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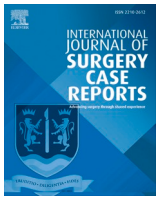

Case report

A perianal conundrum and its management: Condyloma versus carcinoma

Rithvik Govindaraj [a], Shrenik Govindaraj [b,*]

[a] Department of Dermatology, St. John's Medical College & Hospital (SJMCH), Bangaluru, Karnataka, India
[b] Department of General Surgery & Division of MAS, St. John's Medical College Hospital (SJMCH), Bengaluru, Karnataka, India

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ABSTRACT

Introduction: Giant condyloma acuminatum is an uncommon sexually transmitted disease. It also goes by the name Buschke–Löwenstein tumor and develops in immunocompromised patients in the anogenital area [1]. It is caused by human papillomavirus infection, subtypes 6 and 11 [2]. It grows rapidly with the destruction of local tissues, and often recurs [3]. Giant condyloma acuminatum can mimic squamous cell carcinoma. The work has been reported in line with SCARE criteria [4].

Presentation of case: A 44-year-old gentleman had presented with an insidious growing painless mass in the perianal region with anal canal invasion of 2 years duration. Over the last 3 months, it was associated with a rapid increase in size along with an ulcer and bleeding. He was a renal transplant recipient, on immunosuppressive therapy. The dermatologist had referred him to the surgeon with a concern of malignancy. He underwent examination under anesthesia and an incisional biopsy. The pathologist reported it as condyloma acuminata. The dermatologist had tried a few sessions of cryotherapy without success and the fear of malignancy was still lurking. He underwent wide local excision of the tumor and reconstruction of the anocutaneous junction with an advancement flap. The pathologist had reported the lesion as a large verrucous lesion consistent with condyloma acuminata. Short-term follow-up showed good continence of the anal canal and no recurrence.

Conclusion: Giant condyloma acuminatum can mimic squamous cell carcinoma. So when in doubt and conservative treatment fails, surgical excision is a good option both for treatment and pathological confirmation.

1. Introduction

Giant condyloma acuminatum or Buschke-Lowenstein tumor (GBLT) is an uncommon sexually transmitted disease with an incidence of 0.1 % and generally seen in the 3rd or 4th decade with a slight male preponderance. It was first described by Buschke and Lowenstein in 1925. It commonly develops in immunocompromised patients in the anogenital area [1], but lifestyle and sexual practices play a part in their distribution, incidence and etiology. It is caused by human papillomavirus infection (HPV), subtypes 6 and 11 [2]. It grows rapidly with the destruction of local tissues and often recurs after treatment [3]. Giant condyloma acuminatum can mimic a squamous cell carcinoma and in some cases transform into one especially when HPV subtypes 16 and 18 are involved. Multiple treatment options are available and surgical treatment has a very high cure rate. Education regarding safe sex practices and vaccination should help in its prevention. Our case highlights most of these facts and was managed successfully in a tertiary care center involving a multidisciplinary team of dermatologists, surgeons, dermatopathologists, and plastic surgeons. The work has been reported in line with SCARE criteria [4].

2. Presentation of case

A 44-year-old gentleman had presented with an insidious growing painless mass in the perianal region of 2 years duration (Fig. 1). Over the last 3 months, it was associated with a rapid increase in size, pain, bleeding, and foul-smelling discharge during defecation, sometimes with fecal soiling, and obstruction. He was a renal transplant recipient, on immunosuppressive therapy with tacrolimus and mycophenolate, and had undergone a mesh hernioplasty for an inguinal hernia a few years before the transplant. The dermatologist had referred him to the surgeon with a concern of malignancy. Per rectal examination revealed a large 1518 cm ulceroproliferative lesion in the perianal region extending to 1.5 cm into the anal canal (Fig. 1). No active bleeding or pus discharge was noticed. The anal sphincter tone was normal. We also noticed three discrete, painless, firm but enlarged inguinal lymph nodes. Blood tests

Abbreviations: HPV, human papillomavirus; CD, condyloma acuminata; STD, sexually transmitted disease; WLE, wide local excision.

* Corresponding author.
E-mail address: shrenikgovindaraj@gmail.com (S. Govindaraj).

