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RESEARCH ARTICLE

SPECTACULAR RESPONSE OF A LOCALLY ADVANCED VULVAR CARCINOMA IN A RELATIVELY YOUNG PATIENT: SUCCESSFUL MULTIMODAL STRATEGY USING INDUCTION CHEMOTHERAPY AND CONCURRENT CHEMORADIOTHERAPY

Marwa Biyoud, Nouhaila Tnifasse , Fatima Ezzahra Alouan , Rabah Hamlaoui , Nicolas Bauer and Thomas Ohnleiter

1. Department of Radiation Oncology, GHRMSA, Mulhouse, France.

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Vulvar carcinoma, Vulvar cancer, HPV 16, p16, Induction chemotherapy, Concurrent chemoradiotherapy, Locally advanced tumor, Tumor response, Multimodal treatment.

Abstract

Introduction:Vulvar carcinoma is a rare malignancy, and locally advan ced inoperable T4 tumors represent a major therapeutic challenge, particularly in relatively young patients. HPV-associated tumors, often p16-positive, are characterized by rapid and aggressive local invasion.
Case Presentation: We report the case of a 51-year-old woman with HPV 16 and p16-positive T4N1 inoperable vulvar carcinoma. She received weekly induction chemotherapy consisting of paclitaxel and carboplatin for 12 cycles, followed by concurrent chemoradiotherapy using IMRT and cisplatin. The patient experienced a spectacular tumor regression, both clinically and radiologically, with complete disappeara nce of inguinal lymphadenopathy and near-complete regression of vaginal and perineal extensions. Treatment tolerance was excellent.
Discussion: This case highlights the effectiveness of a multimodal strategy in a relatively young patient with inoperable T4 vulvar carcino ma. Induction chemotherapy allows significant tumor downstaging prior to chemoradiotherapy, while maintaining an appropriate interval enhances tolerance and recovery.A multidisciplinary and individualized approach is essential to maximize response, optimize the chance of cure, and preserve quality of life.
Conclusion: The combination of induction chemotherapy followed by concurrent chemoradiotherapy represents a safe and effective therapeuti c option for patients with locally advanced,inoperable vulvarcarcinoma, including relatively young women.

Introduction:-

Vulvar cancer is rare, accounting for less than 5% of all gynecologic malignancies [1,2], and primarily affects older women, most commonly those over 70 years of age [3]. HPV-associated tumors, often p16-positive, occur at a younger age and display rapid and extensive local invasion [4,5]. Locally advanced T4 tumors that are not amenable

Corresponding Author:- Marwa Biyoud, Nouhaila Tnifasse
Address:- Department of Radiation Oncology, GHRMSA, Mulhouse, France.

to surgery require a multimodal approach combining induction chemotherapy and chemoradiotherapy to improve local control and overall prognosis [6,7].

We report the case of a relatively young patient with HPV 16/p16-positive T4N1 vulvar carcinoma who demonstrated a spectacular response to a multimodal therapeutic strategy, underscoring the importance of personalized, multidisciplinary management.

Clinical Presentation:
The patient was a 51-year-old woman, menopausal since age 42, an active chronic smoker (20 pack-years), G3P3 with vaginal deliveries, and with no significant medical, surgical, or family history. She had never undergone HPV screening or regular gynecologic surveillance.

Clinical symptoms began 18 months before presentation with the onset of an ulcerated, pruritic clitoral lesion, initially painless but progressively becoming painful during walking and sexual intercourse. The lesion gradually increased in size and became complicated by persistent pruritus and occasional minimal bleeding. Worsening pain, functional discomfort, and aesthetic concern ultimately motivated her gynecologic consultation.

Initial Clinical Examination
- Vulvar inspection: infiltrating ulcerated–exophytic lesion on the inner surface of the left labia minora, measuring approximately 5–6 cm, with erythematous areas and necrotic crusts, associated with inflammatory deformation of the clitoris.
- Vaginal examination: cervix and vaginal walls macroscopically normal.
- Digital vaginal examination: localized induration at the upper anterolateral left vaginal wall.
- Inguinal areas: no palpable lymphadenopathy bilaterally.

Initial laboratory tests showed:
- Normal CBC, slightly elevated CRP (18 mg/L)
- Normal renal and liver function
- Negative serologies for HIV, syphilis, and hepatitis B/C

Pathology Results from Biopsies
- Multiple biopsies of the left labia minora: VIN3 in several areas.
- Deep biopsy: moderately differentiated non-keratinizing infiltrating squamous cell carcinoma, p16 positive.
- Cervical biopsy: acanthotic mucosa without atypia.

