

MEDICAL EDUCATION SERIES

INCYTE

Issue: November 2017 BREAKTHROUGH NEWS FROM CYTECARE CANCER HOSPITALS

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CANCER**

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Dear Doctor,

Welcome to Incyte, the very first edition of Cytecure Cancer Hospitals' newsletter!

Cancer care is an ever-evolving discipline, and hence, the need for continuous discussions, sharing of new information, and knowledge cannot be overstated.

The aim of Incyte is to share breakthrough news of notable cases at Cytecure Hospitals and initiate a sustained conversation regarding cancer care and research.

In this issue, we go in-depth into three cases of special significance. The first is of a premenopausal woman who came in with an ulcerous mass in the left breast, which had been diagnosed as a breast abscess. A detailed diagnosis at Cytecure revealed it to be a first time reported case of skin cancer, syringocystadenocarcinoma papilliferum. A modified radical mastectomy was done to remove the tumour and affected lymph nodes.

Earlier the better is a maxim that's no truer than in the discipline of cancer care. The second case study is a classic case in point, wherein a patient's mandibular gingival cancer was operated and removed. The patient underwent treatment and recovered well without complications.

The third case is concerning the most common type of cancer among men worldwide - prostate cancer. A 70-year-old man was diagnosed with high-risk localised prostate cancer. This case study highlights the role of Image-Guided Radiation (IGRT) Therapy as an effective treatment for prostate cancer.

I hope this first issue of Incyte provides a brief insight into the kind of work that Cytecure Hospital does, and more importantly will act in encouraging discourse about cancer care in India.

Suresh Ramu
Co-founder & CEO

SYRINGOCYSTADENOCARCINOMA PAPILLIFERUM ON THE BREAST: THE FIRST CASE REPORT

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Abstract

Adnexal carcinomas represent only 1%-2% of all skin cancers. Most of the adnexal skin carcinomas are highly malignant and are difficult to diagnose clinically or even histologically. We present the first reported case of syringocystadenocarcinoma papilliferum in the breast, which had infiltrated to the entire left breast. In this case, we performed a modified radical mastectomy with wide skin excision.

Case Presentation

A 37-year-old woman presented to the hospital with an ulcerated mass in the left breast for the past 3 years (see Fig. 1.1). The mass was painful with a foul smelling discharge. The condition had been diagnosed as a breast abscess for a long time; for which she received multiple courses of antibiotics as part of treatment.



Past Medical History

The patient was a premenopausal woman with two children. Her menstrual cycle was irregular. There was no reported personal history of diabetes, hypertension, benign breast disease, hypothyroidism or surgery. Also, there was no significant family history.

General and Systemic Examination

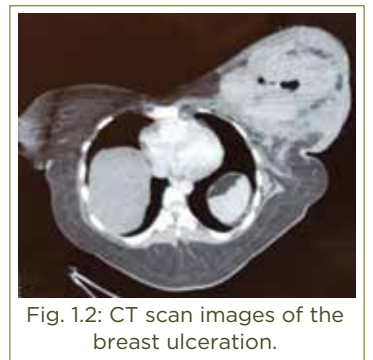
- The patient was moderately built and appeared well nourished. There were no reports of anaemia, jaundice or generalized lymphadenopathy.
- Systemic investigations did not reveal any abnormality. There was no report of organomegaly.

Local Examination

The patient had a large 20x20 cm ulcerated lesion on the left breast, which involved the pectoralis major but not the chest wall. A few nodes were palpable, hard, and non-tender. The supraclavicular fossae were normal. She also had a 2x2 cm naevus, just superior to this lesion on the chest wall. The other breast and axilla were normal.

Investigations

- The routine blood and urine examinations were normal.
- The CT scan showed the lesion arising from the skin with ulceration, involving the entire left breast and some nodes seen in the axilla (see Fig. 1.2).
- Biopsy revealed an adnexal skin tumour.



Diagnosis

The patient was diagnosed as a rare case of syringocystadenocarcinoma papilliferum infiltrating the entire left breast.

Management

Because of the massive involvement of the breast and significantly enlarged lymph nodes, the patient underwent a modified radical mastectomy with wide excision of the skin (see Fig. 1.3). Overall, 33 nodes not involved with cancer were also removed. The post-operative period was uneventful and no complications have been reported so far.