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were within normal limits, and an enzyme-linked immunosorbent assay (ELISA) for human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HbsAg) were negative. The patient underwent examination under anesthesia (EUA) and an incisional biopsy of the lesion. The pathologist had reported it as condyloma acuminata (CA) (Fig. 2). Following this, the dermatologist tried a few sessions of cryotherapy without success and the fear of malignancy was still lurking, so referred back to us. A repeat examination demonstrated the same findings as before but a significant interval increase in size with ulceration. A basic blood workup was repeated, which was normal. He underwent a flexible sigmoidoscopy which showed a normal mucosa but a verrucous perianal lesion and an MRI pelvis which showed a large exophytic verrucous mass epicentred in the perianal region involving the anal verge and sphincter complex (Fig. 3). The patient was placed in a lithotomy position after spinal anesthesia, the urinary bladder was catheterized, and parts were painted appropriately. He underwent an extensive wide local excision (WLE) of the lesion and reconstruction of the anocutaneous junction with a local skin advancement flap by the colorectal surgeon (Fig. 4). The pathologist studied multiple sections and again reported the lesion as a simple large verrucous lesion consistent with condyloma acuminata and no evidence of dysplasia (Fig. 5). Short-term follow-up shows good continence of the anal canal and no recurrence. We have strongly advised him for a long-term follow-up given the nature of the disease which is known for delayed recurrence.

3. Discussion

Condyloma acuminatum (CA) is a sexually transmitted disease (STD) caused by human papillomavirus (HPV) commonly seen in immunocompromised subjects [1,2], like our patient who was on immunosuppression medications for his renal transplant. Simple CA presents as anogenital warts but GBLT resembles CA but grows into large lesions which compress and displace deeper tissues without infiltration [5]. HPV is a double-stranded DNA virus with various subtypes (>70) and oncogenic potential. Based on their oncogenic potential they could be classified into low-risk (LR) and high-risk (HR). CD is often associated with LR subtypes HPV 6 and 11 [3]. The HR subtypes of HPV 16 and 18 are associated with GBLT and squamous cell carcinoma of the cervix and anogenital region [6]. The average age of infection is the mid-20 to 30s and there is an equal distribution between sexes but depends on the age and pattern of sexual activity. Being sexually transmitted other infections like HIV, HCV, HBV, and syphilis are often seen in these patients. HPV infection is transmitted through direct contact and minimal trauma. Once they enter the keratinocyte, the life cycle of HPV is closely linked to the differentiation of the host cell. HPV triggers genes related to cell multiplication, apoptosis, and cytokeratin intermediate filaments in the host cells. HPV E4 gene expression is seen in the parabasal layers of squamous epithelium, which infers that the E4 gene product contributes to the mechanism of differentiation-dependent replication of the virus. This alters the cytokeratin network which in turn helps the release of the virus into the epidermis. An observation of significance is following the invasion of the keratinocyte, CA could clinically manifest within weeks, months, or years later based on the virus-host interaction and immunity [7]. High-risk strains of HPV directly incorporate its genetic material into the host cell and this results in unregulated activation of E 6 and E7 genes and transcription of oncoproteins and inactivation of p53 and retinoblastoma (Rb) tumor suppressor genes. This results in uncontrolled and unregulated cellular proliferation with subsequent evolution toward tumorigenesis [8,9]. So all GBLTs should be biopsied to rule out malignancy [10].

The clinical manifestation of CA and GBLT is seen around the anogenital region and oral cavity. They may present as flat, warty, pedunculated, cauliflower, or cerebriform-like lesions, they may be white, pink, purple, or reddish-brown. The symptoms are pain, itching, bleeding spontaneously or on contact during intercourse or defecation, and discharge with an odd odor. Patients could also have dysuria and haematuria due to intraurethral lesions [11]. Some patients are worried due to the fear of malignancy especially when they have largely ulcerated, bleeding cauliflower-like lesions, like our patient who was worried because it grew very rapidly in the last 3 months with the above complaints. Giant condyloma acuminata can transform into verrucous

