

RESEARCH ARTICLE

VULVAR CANCER: RETROSPECTIVE STUDY RELATING TO 11 CASES

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..... Manuscript Info

Abstract

..... Manuscript History Invasivecarcinomaofthevulvaisarareneoplasticdisease, Received: 19 March 2022 representing5% of gynecological cancers. It occurs most often in Final Accepted: 25 April 2022 elderlywomen. Published: May 2022 Theobjectiveofthisworkwastoevaluatetheepidemiological, clinical. histological and the rapeutic profile of a series of patients with vulvar cancer. Thiswasaretrospectiveanalyticalstudy of a series of 11 patients treated for gynecological vulvar cancer in the obstetrics CHU MohammedVIdepartment in Oujdaduringthe period fromSeptember 2014 to July2022. The average age of the patients was 62 years (range 51-78 years), 82% of patients were multiparous. The averaged elayof consultation was8months, morethan 6 monthsin 60 %. Clinicalsymptomatologywasdominated by the perception of a vulvartumor patients 90,9%,less frequentlypain, by in pruritus.Theulcerous-buddingformsrepresent 54.54% of the cases. And multifocal involvement is themost frequent. The vulvar biopsy was performed in 100% of the cases and concluded to a squamouscell carcinoma in 72,72% of the cases. Assessment of extension revealed a second localization inonepatient. Eight of our patients benefited from total vulvectomysurgerywithbilateralinguinallymphnodedissection.Postsurgical complications are dominated by lymphoedemain fection, suture relea se.Radiotherapyand chemotherapyareothertherapeuticmodels. The prognosis depends on several factors; it is all the better as the tumorissmall and the ganglia arenot invaded.Earlydiagnosis and the adequate management of precancerouslesionshelps to improve heprognosis.

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Introduction:-

Vulvar cancer is an uncommon pathology, which represents 5 % of gynecological cancer.¹It affects usually menopausal women with a middle age between 65-70 years, on the ground of hypoestrogenia and chronic dystrophy². The diagnosis is most often made at an advanced stage by histological examination of a vulvar biopsy. The histological subtype is a squamous cell carcinoma in 90% of cases. The presence of papillomavirus (HPV) and smoking are strongly implicated in the pathogenesis of this neoplasia. Pruritus, swelling vulvar visible or palpable are often the main revealer signs. Generally, patients consult late due to negligence or ignorance. The treatment of vulvar cancer is mainly surgical, it is based on the realization of a total vulvectomy with bilateral inguino-femoral lymph node dissection, this heavy surgical procedure is associated with significant physical and psychological morbidity, from where the interest of conservative therapy. The interest of our retrospective study, relating to 11

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cases of vulvar cancer treated within the department of Obstetrics and Gynecology Mohammed VI University Hospital Center, Oujda, Morocco over a period of 8 years from September 2014 to July 2022 is to report the epidemiology, clinic, therapy, and prognosis in order to discuss them with the help of other scientific works and to draw a conclusion for a better approach therapeutic protocols.

Materials and Methods:-

Our retrospective study, relating to 11 cases of vulvar cancer treated within the department of Obstetrics and Gynecology Mohammed VI University Hospital Center, Oujda, Morocco over a period of 8 years from September 2014 to July 2022. We analyzed our data based on the literature, concerning the epidemiological, clinical and therapeutic aspects of vulvar tumors. An exploitation sheet produced for this purpose allowed the collection of the following data: epidemiological data: age, parity, history, pre-existing lesions, clinical data, data macroscopic and histological anatomo-pathological, therapeutic data and evolutionary data. Results: The extreme ages of our patients were between 51 and 78 years old, and the average age of the patients being 62 years old. In our series, 82% of patients were multiparous while 18% were pauciparous. In our series 11 patients are menopausal or 100%, with an average age of menopause of 55 years. In our series, 2 patients were followed for cancer of the gynecological sphere, of which 29%. A patient was followed for colon cancer. In our series, diabetes was noted in 2 patients, arterial hypertension in a single patient, and a case of thrombophlebitis of both lower limbs. In our series, the most common warning sign is the perception of vulvar swelling by patients, it is observed in 90.9% of cases (10 patients), in our study, patients consult less frequently for pain, vulvar pruritus and bleeding. The diagnostic delay greater than 6 months in 60% of cases. In our study, ulcero-budding tumors were the most frequent forms, since they represented 54.54% followed by other budding 36.36% and ulcerated (9.09%) forms. In our study, multifocal localization is the most frequent. It associates damage to the clitoris, labia minora and labia majora in 36.36% of cases. The uni-focal localization is less frequent in our study represented by the damage of the labia minora in 9.09%. The sizes of the lesions vary between 4 cm and 8 cm with an average size of 6 cm. In our series, we noted 03 cases of invasion of the urethral meatus, one case of extension to the vagina and one case of extension to the anus. On clinical examination, the perception of lymphadenopathy was noted in 6 patients (54.54%), in 4 patients the involvement is bilateral and in two patients the involvement is unilateral. The nodal areas were free in 5 patients (45.45%). At the general examination, 63.63% of the cases of our patients (7 patients) had a preserved general state. The speculum examination was difficult to perform in 5 patients due to the presence of painful ulcero-budding lesions. The cervix pap smear was performed in 6 patients (54.54%).