Fig. 1.3: Excised mass from the breast

Discussion

Melanomas account for 4%–7% of skin cancers, while the remaining 93%–96% are non-melanomas. Adnexal tumors, which are derived from sweat glands, sebaceous glands, and hair follicles, represent 1%–2% of all skin tumours.¹ Most of the skin adnexal tumours are benign and curative with local complete surgical

excision. On the contrary, their malignant counterparts are rare, locally aggressive, with the potential for nodal involvement and distant metastasis. Thus, detecting the malignancy in skin adnexal tumours is critical for therapeutic and prognostic purposes.²

Syringocystadenocarcinoma papilliferum is an extremely rare, cutaneous adnexal carcinoma, considered as the malignant form of its benign counterpart, syringocystadenoma papilliferum (SCAP).^{2,3} First described in 1980, a typical syringocystadenocarcinoma papilliferum presents as a long-standing lesion, commonly on the head and neck (though also reported on scalp, back, chest, suprapubic area, and perianal region) in middle-aged or elderly individuals. They are generally seen as raised and nodular neoplasms with possible ulceration, secretion, or pain.³

Cases of syringocystadenocarcinoma papilliferum have been reported as individual case reports and case series. Our case is distinctive in the aspect that it is the first reported case of syringocystadenocarcinoma papilliferum involving the breast tissue. Distinguishing syringocystadenocarcinoma papilliferum from mammary carcinomas is particularly challenging, considering the apocrine histologic features and possibly shared estrogen receptor expression.³

Surgery is the preferred treatment modality for malignant adnexal tumour cases. In this case, a modified radical mastectomy with wide skin excision was performed to remove all of the tumours.

CONCLUSION

We presented a rare, mammary tissue involvement of a rare clinical entity, syringocystadenocarcinoma papilliferum. This case emphasizes the need for a careful and broad spectrum of differential diagnosis in the patient presenting with mammary lesions to arrive at accurate diagnosis and achieve optimal treatment outcomes.

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THE NEED FOR AN EARLY DETECTION AND QUICK REFERRAL IN MANDIBULAR GINGIVAL CANCER: A CASE REPORT

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Abstract

Oral cancers are among the highly preventable and easily identifiable cancers. Despite this, the diagnosis is often delayed and hence the prognosis is poor. In addition to the delay by patients in initial presentation to the physician, there is a significant time lag in referral by the physician to the oncologists. An early detection followed by an early initiation of treatment can significantly improve survival. Here, we present a case of mandibular gingival cancer, referred to our hospital with the diagnosis of oral cancer. After the biopsy and relevant investigations, the case was discussed in a multi-disciplinary tumour board; where it was unanimously agreed that a primary surgical approach/treatment with curative intent would be adopted and the need for adjuvant treatment would be decided based on the final histopathology report. The patient was counseled for proposed treatment plan, which he underwent and recovered well without any complications.

Case Presentation

A 45-year-old man presented to the hospital with the complaints of non-healing ulcer over his left lower jaw (see Fig. 2.1) for the past 2-3 months, with associated mild to moderate pain and progressive decreased mouth opening for the past 3-4 years.



Fig. 2.1: Non-healing ulcer in the patient.

History of Present Illness

The patient had consulted an Onco-Surgeon 8 months ago for some oral symptoms. Since he was a tobacco chewer for over 10 years, and already had significant changes in the mouth in the form of oral potentially malignant disorders (OPMDs) (viz., oral submucous fibrosis and erythroplakia), he was advised to abstain from tobacco usage. He was also suggested for a regular follow up. On a recent follow up for a non-healing oral ulcer, biopsy was recommended, which confirmed the diagnosis of oral cancer. The patient was then referred to a specialty hospital for further treatment.

Past Medical History

The patient was a known hypertensive for the past 3-4 years and was recently diagnosed with diabetes mellitus. There was no relevant family history.

General and Systemic Examination

- The patient was moderately built and appeared well nourished. There was no anemia, jaundice or generalized lymphadenopathy.
- Systemic investigations did not reveal any abnormality. There was no organomegaly.

Oral Examination

The patient was able to open his mouth only up to 2 fingers width. Overall, the oral hygiene was poor. There was an ulceroproliferative lesion over the left mandibular buccal gingiva, lower gingivobuccal sulcus

and buccal mucosa with respect to the anterior and posterior teeth, measuring 3.0x2.0 cm. The overlying cheek skin was free. Moderate to severe oral submucous fibrosis was noted along with leukoplakia on the left upper buccal gingiva with respect to the posterior teeth.

