



METASTASIS TO VULVA IN OROPHARANGEAL CANCER: A RARE CASE REPORT

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ABSTRACT Introduction: Metastasis to vulva from head and neck cancer is a rare event. It is usually a late manifestation of the primary tumour and may be the first evidence of widespread dissemination of the disease. The diagnosis is difficult and is usually done by histopathological examination. Case Summary: A 75-year old female presented with complaints of pain in throat and difficulty in swallowing for 15-20 days and was diagnosed as a case of oropharyngeal cancer involving soft palate and uvula. The patient was treated with palliative EBRT followed by supplementary EBRT to face and neck. The patient was later found to have recurrence with metastasis to vulva despite completion of primary treatment. The patient presented with pain in groin and swelling over perineal region with histopathology report revealing poorly differentiated malignant tumour. The patient was given palliative EBRT single session to local site which resulted in good relief of symptoms. Conclusion: The case report showed that palliative radiotherapy can yield a good symptomatic response in vulvar metastasis. Further studies are required to standardize an approach to manage such patients.

KEYWORDS : -Carcinoma oropharynx, vulval metastasis, palliative

Introduction

The appearance of local recurrence in oropharyngeal cancer is not uncommon. But, involvement of distant locations from a primary head and neck tumour continue to be problematic question. Oropharyngeal cancers mostly metastasize to cervical lymph nodes, lung, liver, bone etc. Metastasis to vulva from oropharyngeal cancers has been rarely reported, probably due to its infrequent presentation. It is usually a late manifestation of the primary tumour and may be the first evidence of widespread dissemination of the disease. The treatment is usually palliative; for symptomatic relief and to avoid any unnecessary morbidity. Here we report an unusual case of vulvar metastasis from oropharyngeal carcinoma.

Case Summary

A 75-year old female, without any comorbidities, presented to our department with complaints of pain in throat and difficulty in swallowing since 20 days. The pain was insidious in onset, gradually progressive in intensity and got relieved on medications. Difficulty in swallowing was more for solids as compared to semi-solids and liquids. Patient had no history of fever, weight loss, anorexia or bleeding from any natural orifice. General physical and systemic examination was within normal limits. Local examination revealed a proliferative growth of about 5x5 cm on left sided soft palate and tonsil, which was non bleeding on touch and was associated with palpable left level II cervical lymph nodes of size around 2x2 cm [clinical stage T3N1M0, III].

USG guided FNAC from swelling in left cervical region suggested poorly differentiated malignant tumour. A contrast enhanced CT scan was done which confirmed the lesion of size 35x30x45 mm involving left tonsil, left lateral and posterior wall of oropharynx along with multiple enlarged lymph nodes at left level IB, II and III; largest measuring 34x25 mm [pathological stage T2N2BM0, IVA]. The patient was given palliative external beam radiotherapy (20 Gy in fractions over 5 days) to face and neck by Cobalt-60 machine. Following good response, the patient again received supplementary external beam radiotherapy to face and neck in the dose of 20 Gy in 5 fractions over 5 days again by Cobalt-60 machine.

7-months after completion of treatment, patient started complaining of pain in groin and swelling over perineal region (Image 1). On local examination, a 5x5 cm growth was found on labia majora on the left side, which was hard, fixed and tender. The patient was referred to gynaecology department for vulvar biopsy and histopathology

revealed poorly differentiated malignant tumour (Image 2 and 3). The patient was then referred back to our department for further management. She was then given palliative external beam radiotherapy single session in the dose of 800 cGy to local swelling by direct incident dose in lithotomy position on Cobalt-60 machine. Post radiotherapy, the patient showed symptomatic relief in pain and on examination, the growth started to regress. The patient was then started on oral metronomic chemotherapy with Tab Cyclophosphamide 50 mg BD after routine investigations.



Image 1: Clinical image showing swelling over perineal region.