Initial Imaging
- Pelvic MRI: lesion centered on the left labia minora and clitoris, measuring 7.7 × 5 × 1.85 cm, with moderate extension to the lower vaginal walls, early infiltration of the left levator ani muscle, partial involvement of the puborectal and iliococcygeal bundles, contact with the ischiopubic ramus, and limited infiltration of the ischiorectal fossa. Partial invasion of the left anterolateral anal canal wall (1.2 cm).
- Right inguinal lymph nodes: up to 1.4 cm.
- PET-CT: SUVmax 17, no other suspicious foci.

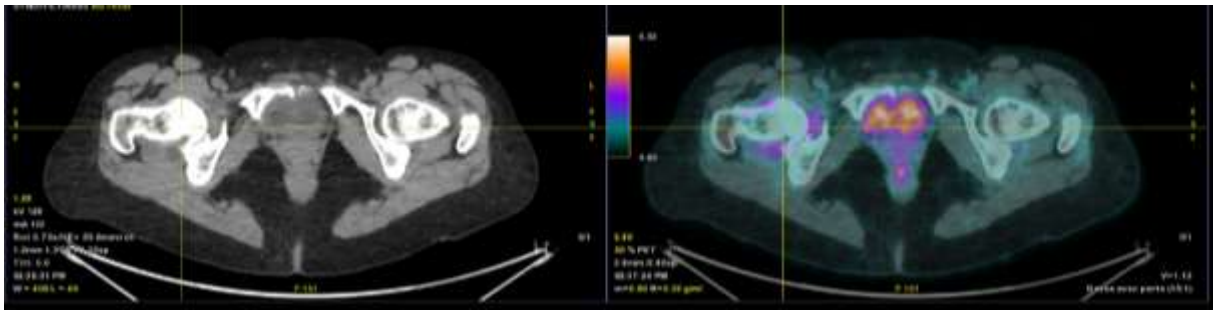

Image 01: PET-CT findings showing the initial involvement of the vulva (axial view).

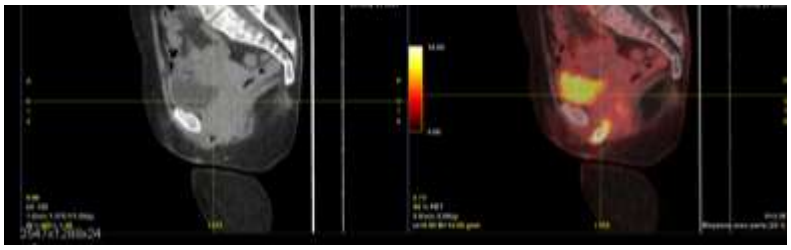

Image 02: PET-CT findings showing the initial involvement of the vulva (sagittal view).

Initial RCP Decision
Radical total vulvectomy with bilateral lymph node assessment.
The patient refused treatment and was lost to follow-up for six months.

Clinical Evolution After 6 Months
- Ulcerated necrotic mass >15 cm, very painful
- Decline in general condition, 6 kg weight loss, anemia 10.8 g/dL
- Dysuria and tenesmus
- No significant lymphedema
- Inguinal lymph nodes likely inflammatory

Repeat MRI: extensive left pelvic involvement, large infiltration of the levator ani, abscessed areas, contact with the ischiopubic ramus.

PET-CT: major local progression and evolving lymph node involvement.
Final staging: T4N1M0, inoperable.

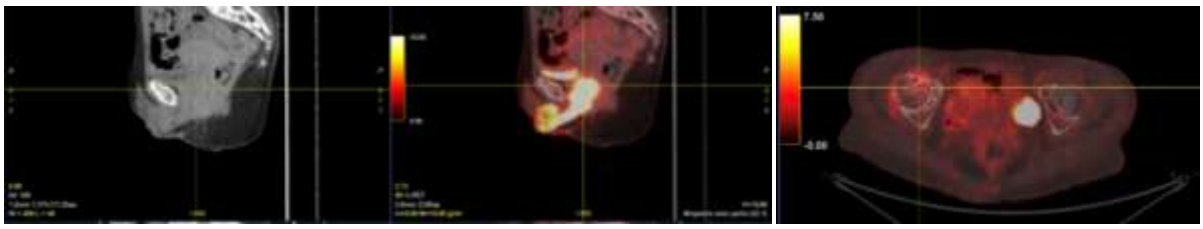

Image 03: PET-CT findings showing involvement of the vulva following progression to a T4N1M0 lesion (sagittal and axial views).

Therapeutic Management (RCP Decision)
Induction Chemotherapy
- Paclitaxel 80 mg/m² weekly
- Carboplatin AUC 2 weekly
- 12 cycles
- Premedication with corticosteroids and antihistamines

Clinical evolution:
Progressive improvement in pain, disappearance of bleeding, improved appetite and sleep, better mobility, ECOG 1, and complete resolution of inguinal lymphadenopathy.

Post-chemotherapy MRI: major regression, near-complete disappearance of the clitoral component, and significant reduction in vaginal, perineal, and levator ani extension.