Investigations

- The routine blood and urine examinations were normal.
- **Punch Biopsy:** Reports revealed a well-differentiated squamous cell carcinoma of the left lower buccal gingiva.
- A **CT Scan** of the **neck** showed 3.6x1.1x1.2 cm left lower gingival mass with subtle osteolysis in the left lower first premolar socket and loosening of left lower first molar.

excision with left marginal mandibulectomy, left selective neck dissection (*level* I-IV), and radial forearm free flap reconstruction (see Fig. 2.2). The patient recovered well without any complications. He is currently taking normal oral diet and is back to routine activities.

Discussion

Oral squamous cell carcinomas (OSCC) contribute over 90% of all oral cancers. It is the sixth most common cause of cancer mortality worldwide and second most common cause of cancer mortality in India.¹

Gingival carcinomas contribute about 10% of the OSCCs; with mandibular gingiva carcinomas being more common than maxillary gingiva carcinomas.¹ Although an early diagnosis is difficult due to the



Fig. 2.2 : Intra-operative images.

- a. Left cheek flap raised to access and expose the primary lesion for resection.
- b. Post-ablative defect
- c. Final inset of radial forearm free flap and after the microvascular anastomosis.

- Left submandibular and level II cervical lymphadenopathy (metastatic disease) was also noted.

Diagnosis

The patient was diagnosed as a case of carcinoma in the left mandibular gingiva (cT2N2bM0).

Management

The patient underwent surgery, involving wide local

symptoms mimicking other oral inflammatory conditions, it is crucial due to a high likelihood of metastasis.²

The stage of lesion at the time of presentation directly affects the survival. With an advanced stage cancer at the time of diagnosis (stage III and IV), the 5-year survival rate is reported to be $\leq 50\%$. On the contrary, an early stage at the time of diagnosis (stage I and II lesions) is associated with a 5-year survival rate of 80% .³

There is a general patient delay of 3.5–5.4 months, from the first appearance of symptom/lesion to first presentation to the physician. Unfortunately, the time taken by squamous cell carcinoma to double in size (doubling time) is approximately 3 months. Hence, any further delay in treatment initiation tremendously decreases the prognosis. The overall professional delay, from first presentation to the physician, to the initiation of definitive treatment is 14–21 weeks; this duration includes investigations, biopsy, histopathological diagnosis, and referral to a specialist for further treatment. Reducing this professional delay in referral can help in early initiation of treatment.³ Since there is a possibility to identify potentially malignant oral lesions through visual examination, creating awareness among the patients as well as primary healthcare team, including the dentists and

physicians, can help in early detection of oral cancers. This might help in reducing the disease burden and downstaging the cancer.⁴

The treatment of oral cancers remains a challenge despite the advancements in surgical techniques and radiation therapy.⁵ Furthermore, since occult cervical metastasis is common even in early stages, elective treatment of the neck is necessary in many cases.⁶ In the present case, a wide excision, to remove the affected tissue, was performed along with level I–IV neck dissection and appropriate microvascular soft tissue free flap.

The final histopathological reports indicated an early cancer (Stage II); hence, no adjuvant treatment (radiation therapy) was advised after discussion in the multi-disciplinary tumour board at our hospital.

CONCLUSION

We presented a case of left mandibular gingiva squamous cell carcinoma. This case indicates the need to consider a differential diagnosis of gingival squamous cell carcinoma in patients presenting with gingival lesions; an early detection can improve the prognosis. Along with the surgical excision of the cancerous tissue, elective neck dissection may be required to remove possible metastasis.

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GOLD FIDUCIAL MATCHING OFFERS BETTER IMAGE GUIDANCE FOR **IGRT**

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Abstract

Prostate cancers are the most common cancers among men worldwide. Despite metastasis, the overall prognosis is high. Image-guided intensity-modulated radiation therapy (IG-IMRT) is an advanced, safe, and highly effective form of radiation therapy, which provides high radiation dose to limited tumour volume. Here, we present a case of high-risk localized prostate cancer. Radical radiation therapy (RT) was administered in this case with the help of gold fiducial markers, which offer better image guidance for image-guided radiation therapy (IGRT). The treatment was well tolerated and no major toxicity was reported.

Case Presentation

A 76-year-old male from Tanzania, Africa, was presented with the complaint of difficulty in passing urine for the past 6 months. He was diagnosed as a case of prostate cancer and was referred to our hospital for appropriate RT.