All our patients benefited from a systematic vulvar biopsy, which confirmed the diagnosis.Squamous cell carcinoma is found in 72.72% of cases, a single case of vulvar Bowen's disease 9.09% and 2 cases of vertucous carcinoma with a percentage of 18.18%.All the patients benefited from a Thoraco-abdomino-pelvic scanner, it revealed a mass of the root of the thigh, a tumoral thrombosis of the lower limb in one patient, an extension to the vagina over its entire length to the bladder and the anal canal in another patient, the others without secondary localizations. Pelvic MRI was performed in 3 patients (27.27%).

In our series, we noted the predominance of the T2 form in 08 patients (72.72%), the T3 form is present in 2 patients (18.18%), while the T1 form was absent. The analysis of lymph node status shows a predominance of N1 status in 6 patients (54.54%). While the N0 state is found in 5 patients (45.46%).No cases of metastasis. In our study, we adopted the classification (F.I.G.O.) and it was noted that 6 patients had stage II, 54.54% of cases, 3 patients had stage III, 27.27% of cases, and 2 patients had stage IV, 18.18% of cases, while stage I was absent. Surgical treatment was the mode of treatment used in most of our patients since it was performed in 8 patients (72.72%, while two patients 18.18% received palliative treatment at an advanced stage of the disease and one patient refused therapeutic treatment. 3/11 patients benefited from adjuvant radiotherapy. 1 patient benefited in addition to radiotherapy from 5 sessions of carboplatin.

The complications that were found in our series were one case of suture release in an infectious context was noted in a patient and two cases of pain in the vulvar region, one case of recurrence was observed in a patient one year after stopping adjuvant treatment, 3 patients died: 1 patient related to the refusal of care and the two others after palliative treatment related to the advanced stage of the disease.

Discussion:-

Vulvar cancer is a rare gynecological disease ³. Its incidence is estimated between 1 and 2 per 100,000 women per year^{1, 2}. As for the prevalence, it represents approximately between 3-5% of cancers developed on the female genitalia.^{1, 2}, it mainly affects postmenopausal women, aged over 65 with a peak in the incidence curve between 60 and 70 years of age⁴. In our study, the extreme ages of our patients were 51 and 78 years old, and the average age of the patients being 62 years old. Our results are therefore similar to those of the literature.

With regard to reproductive life, the risk of vulvar cancer is increased with multiparity. In our series, 82% of our patients were multiparous. Estrogen deficiency plays an important role in the genesis of vulvar cancer. It occurs long after the menopause, also with greater frequency in women who have had a reduced estrogen impregnation. In 1984 R. Erny and collaborators specify that it is a cancer which develops in a context of hypo-estrogenism (early menopause and/or surgical castration) which would be responsible for the dryness of the vagina, the rarefaction of the mucus, atrophy of the labia minora and the frequency of infectious, fungal or parasitic vaginitis. Thus scratching is the cause of erosions of the mucous membranes, superinfections and leukoplakia that are real lesions on which the cancer will be grafted⁵.Robert⁶ describes that more than 90% of women are postmenopausal, and the small percentage of premenopausal women show clinical signs of hypoestrogenism (atrophy of the labia minora, dry vagina, and scanty cervical mucus). In our series, 100% of patients are postmenopausal.