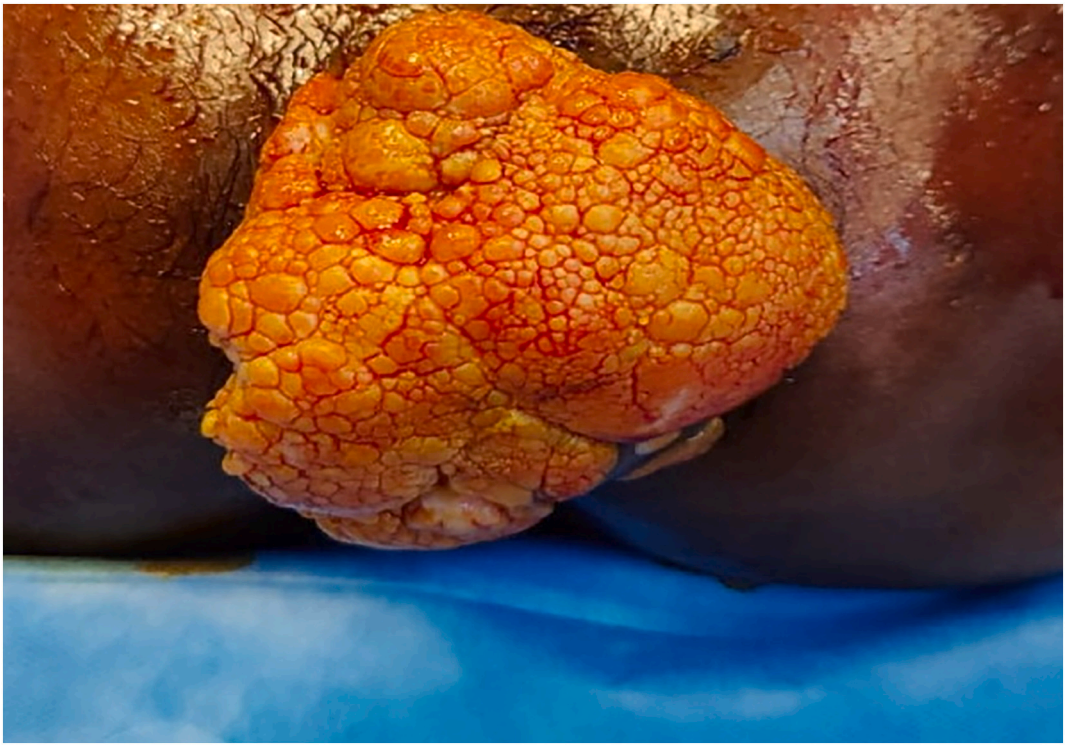

Fig. 1. A large ulceroproliferative lesion in the perianal region.