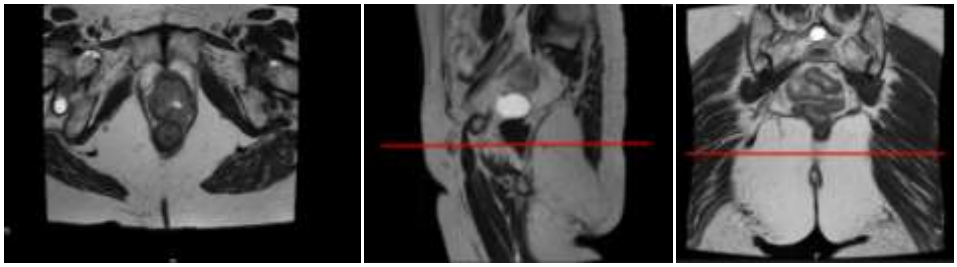

Image 04: Magnetic resonance imaging (MRI) performed after induction chemotherapy.

Interval before chemoradiotherapy: a 3-week delay was respected after the final induction chemotherapy cycle to allow hematologic and general recovery, according to current recommendations [8,9].

Concurrent Chemoradiotherapy :

- Initiated 3 weeks after completion of induction chemotherapy
- IMRT radiotherapy:
  - Pelvis 46 Gy (2 Gy/fraction, 23 fractions)
  - Vulvar tumor boost 20 Gy (2 Gy/fraction, 10 fractions)
  - Total dose: 66 Gy
- Cisplatin 40 mg/m² weekly × 5 cycles
- Observed toxicity: Grade 2 radiodermatitis, well managed with local care

Post-Treatment Evaluation

- Nearly normal vulvar anatomy
- No residual induration
- Sphincter tone preserved
-

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

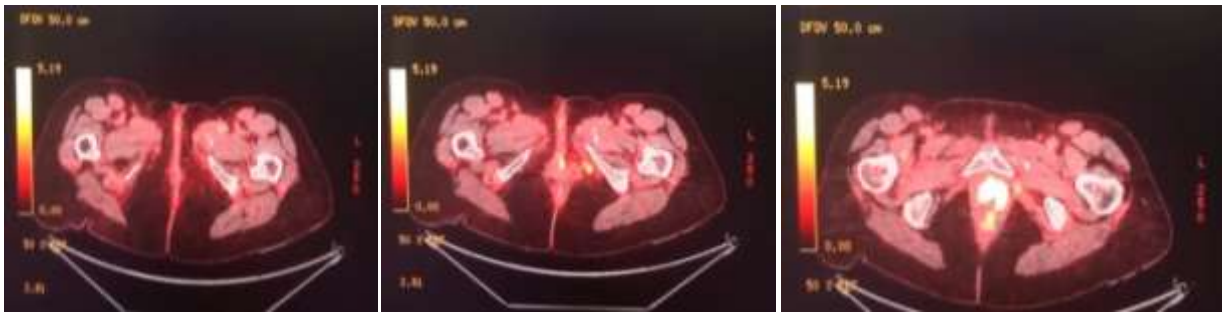

Image 05: Follow-up PET-CT scan performed three months after completion of induction chemotherapy and concurrent chemoradiotherapy.

Follow-Up

- At 3 months post-chemoradiotherapy: ECOG 0, no pain, no lymphedema, full return to normal daily activities, no clinical or radiologic recurrence, and significant improvement 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 vulvar carcinomas occur after the age of 70, but HPV-associated forms (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 relatively young age and a large initial tumor burden makes this case clinically interesting and scientifically significant [5,6].

Diagnosis and initial management
Precancerous lesions (VIN3) were identified on multiple biopsies, with a deep area showing infiltrating, moderately differentiated non-keratinizing squamous cell carcinoma, p16 positive. The detection of VIN3 and p16 positivity highlights the major role of HPV in vulvar carcinogenesis and allows differentiation between two main pathways: HPV-dependent and HPV-independent [7,8].

Initial MRI revealed a more extensive tumor than clinically appreciated, reflecting the limitation of physical examination in assessing deep pelvic and perineal extension [9]. Inguinal lymph nodes were detected on MRI and confirmed by PET-CT, guiding the multimodal treatment approach [10].

Therapeutic strategy
Standard treatment for T4 vulvar cancers typically includes radical surgery; however, in our case, the patient initially refused surgery and the tumor was deemed inoperable [11].

Induction chemotherapy (paclitaxel + carboplatin) resulted in significant tumor regression, marked clinical improvement, and complete disappearance of inguinal lymphadenopathy. This type of induction chemotherapy is recommended for locally advanced, inoperable tumors to reduce tumor volume prior to chemoradiotherapy [12,13].
A three-week interval was observed between the end of induction chemotherapy and the start of chemoradiotherapy to allow hematologic and general recovery, consistent with international guidelines [14,15].

