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CASE REPORT

Squamous Cell Carcinoma Bartholin's Gland: Management Challenges: Case Report and Review of Literature

Pallavi Verma[1], Sushil Chawla[2], Sandhyarani[3], Sunil Anand[4], Rahul Mahajan[5], Divya Shelly[6]

[1]Associate Professor, Obstetrics and Gynecology (Gynaecologic Oncology), INHS Asvini Mumbai, India. [2]Professor and Head of department, Obstetrics and Gynaecology, INHS Asvini Mumbai, India. [3]Postgraduate Resident, Obstetrics and Gynecology, INHS Asvini Mumbai, India. [4]Associate Professor, Reconstructive surgery, INHS Asvini Mumbai, India. [5]Associate Professor, Obstetrics and Gynaecology, INHS Asvini Mumbai, India. [6]Professor, Pathology, INHS Asvini Mumbai, India.

Abstract

Bartholin gland carcinoma is an unusual malignancy, accounting for less than 5% of all vulval cancers. Squamous cell carcinoma is the most common histological type, followed by adenocarcinoma. Bartholin's gland carcinomas develop into masses of varying sizes and may be ulcerated or deep to the surface with the overlying skin intact. Because little is known about bartholin's gland cancer, it is frequently misdiagnosed as an abscess or a cyst. Diagnosis is often delayed until discovered at advanced stages. To add to the literature, we report a case of locally advanced stage bartholin's gland carcinoma in a postmenopausal lady, who is managed with radical partial vulvectomy with bilateral inguinofemoral lymphadenectomy with vulvar-vaginal reconstruction by gracilis myocutaneous flap followed by adjuvant concurrent chemoradiation. We aim to create awareness among clinicians and provide new insights for the diagnosis and treatment of this rare malignancy.

Keywords: Bartholin's gland carcinoma- Squamous cell carcinoma- Human Papilloma Virus

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Introduction

Bartholin's gland carcinomas are primary vulvar carcinomas, accounting for less than 1% of female genital tract malignancies and less than 5% of vulvar neoplasms [1]. Bartholin's gland carcinoma typically occurs in middle-aged to elderly women. Bartholin's gland carcinomas are most commonly squamous cell carcinomas or adenocarcinomas; occasionally adenoid cystic carcinomas, adenosquamous, and transitional cell carcinoma may develop [2]. We reported a case of Human Papilloma Virus (HPV) associated squamous cell carcinoma bartholin's gland, hoping to provide insight to avoid misdiagnosis and the need for vigilance for timely management among clinicians. We present this case in accordance with the CARE guidelines (available at https://www.care-statement.org/checklist).

Case Presentation

A post-menopausal P2L2A1 lady in her late 50s, without any co-morbidities, presented with a history of swelling over the vulva for 1 year at our tertiary care centre. She had complaints of off and on pain and bleeding at the site of swelling for the last 1 month. She had a history of recurrent Bartholin's cyst of the same site, for which she underwent marsupialization twice, 8 years ago in a private hospital.

Clinical findings

On examination, she is Eastern Cooperative Oncology Group (ECOG) Performance Status 1. General and systemic examination was normal. On local examination, 5x3x4cm ulcero-proliferative growth predominantly at the site of left labia minora in the anatomical position of the left Bartholin's gland, extending to lower part of the

Corresponding Author:
Dr. Pallavi Verma
Associate Professor, Obstetrics & Gynecology (Gynaecologic Oncology), INHS Asvini Mumbai, India.
Email: drpallavi4@gmail.com

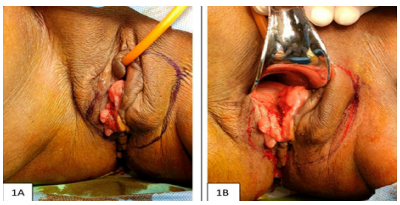

Figure 1. Clinical Picture of Bartholin's Gland Carcinoma Left Side. 1A, 5x3x4cm ulcero-proliferative growth predominantly at the site of left labia minora in the anatomical position of the left Bartholin's gland, with overlying skin of labia majora intact. 1B, Tumor extension to lower part of left postero-lateral vagina, involving posterior fourchette, crossing the midline

left postero-lateral vagina, involving posterior fourchette, crossing the midline (Figure 1). The growth was hard, friable, bleed on touch, fixed with underlying structure but not bone. Urethral meatus, clitoris, and anus were not involved by the lesion. There were no clinically palpable groin nodes. Thorough pelvic examination including cervical examination with Papanicoalou smear was unremarkable.