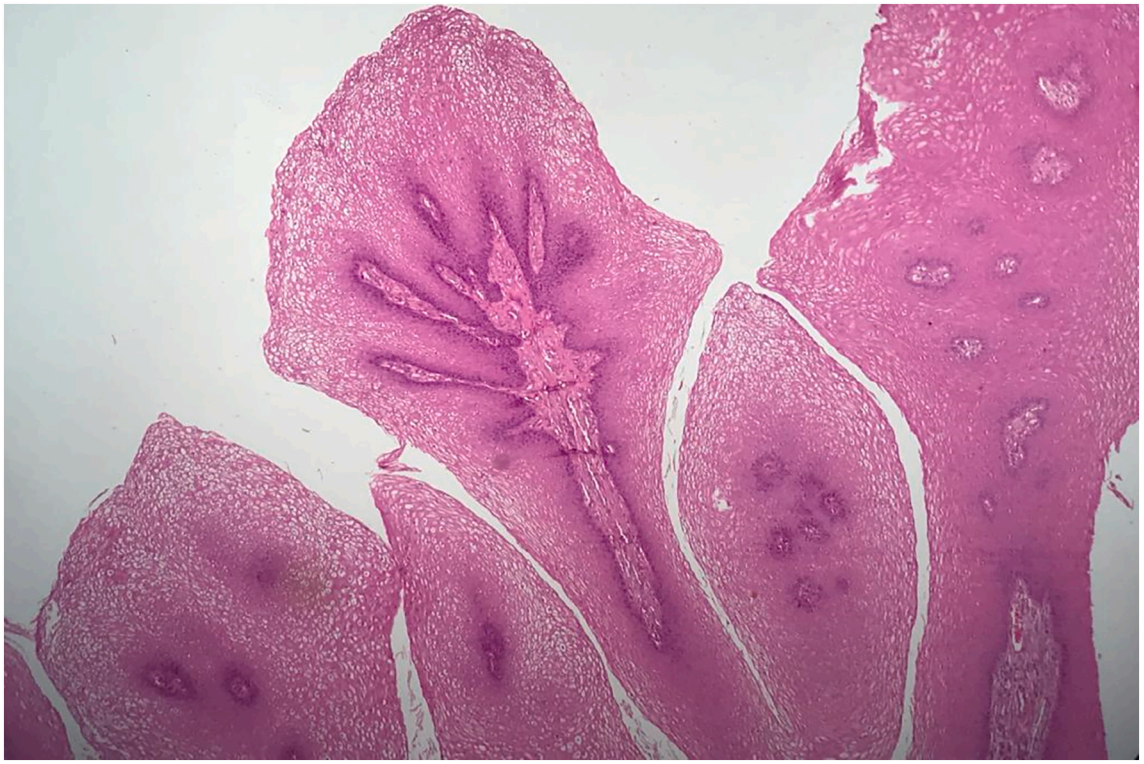

Fig. 2. Pathology showing marked acanthosis, hyperplasia, papillomatosis, and dense lymphocytic infiltration.