Concomitant chemoradiotherapy with IMRT and weekly cisplatin was well tolerated and led to normalization of vulvar and nodal hypermetabolism. The use of IMRT optimized dose distribution while minimizing cutaneous and intestinal toxicity [16,17].

Results and prognosis:-
The spectacular response observed in our patient underscores the efficacy of this multimodal strategy in advanced vulvar carcinomas. Studies report that the combination of induction chemotherapy and chemoradiotherapy can induce partial to complete responses in 40–70% of cases [18,19]. Clinical tolerance was excellent, with only mild peripheral neuropathy and grade 2 radiation dermatitis, both resolving [20].

Implications for practice
This case highlights several key points:
1. The importance of multimodal evaluation (clinical examination, MRI, PET-CT) to plan treatment for locally advanced vulvar cancers.
2. The effectiveness of induction chemotherapy followed by concomitant chemoradiotherapy in inoperable tumors.
3. The necessity of respecting an appropriate interval between treatments to optimize tolerance and recovery.
4. The value of multidisciplinary management to maximize response rates and preserve quality of life [1–20].

Conclusion:-
Advanced vulvar cancer in a relatively young, HPV/p16 positive patient is rare. The combination of induction chemotherapy followed by concomitant chemoradiotherapy achieved spectacular tumor regression, disappearance of lymphadenopathy, and functional recovery. This case illustrates the efficacy of an individualized, coordinated, multimodal approach and emphasizes the importance of innovative strategies for inoperable tumors.
The patient provided written informed consent for the publication of this case, including clinical data and associated images. The authors declare no conflicts of interest.

Consent and Conflicts of Interest:
Written informed consent was obtained from the patient for publication of this case report.
The authors declare that they have no conflicts of interest related to this study.

Tables:

Table 1: Therapeutic Scheme

Phase	Treatment	Dose / Cycle	Frequency	Number of Cycles	Objective
Induction Chemotherapy	Paclitaxel	80 mg/m²	Weekly	12	Tumor reduction
Induction Chemotherapy	Carboplatin	AUC 2	Weekly	12	Tumor reduction
Concomitant Chemoradiotherapy	IMRT Pelvis	46 Gy	2 Gy/fraction	23	Inclusion of lymph nodes
Concomitant Chemoradiotherapy	Vulvar Tumor 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	Clinical Findings	MRI	PET-CT	Comments
Initial	5–6 cm lesion, vaginal induration	7.7 × 5 × 1.85 cm, early involvement of the levator	SUVmax 17	Tumor extension underestimated on clinical examination
6-Month Follow-Up	Ulcero-necrotic mass >15 cm, pain, tenesmus	Extensive left pelvic involvement, abscessed areas, levator infiltration	Significant local and nodal progression	T4N1M0, inoperable
Post-Induction Chemotherapy	Pain improvement, ECOG 1	Major regression of tumor and lymph nodes	SUVmax decreased	Spectacular partial response
Post-Chemoradiotherapy	Nearly normal vulvar anatomy	Resolution of clitoral lesion, regression of vaginal, perineal, and levator involvement	Normalization of vulvar and nodal uptake	Complete response in vulva and lymph nodes

List of Figures and Tables :

Figures

- Figure 1: Axial PET-CT showing initial vulvar involvement.
- Figure 2: Sagittal PET-CT showing initial vulvar involvement.
- Figure 3: PET-CT after disease progression showing T4N1M0 vulvar lesion (sagittal and axial views).
- Figure 4: MRI images after induction chemotherapy showing major tumor regression.
- Figure 5: PET-CT follow-up 3 months after completion of induction chemotherapy and concurrent chemoradiotherapy showing normalization of vulvar and nodal hypermetabolism.

Tables

- Table 1: Therapeutic schema: induction chemotherapy and concurrent chemoradiotherapy (dose, frequency, number of cycles, objective).
- Table 2: Summary of clinical and imaging results at different treatment stages (initial, 6 months later, after induction chemotherapy, and after chemoradiotherapy).

Abbreviations:-

- **VIN:** Vulvar Intraepithelial Neoplasia
- **HPV:** Human Papillomavirus
- **RCP:** Multidisciplinary Tumor Board Meeting
- **ECOG:** Eastern Cooperative Oncology Group
- **IRM:** Magnetic Resonance Imaging (MRI)
- **TEP-TDM:** Positron Emission Tomography – Computed Tomography (PET-CT)

- **SUV:** Standardized Uptake Value
- **IMRT:** Intensity-Modulated Radiation Therapy
- **OS:** Overall Survival
- **PFS:** Progression-Free Survival
- **LVSI:** Lymphovascular Space Invasion

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