Diagnostic assessment

A long-standing abscess or malignancy of the Bartholin's gland was one of the differential diagnoses. Nevertheless, the clinical features of the tumor on examination were supportive of malignant pathology. The histopathology of incisional biopsy from the vulvar growth revealed moderately differentiated squamous cell carcinoma likely HPV associated, positive for P16 on immunohistochemistry (Figure 2). Magnetic resonance imaging (MRI) showed a well-defined lobulated mass of 40.3 x 32.36 x 39.9 mm in the left vulvar region, showing intermediate signal intensity on both T2WI and T1WI with restriction of diffusion. The lesion was abutting the lowermost aspect of the vagina with loss of intervening fat planes. Posteriorly it was abutting the anal canal with the preserved interface. The urethra and urinary bladder were not involved. No involvement of pelvic floor muscles or bones was noted. A well-defined enlarged left medial superficial inguinal lymph node (LN) measuring 17 mm with restriction of diffusion was seen. It showed lobulated outlines with loss of fatty hilum. On contrast administration, it showed peripheral rim enhancement with a non-enhancing center. There was no evidence of distant metastases (Figure 3).

Therapeutic intervention

This case was discussed at a multidisciplinary tumor board (MDT) meeting as a locally advanced (stage III) squamous cell carcinoma of Bartholin's gland, and a decision was made to offer primary surgical treatment. The patient and her relatives were explained about the potential need for flap reconstruction or stoma formation as additional procedures, depending upon the extent of resection required to obtain clear surgical margins. Consent for surgery was taken, and the need for postoperative adjuvant chemoradiotherapy was explained.

Radical partial vulvectomy with bilateral inguino-femoral lymphadenectomy with vulvar-vaginal reconstruction by gracilis myocutaneous flap was done (Figure 4). Intra-operatively, on the right side, multiple superficial and deep inguinofemoral groups of lymph nodes were enlarged, the largest superficial inguinal LN 1x2 cm, on the left side; the largest deep inguinofemoral LN 2x1.5 cm, necrotic on the right side was removed. Most of the Left labia majora, minora, a part of right labia majora and minora, posterior fourchette, and the lower 3-4 cm of the vagina were sacrificed. Clitoris and Urethral meatus were spared. Vulvar and upper vagina reconstruction was done of gracilis myocutaneous flap. The post-op period was uneventful.

Follow-up and outcomes

Post-op histopathology report showed moderately differentiated squamous cell carcinoma, HPV associated of bartholin's gland vulva with ipsilateral inguinal lymph node metastasis, tumor deposit >5 mm with extranodal metastasis pT1bN2cMx/ FIGO stage IIIC. The patient was further given adjuvant chemoradiotherapy. She reported for follow-up 3 months after surgery. Careful history and clinical examination showed no evidence of recurrent tumour, in either the groin or the pelvis. A CT scan performed 3 months after treatment showed no evidence of disease other than postoperative changes related to the resection and myocutaneous flap. She will undergo follow-up in our clinic approximately every 3 months for 2 years, then every 6 months for the next 3 years, and annually thereafter.

Discussion

Primary Bartholin's gland carcinoma is a rare type of gynecologic tumor that accounts for 2-7% of all vulvar cancers [3]. Because Bartholin's glands typically shrink

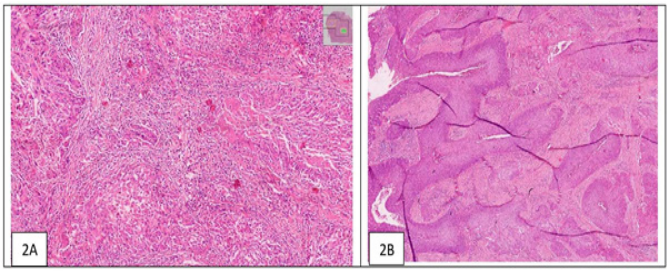

Figure 2. Histopathological Images of Vulvar Growth Biopsy. 2A, Section from the growth showed infiltrating keratinizing squamous cell carcinoma (H and E, 40x). 2B, The tumor cells show intercellular bridges and individual cell keratinization (H and E, 100x)

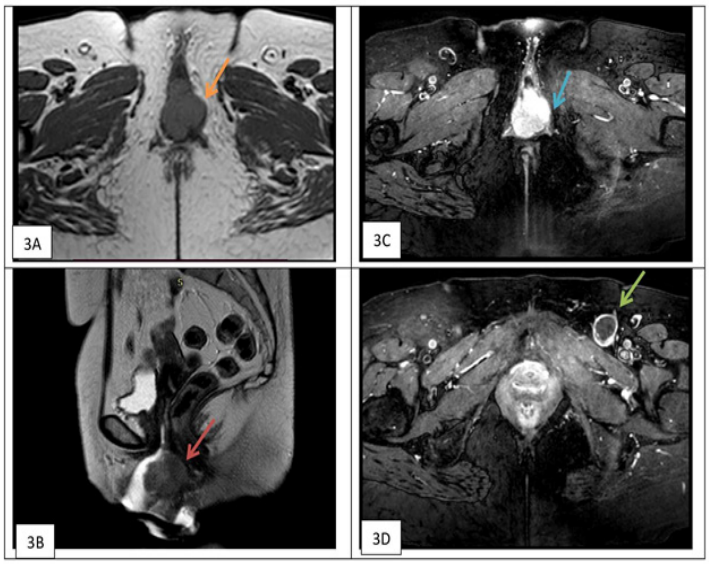

Figure 3. MRI Images of Pelvis and Groin. A, T1W1 axial MRI showing Bartholin's gland tumor with intermediate signal intensity (orange arrow). 3B, T2W1 sagittal MRI showing Bartholin's gland tumor with intermediate signal intensity (red arrow). 3C, T1 post-contrast axial MRI showing Bartholin's gland tumor. 3D, T1 post-contrast axial MRI showing enlarged left medial superficial inguinal lymph node peripheral rim enhancement with non-enhancing center (green arrow)