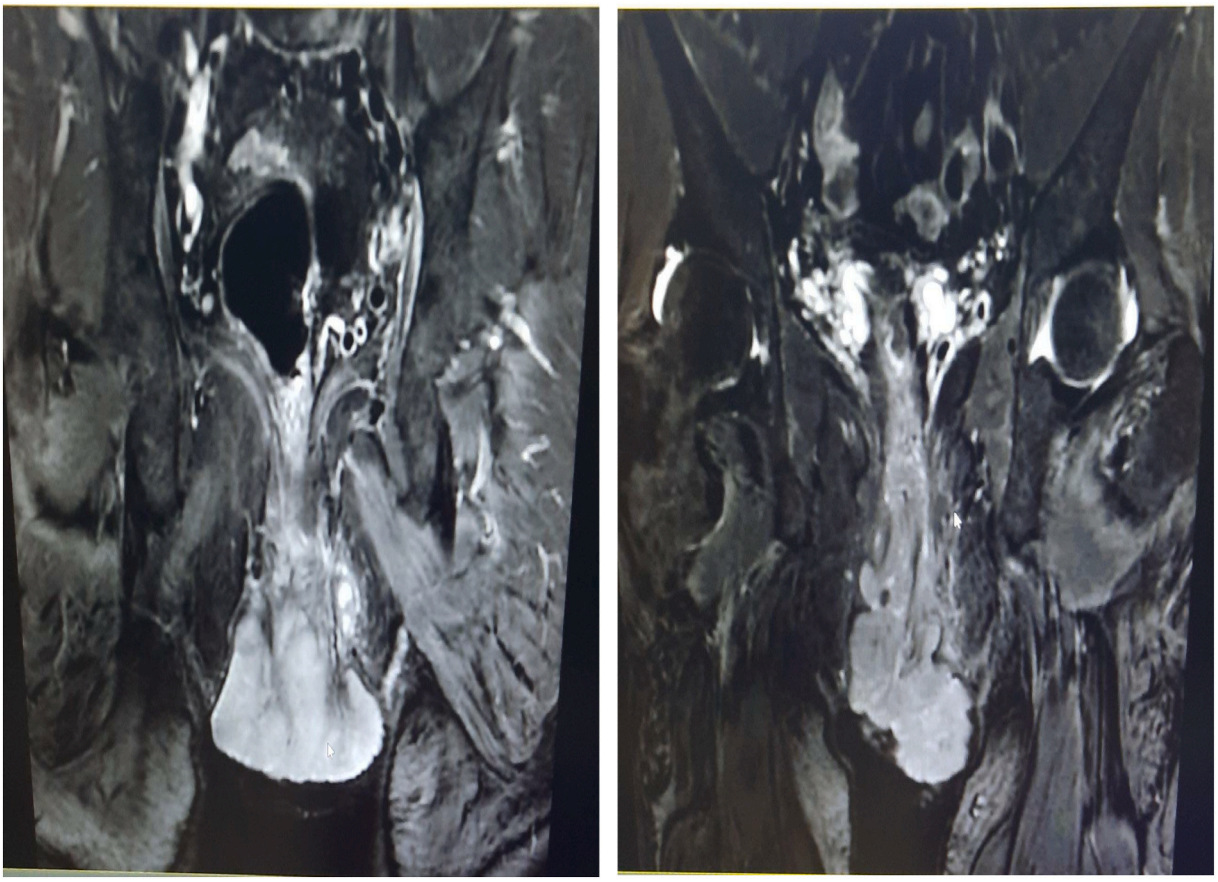

Fig. 3. MRI pelvis showed a large exophytic verrucous lesion on the anal verge.