A deficient terrain is found in vulvar cancer in variable proportions for most authors. Obesity, diabetes and hypertension are frequently encountered in patients with vulvar cancer ^{7, 8, 9}. In our series, diabetes was noted in 2 patients, and arterial hypertension (AH) in a single patient, a case of thrombophlebitis of both lower limbs.

| Authors | Obesity(%) | AH(%) | Diabetes(%) |
|-------------------------|-------------|-------|-------------|
| Ouguerri ¹⁰ | 15,18 | 18,75 | 6,25 |
| Lakhdar ¹¹ | Not studied | 23,07 | 23,07 |
| Belghmi ¹³ | 12,5 | 18,75 | 14,06 |
| Aboulfath ¹⁴ | Not studied | 18,18 | 9,1 |
| Lansac ¹² | 2,22 | 14,44 | 14,44 |
| Bennani ¹⁵ | Not studied | 23,08 | 7,69 |
| Our series | Not studied | 9,09 | 18,18 |

Table1:- The frequency of medical history in patients according to the authors.

HPV infection of the female lower genital tract appears to favor the development of certain precancerous and cancerous lesions of the cervix, vagina and vulva. Recent studies¹⁶have been done on the epithelium of the vulvar skin and have shown that there are changes in the expression of the P53 protein, which may precede the appearance of intraepithelial carcinomas of the vulva, this has led to the suggestion that P53 mutations may be an early event in the genesis of vulvar carcinoma.Dynes¹⁷ reports that more than 50% of P53 protein mutations are found in vulvar cancers, and that genital HPV infection increases the risk of the occurrence of P53 mutations.In our series, one patient presented an HPV infection confirmed by anatomopathological examination.

Dystrophic lesions are varied vulvar conditions, the most common of which is lichen sclerosus, with malignant potential with a cancerization rate estimated at 5%, In 80% of cases, it is manifested by chronic vulvar pruritus with or without orificial dyspareunia or cracks during intercourse. Vulvar biopsy should be performed to confirm the diagnosis and on all suspicious lesions that do not regress under treatment, regardless of leukoplakia, erosive or ulcerated lesions.

Vulvar intraepithelial neoplasias constitute a precancerous state; their definition is purely anatomopathologic, a disorganization of the architecture, a hyperchromasia of the parabasal cells, a pleomorphism and abnormal mitoses. 3 types of vulvar intraepithelial neoplasia (VIN) are characterized, differentiated non-HPV induced VIN and are usually associated with lichen sclerosis, classic VIN which are subdivided by some authors into two entities, classic basaloid VIN which are often well limited single lesions, affecting older women and condylomatous classic VIN willingly multifocal, affecting young women smokers, and finally Bowen's disease vulvar which mainly affects women over 50, postmenopausal, the revealing signs are essentially vulvar pruritus.

The majority of studies reported in the literature indicate that pruritus is the most frequently found revealing symptom (in 70%)¹⁸. Vulvar pruritus is found in 81.25% by Belghmi¹³, in 75% by Ouguerri¹⁰ and in 76.92% in the Lakhdar¹¹series. It was found in our series in 63.63% of cases. This pruritus is characterized by its intensity, its chronicity and its resistance to any symptomatic treatment. The perception of a tumor is an equally frequent symptom which can be budding, ulcero-budding, ulcerated and/or bleeding. It is found by Belghmi¹³ in 75% of cases, by Ouguerri¹⁰ in 38.40% of cases, and by Lakhdar¹¹ in 92.3% of cases.In our series, it was found quite frequently, it was noted in 90.9% of cases.vulvar pain can be found and represents 27.27% of cases in our study.

| Authors | Pruritus(%) | Tumor(%) | Bleeding(%) | Pain(%) | Inguinal |
|-------------------------|-------------|----------|-------------|---------|------------|
| | | | | | adenopathy |
| Ouguerri ¹⁰ | 75 | 38,4 | 13,4 | 20,54 | 2,68 |
| Belghemi ¹³ | 21 | 75 | 28,12 | 32,35 | 7,8 |
| Body ¹² | 20 | 49 | 12 ,2 | 14,4 | 1,1 |
| Lakhdar ¹¹ | 76,92 | 92,3 | 7,7 | 7,7 | 0 |
| Aboulfath ¹⁴ | 100 | 100 | 18,8 | 45,45 | 54,54 |
| Bennani ¹⁵ | 84,26 | 92,3 | 0 | 23,07 | 0 |
| OurSeries | 63,63 | 90,9 | 9,09 | 27,27 | 9,09 |

Table 2:- Distribution according to the signs of calls according to the authors.

Budding and ulcero-budding tumors are the anatomoclinical forms most frequently encountered in vulvar cancer and are generally accompanied by more or less deep infiltration. Although any part of the vulva may be involved, for some authors the elective seat of the lesions is represented by the clitoris or the labia majora^{1, 2}. In most series, the budding ulcer form is the most frequent. This is the case even in our series. In our study, multifocal localization is the most frequent. It associates damage to the clitoris, labia majora and labia minora in 36.36% of patients. Followed by involvement of the small right lip in 9.09% of cases. In Abdi's series¹⁹, the multifocal localization also predominates, it associates the involvement of the labia majora, labia minora and clitoris in 57.1% of cases.