during menopause, vulvar lesions in older women are more likely to be malignant and must be distinguished from other benign vulvar lesions. This is particularly true in cases where the mass is nodular, solid, irregular, friable, and persistently indurated.

The diagnostic criteria for Bartholin's gland carcinoma were initially described by Honan in 1897, then revised by Chamlian and Taylor to include: (1) The tumor involving the Bartholin's gland area is histologically consistent with the origin from the Bartholin's gland; (2) Histological examination reveals clear transition areas from normal to tumor elements; and (3) No evidence of a primary tumor has been found elsewhere [4]. However, in reality, not all of these criteria are always met. Presentation of primary BGC is usually late as lesions are deep within the vulva and often misdiagnosed as a Bartholin's gland abscess or cyst.

Wang K et al analyzed 6 cases of Bartholin gland carcinoma and found that it accounted for 4.4% of all vulvar malignancies. Patients with Bartholin's gland cancer aged ranging from ranging from 28 to 57 years old, and the tumor size varied from 2 to 5 cm. Squamous cell carcinoma was the most common histology [5]. The association between HPV and carcinogenesis of squamous bartholin's gland carcinoma has now become well established. Most of squamous cell carcinoma bartholin's glands are high-risk Human Papilloma Virus (HPV) associated neoplasm [6]. Bartholin's gland carcinoma is diagnosed as stage I in about 17% of cases, and stage II in about 28% of patients. Stage III, in which the disease has spread to the inguinofemoral lymph nodes, is detected in about 32% of individuals. About 23 percent of patients are detected as stage IV at the time of diagnosis. The 5-year survival rate for patients amenable to primary surgical treatment is 70% to 93% [7].

A retrospective analysis by Bhalwal AB from MD Anderson Cancer Center of 33 (7.7%) cases of primary Bartholin's gland carcinoma among 429 patients with invasive vulvar carcinoma. 29 (87.9%) patients had squamous cell histology and only four (12.1%) had adenocarcinoma. Compared to vulvar cancers not involving the Bartholin glands, patients with primary Bartholin's gland cancers were younger at the time of diagnosis (median 57 years vs. 63 years, p=0.045), had more incidence of stage III/IV disease (60.6% vs. 35.8%, p=0.008), and were higher likelihood of receiving radiotherapy (78.8% vs. 43.9%, p<0.001). Regarding histological subtype, lymphovascular space invasion, perineural invasion, positive margins, disease-free survival, and overall survival, there was no significant difference between the two groups [8].

There is no definite recommendation regarding the best treatment of Bartholin's gland carcinoma, due to limited existing retrospective studies. Information regarding standard treatment is scarce and there is no strict consensus on best practices [9]. Although surgery remains

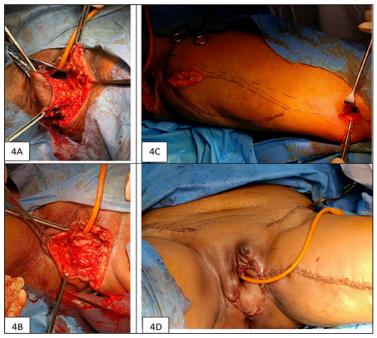

Figure 4. Intra-operative Images. 4A, Radical partial vulvectomy with depth till perineal membrane. 4B, Upper part of vagina excised to achieve negative margins, urethra and clitoris spared. 4C, vulvar-vaginal reconstruction by gracilis myocutaneous flap. 4D, Immediate post-operative image

the cornerstone of treatment, chemoradiation is invariably required especially in advanced stages. Bone and lung are the most common sites of distant recurrence. Lymph node metastasis directly affects the stage of patients. Inguinofemoral lymph node status has a significant impact on patients' survival [10].

In conclusion, primary Bartholin's gland cancer is an unusual form of vulvar cancer. Diagnosis is often delayed due to the lack of specific symptoms and the possibility of being misdiagnosed as a benign Bartholin cyst or abscess. This case report highlights a rare and aggressive malignancy and the importance of being extremely vigilant for Bartholin's gland cancer, especially in older women presented with glandular tumors.

Acknowledgments

Statement of Transparency and Principals

- Author declares no conflict of interest
- Study was approved by Research Ethic Committee of author affiliated Institute.
- Study's data is available upon a reasonable request.
- All authors have contributed to implementation of this research.

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