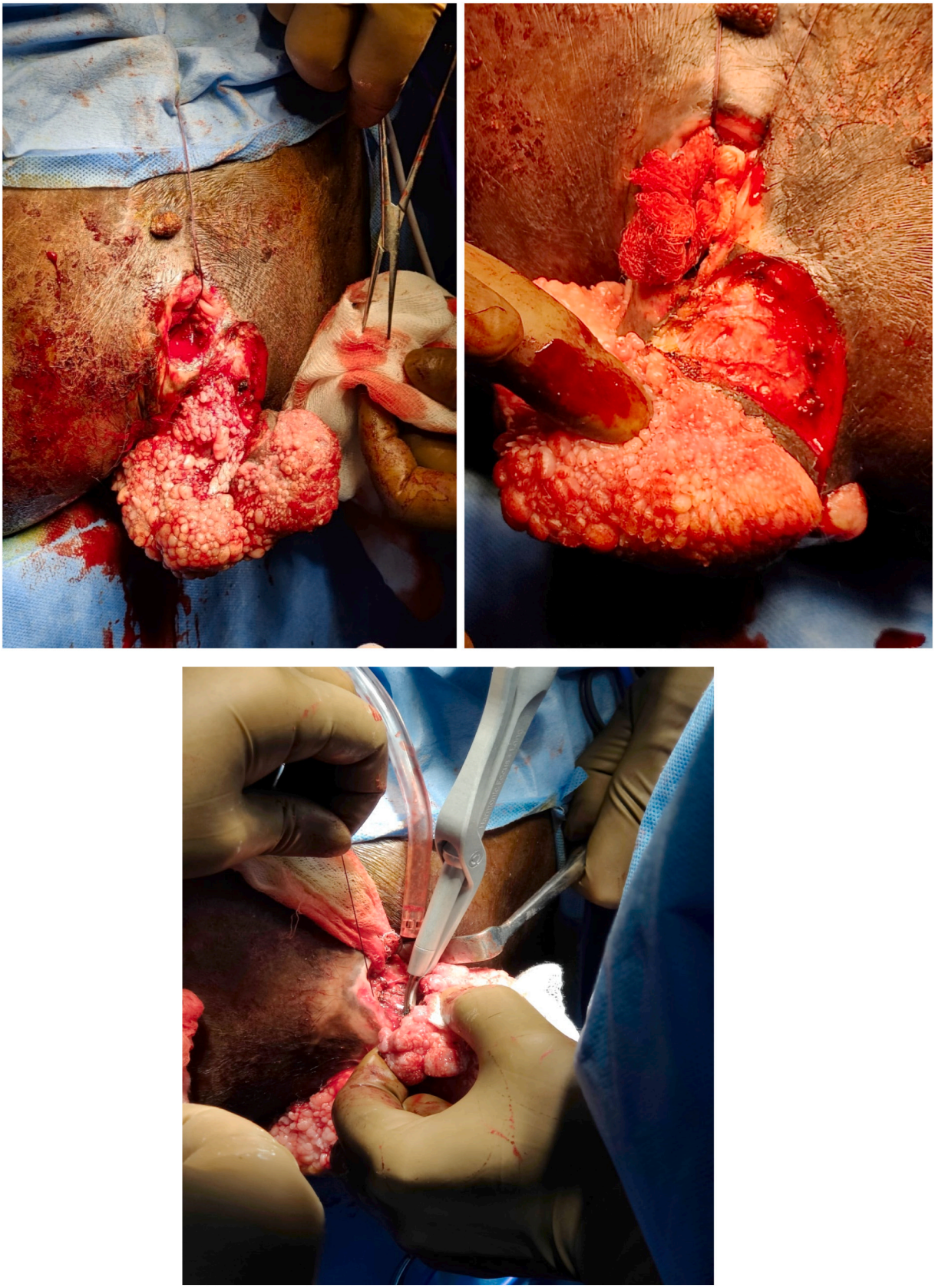

Fig. 4. Intraoperative photographs during wide local excision (WLE) surgery.

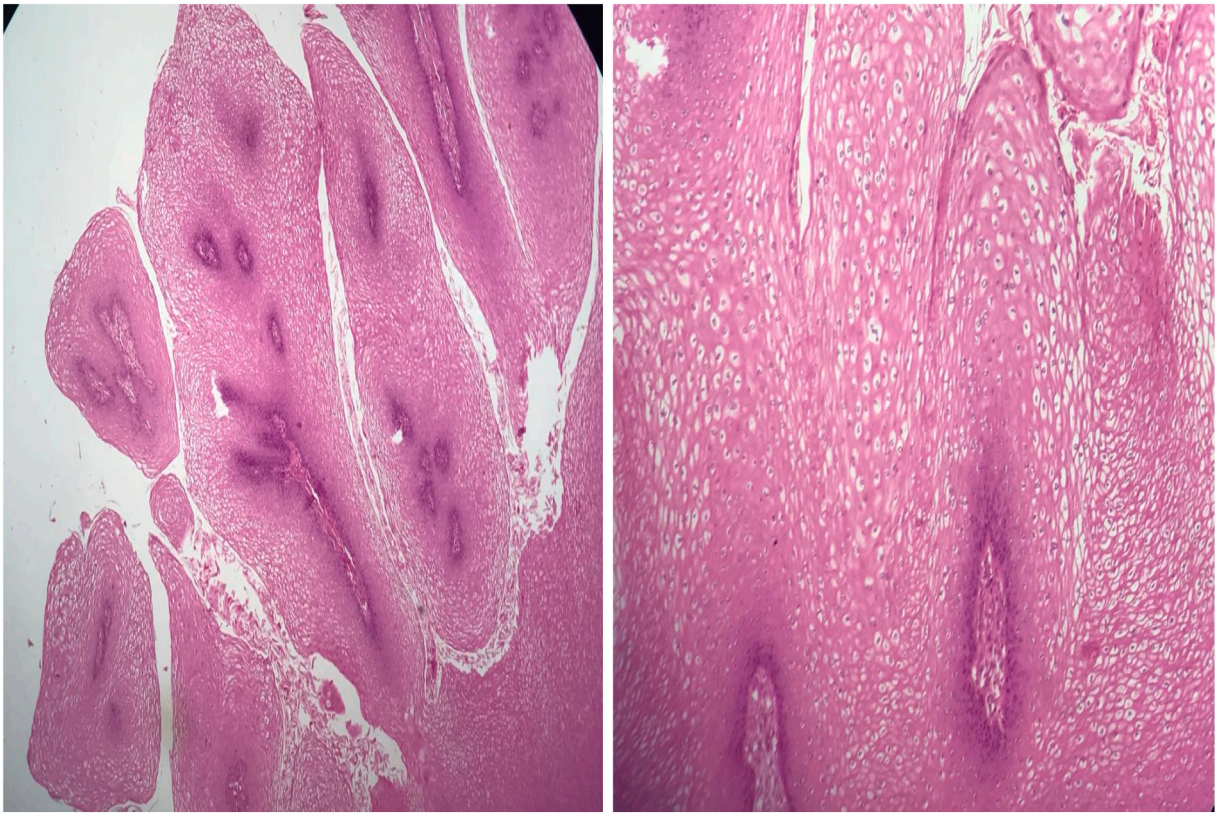

Fig. 5. The epidermis shows marked acanthosis with papillomatosis and koilocytic changes but no atypia. The dermis shows fibrosis with dense lymphocytic infiltration.

