main pathways: HPV-dependent and HPV-independent [7,8].
Initial MRI revealed a more extensive tumorthanclinicallyappreciated, reflecting the limitation of physicalexamination in assessingdeeppelvic and perineal extension [9]. Inguinal lymphnodesweredetected on MRI and confirmed by PET-CT, guiding the multimodal treatmentapproach [10].

Therapeuticstrategy

Standard treatment for T4 vulvar cancers typicallyincludes radical surgery;however, in our case, the patient initiallyrefusedsurgery and the tumorwasdeemedinoperable [11].
Induction chemotherapy (paclitaxel + carboplatin) resulted in significanttumorregression, markedclinicalimprovement, and completedisappearance of inguinal lymphadenopathy. This type of induction chemotherapyisrecommended for locallyadvanced, inoperabletumors to reducetumor volume prior to chemoradiotherapy [12,13].
A three-weekintervalwasobservedbetween the end of induction chemotherapy and the start of chemoradiotherapy to allowhematologic and generalrecovery, consistent with international guidelines [14,15].
Concomitant chemoradiotherapywith IMRT and weeklycisplatinwaswelltolerated and led to normalization of vulvar and nodal hypermetabolism. The use of IMRT optimized dose distribution whileminimizingcutaneous and intestinal toxicity [16,17].

Results and prognosis

The spectacularresponseobserved in our patient underscores the efficacy of this multimodal strategy in advancedvulvarcarcinomas. Studies report that the combination of induction chemotherapy and chemoradiotherapy can induce partial to completeresponses in 40–70% of cases [18,19].
Clinicaltolerancewas excellent, withonlymildperipheralneuropathy and grade 2 radiation dermatitis, bothresolving [20].

Implications for practice

This case highlights several key points:

1. The importance of multimodal evaluation (clinicalexamination, MRI, PET-CT) to plan treatment for locallyadvancedvulvar cancers.
2. The effectiveness of induction chemotherapyfollowed by concomitant chemoradiotherapy in inoperabletumors.
3. The necessity of respecting an appropriateintervalbetweentreatments to optimizetolerance and recovery.
4. The value of multidisciplinary management to maximizeresponse rates and preservequality of life [1–20].

Conclusion

Advanced vulvar cancer in a relativelyyoung, HPV/p16 positive patient is rare. The combination of induction chemotherapyfollowed by concomitant chemoradiotherapyachievedspectaculartumorregression, disappearance of lymphadenopathy, and functionalrecovery. This case illustrates the efficacy of an individualized, coordinated, multimodal approach and emphasizes the importance of innovative strategies for inoperabletumors.
The patient providedwritteninformed consent for the publication of this case, includingclinical data and associated images. The authorsdeclare no conflicts of interest.

Consent and Conflicts of Interest:

Writteninformed consent wasobtainedfrom the patient for publication of this case report.
The authorsdeclarethatthey have no conflicts of interestrelated to thisstudy.

Tables:

Table 1:Therapeutic Scheme

Phase	Treatment	Dose / Cycle	Frequency	Number of Cycles	Objective
Induction Chemotherapy	Paclitaxel	80 mg/m²	Weekly	12	Tumorreduction
Induction Chemotherapy	Carboplatin	AUC 2	Weekly	12	Tumorreduction
Concomitant Chemoradiotherapy	IMRT Pelvis	46 Gy	2 Gy/fraction	23	Inclusion of lymphnodes
Concomitant Chemoradiotherapy	VulvarTumor Boost	20 Gy	2 Gy/fraction	10	Total dose 66 Gy
Concomitant Chemoradiotherapy	Cisplatin	40 mg/m²	Weekly	5	Concurrent with RT

Table 2:Summary of Clinical and Imaging Results

Step	ClinicalFindings	MRI	PET-CT	Comments
Initial	5–6 cm lesion, vaginal induration	7.7 × 5 × 1.85 cm, earlyinvolvement of the levator	SUVmax 17	Tumor extension underestimated on clinicalexamination
6-Month Follow-Up	Ulcero-necrotic mass >15 cm, pain, tenesmus	Extensive leftpelvicinvolvement, abscessed areas, levator infiltration	Significant local and nodal progression	T4N1M0, inoperable
Post-Induction Chemotherapy	Pain improvement, ECOG 1	Major regression of tumor and lymphnodes	SUVmaxdecreased	Spectacular partial response
Post-Chemoradiotherapy	Nearly normal vulvaranatomy	Resolution of clitorallesion, regression of vaginal, perineal, and levatorinvolvement	Normalization of vulvar and nodal uptake	Complete response in vulva and lymphnodes

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