History of Present Illness

The patient had consulted a urologist in Tanzania for the above mentioned symptoms. His clinical examination reports revealed high serum prostate specific antigen (PSA) levels (21.36 ng/mL). Results of a transurethral resection (TUR) biopsy of the prostate revealed Adenocarcinoma Grade II (involving all six cores more than 60%) with Gleason score 3+4 =7/10. The patient received hormonal injection (one dose of subcutaneous 45 µg leuprolide). He then decided to take a second opinion at a hospital in India, where repeat PSA levels were noted to be 1.87 ng/mL. On the basis of MRI scans, PSA levels, no bone metastases, and

Gleason score, the carcinoma was staged as cT_{2c}N₀M₀, high-risk prostate cancer. The urologists concurred with the medical management of combined androgen blockade protocol along with curative radical RT.

Past Medical History

The patient was a known hypertensive and also had type 2 diabetes mellitus, and was being treated with medications. His coronary angiogram showed minor coronary artery disease.

General and Systemic Examination

- The patient was moderately built and appeared well-nourished, with ECOG performance score of 1.
- Systemic examinations did not reveal any abnormality.
- Pelvic examination did not reveal any palpable pelvic/inguinal lymphadenopathy.
- Testis and scrotal examinations were unremarkable.

Investigations

- PSA levels were 1.87 ng/mL
- MRI reported 4.3 cm prostate gland with small 1.3x1.1 cm nodule in the right half of the central zone and small ill-defined nodule in the right half of the peripheral zone, a few sub-centimeter lymph nodes in the internal iliac region, non-significant by size criteria.

Diagnosis

The patient was diagnosed with localized high-risk prostate cancer (T_{2c}, GLS-7, PSA 21.3 ng/dL).

Management

The treatment protocol for high risk localized prostate cancer was discussed with the patient. The patient underwent radical RT with 76Gy in 38 fractions (2 Gy/fraction) with IGRT and volumetric-modulated arc therapy (VMAT) planning. Before the initiation of RT, gold fiducials were inserted into the prostate to assist in IGRT. Combifix (a customized knee rest and foot rest combination) was used for uniform patient positioning for CT simulation as well as treatment. A reproducible

protocol were provided. For targeting the tumour, it was planned that 95% of the contoured PTV should get 76Gy and <5% should get 81 Gy (hot spot/high dose region). Accordingly, double arc VMAT was planned. The plan was then evaluated with dose volume histogram (DVH). A modern cone beam computed tomography (CBCT), built in Elekta system, along with Gold fiducials, was utilized and matched to correct the errors for maximum accuracy in radiation delivery. The treatment was well tolerated by the patient, with no