Figure 1:- Budding ulcerative tumor of the vulva.

Speculum examination and cervical-vaginal smears should rule out associated cervical neoplasia. Pelvic touches are systematic: the vaginal examination checks the state of the internal genitalia, and rectal examination with a detailed

examination of the anal region, looking for condylomatous lesions and/or invasion of the rectum and the rectovaginal septum.

Examination of lymph node areas look for pelvic lymphadenopathy. Invasive vulvar cancer is a slow growing and essentially locoregional disease. It has two common modes of metastasis: migration of emboli through the lymphatic system to regional lymph nodes and by contiguity to neighboring tissues and organs²⁰.

The vulvar biopsy remains the key examination which provides the histological diagnosis of certainty and which must be carried out at the slightest doubt on a vulvar lesion, and must be done at the level of clinically suspicious areas, and avoid necrotic areas to be interpretable, cancer squamous cell represents more than 90% of vulvar cancers, the remaining 10% include a wide variety of tumors ranging from basal cell carcinoma to secondary vulvar tumors.³⁴ In our series, squamous cell carcinoma is found in 72.72% of cases and is characterized by the multiplicity of its variants, a single case of carcinoma in situ (Bowen's disease) and verrucous carcinoma with a percentage of 18.18%. For the other series, squamous cell carcinoma is found in more than 90% of cases.

Concerning the extension assessment, the chest X-ray is practiced in a systematic way in search of an associated pathology; an operative contraindication or a thoraco-pulmonary metastasis. Abdominal ultrasound, on the other hand, makes it possible to study the deep lymph nodes and pelvic organs as well as the liver, bile ducts and kidneys ²²; a skeleton x-ray is indicated in the event of suspicion of bone metastases. The thoraco-abdominal-pelvic CT scan can be used to search for distant metastases. The extension assessment allows the classification of the tumor according to its dimensions and its nodal or metastatic extension. This classification is necessary because it allows the natural history to be traced, the prognosis to be established and the appropriate therapeutic indication to be drawn ²³.

Surgery is considered the cornerstone in the treatment of vulvar cancers in most cases and consists of total vulvectomy with bilateral inguino-femoral dissection as soon as the depth of invasion exceeds one millimeter on the assumption that radical treatment improves prognosis. The postoperative care is essential to obtain the fastest possible healing ^{21,23}. Patients with vulvar cancer are at high risk of venous thrombosis ²⁴.



Figure 2:- Total Vulvectomy.

Radiotherapy is indicated in case of positive edges or margins < 8 mm and in the absence of possibility of revision surgery, in the event of emboli or infiltration in depth > 5 mm, or If positive lymphadenectomy regardless of the number of N+ or in the absence of cleaning; concomitant potentiation chemotherapy discuss based on risk factors

and comorbidities. When due to age, general condition or the extent of the lesion, a curative treatment cannot be applied, it is then necessary to rely on the choice of a palliative therapy, which can be decided according to the extent of the lesion, the site and the side effects metastasis, the necrotic nature of the lesion or its complications 20 . Survival according to stages and lymph node involvement and the prognosis depends on several factors, age, size and location of the tumor, the type histology of the lesion and the degree of differentiation and the histological status of the lymph nodes 20 .

Monitoring of treated invasive lesions should include a clinical examination of the vulva and perineum every 4 month the first year, every 6 months for 2 years, every year thereafter. The risk of recurrence becomes low after 5 years, but second localizations are always possible given the persistence of etiological factors. Examination of lymph node areas possibly supplemented by ultrasound and fine needle aspiration in case of doubt. A regular complete gynecological examination with smear screening.

Conclusion:-

Vulvar cancer is a rare neoplastic condition. Currently, interest has focused on the role of HPV in the genesis of vulvar cancer. The time to diagnosis issually long. Hence, the importance of not neglecting all symptoms and vulvar lesions, and the needof a well-done and complete gynecological examination and he does not hesitate to have recourse to the vulvar biopsy, which provides definitive diagnosis treatment is primarily surgical vulvectomy with lymphadenectomies inguinales are part of the treatment of invasive carcinomas. The morbidity of this inguino vulvar surgery is important and sometimes leaves lasting and disabling sequels. Prevention of vulvar cancer by early detection of risk groups and precancerous lesions remains the best way to fight against this illness.

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