carcinoma which is locally invasive but rarely metastasize [12]. Based on the location, they are called oral papillomatosis when they occur in the oral cavity, giant condyloma acuminata of Buschke and Lowenstein in the anogenital region, and carcinoma cuniculatum when seen in the palmoplantar region [13]. The clinical diagnosis is made based on the morphology of the lesion, but a biopsy of the lesion for histopathology is important to differentiate a benign GBLT from malignancy, especially when the lesion ulcerates and bleeds or doesn't respond to the usual standardized nonsurgical therapy. When the pathology is associated with marked atypia or uncertainty exists in routine H&E staining, immunohistochemistry (IHC) will help [14]. The current treatment modalities for CA and benign GBLT are topical application (Podophyllin, 5-FU, Imiquiod, cidofovir), local destruction (cryotherapy, electrocautery, and laser), surgical excision, and systemic treatment with interferon [15]. Most of these treatments are aimed at removing the lesion, not at eradicating the virus. However early surgery in the form of radical or wide local excision (WLE) remains the mainstay of treatment for GBLT [16]. Abdominoperineal resection (APR) with end colostomy, a radical procedure may be indicated in cases when the sphincter is invaded with incontinence, diffuse rectal and lateral pelvic wall invasion, multiple recurrences and malignancy [17]. In our case, we felt it was better to undergo WLE of the lesion with n advancement flap to reconstruct the perianal region. There were multiple reasons for this decision, the sudden rapid growth of the lesion along with ulceration and bleeding, failed initial conservative treatment, more importantly, a fear of hidden malignancy, the lesion confined to the skin and subcutaneous tissue, sphincter function was preserved, and an immunocompromised state. However, the most important factor was the possibility of complete excision of the GBLT. The recurrence rates are quite high at 18 to 67 % (16,17) with significant morbidity. With the proven benefit of Nigro's chemoradiation as a gold standard treatment in squamous cell carcinoma of the anal canal, we could extend this to treat GBLT in the neoadjuvant or adjuvant setting to treat recurrences or extensive pelvic invasive disease or patients not willing for APR and also to reduce local recurrence [18]. External beam radiation alone or as adjuvant to surgery could also be used as salvage therapy to surgery or as a primary modality [19]. In view of the recurrence rate being so high, long-term follow-up is important. Studies have shown a decrease in the incidence of recurrence and also a decrease in the incidence of genital warts in the population vaccinated with the HPV vaccine [20]. So vaccination programs in selected high-risk groups should be strongly recommended.

4. Conclusion

A perianal giant condyloma acuminatum can mimic squamous cell carcinoma. So when in doubt surgical excision is the best option for pathological confirmation and it also has a high success rate with low recurrence. However, a careful long-term follow-up is required.

Patient consent for publication

Obtained.

Ethical approval

Obtained from institutional ethics committee.

Funding

Not applicable.

Patient perspective

I was satisfied with the treatment and its final outcome. The

counseling sessions by the lead clinician regarding the diagnosis, the need for surgery, and the risk involved with fecal continence were very well explained. This helped me to make an informed decision to undergo surgery. Also, the need for long-term follow-up has been emphasized.

Guarantor

Dr.John Stephen, Professor and Head, Department of Dermatology, St.John's medical College Hospital and Dr.Sridar Gj, Professor & Head, Department of Surgery, St.John's medical college hospital.

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Ethical approval

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Consent

Written patient consent obtained.

Registration of research studies

1. Name of the registry:
2. Unique identifying number or registration ID:
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

CRediT authorship contribution statement

RG (Rithvik Govindaraj): Data acquisition, interpretation and analysis, drafting of the article, final drafting, and approval of the manuscript.

SG (Shrenik Govindaraj): Article design, critical review for intellectual content, final drafting, and approval of the manuscript.

Declaration of competing interest

Not Applicable i.e., N/A.

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