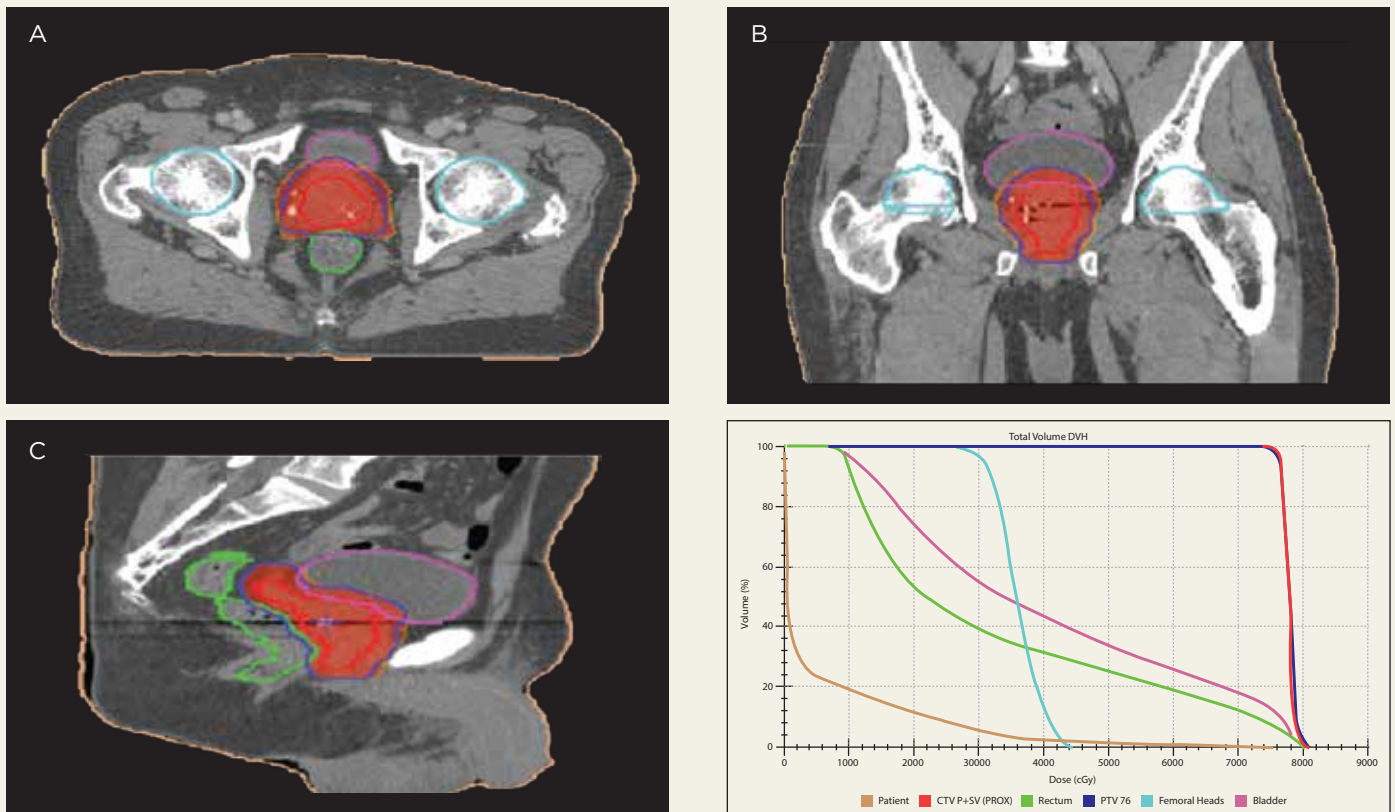


Fig. 3.1: (A) (B) and (C) depict the contours of the PTV 76 Gy (encompassing CTV prostate plus 2 cms seminal vesicles) along with distribution of the 76 Gy isodose (A) Axial section (B) Coronal section; (C) Sagittal section; (D) Depicts the dose volume histogram (DVH).

Pink: bladder; Green: rectum; Blue: bilateral femoral heads; Red: PTV prostate plus seminal vesicle

bladder protocol* was followed for CT simulation and RT. The CT simulation scan with i.v. contrast was shared with the treatment planning system. The reconstructed images were contoured for clinical target volume (CTV). The planning target volume (PTV) included margins (1 cm overall, except 0.7 mm on the posterior side to protect the rectal area) for setup errors. The organs-at-risk (bladder, rectum, and femoral heads) were also marked (see Figure 3.1).

Dose constraints as per the Fox Chase Cancer Center

major complications, except slight painful micturition, which was treated with antispasmodics.

The ongoing hormonal therapy was continued with second dose of leuprolide injection (22.5 µg) during RT. The patient was advised to continue the hormonal therapy every 3 months for the next 1.5 years in Tanzania and follow-up regularly with future reports. It is anticipated that PSA levels <1 ng/mL would be achieved. He was also advised evaluation of PSA every three months for the next five years, which would determine whether he is completely cured.

*complete urination, followed by oral intake of 500 ml of water and 45 minutes of waiting period for bladder expansion, before imaging)

Discussion

Several prospective, randomized studies have established the role of RT in the management of high-risk prostate cancer.¹ Higher doses of RT have been shown to improve the biochemical relapse-free survival, compared with conventional-dose RT. However, considering the higher risk of acute and late toxicities associated with higher radiation doses, it is crucial that higher dose radiation be confined to a minimal target volume.²

Currently, IGRT and reverse planned IMRT are being used to deliver high doses to the target together with minimizing the dose to the surrounding normal tissues. Often, IGRT is based on the implantation of fiducial gold markers in the prostate, which help in verification of prostate position before each treatment fraction. By

limiting the interfractional variability in the prostate position, PTV can be downsized. In a retrospective study by Sveistrup *et al.*, involving 503 patients with high-risk prostate cancer, the toxicities with 3D-CRT and IG-IMRT based on implanted markers, were compared. It was reported that 2-year actuarial likelihood of developing grade ≥ 2 gastrointestinal toxicity was significantly lower with IG-IMRT (5.8%) compared with 3D-CRT (57.3%; $p < 0.0001$). Similarly, IG-IMRT was associated with lower incidence of genitourinary toxicity (29.7%), compared with 3D-CRT (41.8%; $p = 0.011$).³

In this case, with the help of gold fiducial matching, sub-millimeter accuracies were achieved in the verification of prostate treatment and better correction of systematic and random errors.

CONCLUSION

In the present case of high risk prostate cancer, we delivered IG-IMRT with the help of CBCT and gold fiducial implanted markers for a more accurate matching of the prostate (relative to matching the prostate and rectum interface, where the CT resolution is very similar and may result in inaccuracies). The patient tolerated the treatment well, without any major toxicity.

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