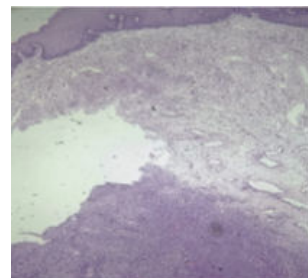


Image-2

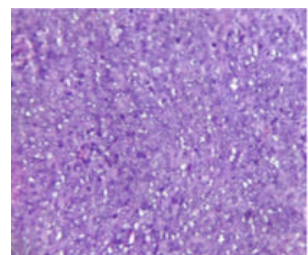


Image-3

Image 2 & 3: H&E stained microsections from vulvar biopsy revealing poorly differentiated malignant tumor (40X, 100X).

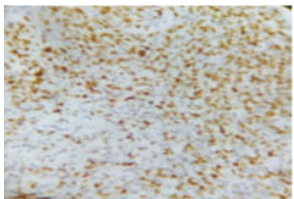
**Image-4****Image-5**

Image 4 & 5: Immuno-histochemical staining for Ki67 revealing 60-70% positivity in tumor cells (40X, 100X).

Discussion

Oropharyngeal cancer is the sixth most common cancer worldwide.² Two types of oropharyngeal cancer can be distinguished, HPV-associated, due to an oral human papillomavirus infection, and non-HPV-associated, mainly due to tobacco smoking and alcohol use.³ The prevalence is higher in males than females. There are approximately 1 lac new oropharyngeal cancers in 2020 (0.13% of total cancer incidence).⁸

Patients with oropharyngeal cancer can present with a variety of symptoms depending on the location of the tumor. The most common presentation includes persistent sore throat, dysphagia, odynophagia, dysarthria, presence of a lump in the neck, and otalgia. In addition, the patients may also complain of voice changes (hoarseness), unexplained weight loss, and hematemesis.

The conditions with presentations similar to oropharyngeal squamous cell carcinoma and which need to be excluded include: Actinic keratosis, erythroplasia, lichen planus, leukoplakias, lichenoid lesions, oral candidiasis, tonsillitis, traumatic lesions. A biopsy of the suspicious area is performed to make a definitive diagnosis.

The most common site for metastasis from oropharyngeal cancer is the cervical lymph nodes, with variability among the different levels of nodal metastasis based on the position of the primary tumor. The overall incidence of cervical lymph node involvement from cancer of the oropharynx is approximately 70%.⁸ Bilateral cervical lymph node metastases are common, as well—up to 50%.⁹

Distant metastasis is a significant problem in patients with carcinoma of the oropharynx, occurring in approximately 15-20% off all patients over the course of the disease.⁸ It generally occurs in patients who present with advanced disease, especially in those with pathologically proven lymph nodes at multiple levels of the neck or in the lower neck. Distant metastases of oropharyngeal cancer generally occur in the lung (55.8%); bone (9.9%); liver (3.9%) and are usually due to lymphatic spread.⁴ Metastasis from oropharyngeal carcinoma has also been observed to involve the central nervous system in 1 to 2% of patients throughout the course of the disease.¹⁰ Since distant metastases occur infrequently in carcinomas of oropharynx, data about them are scarce. However unusual oropharyngeal cancer metastatic sites should not be ruled out: metastases have been reported in thyroid, colon, orbits, cavernous sinus and vulva. Metastases to vulva has rarely been reported.

A review of the current head and neck tumor literature describes the aforementioned distribution of distant metastasis, with each study citing the lung as the most common site of distant metastasis.¹¹⁻¹³ Other, less common, sites of metastasis from various head and neck SCCs

include skin, brain, adrenal gland, heart, kidney, peritoneum, soft tissue, spleen, and prostate. A review of 546 patients with oropharyngeal SCCs by Merino et al yielded distant metastasis in the following locations: lung in 52% of patients, bone in 20.3%, liver in 6%, mediastinum in 2.9%, lung and bone in 3.3%, and others in 15.4%.¹¹ Another review of 89 patients with metastatic oropharyngeal SCC by Kowalski et al revealed metastasis in the following locations: lung in 58.4% of patients, bone in 37.1%, liver in 3.4%, brain in 3.4%, and soft tissue in 2.2%.¹² Finally, a review of 39 patients with various head and neck SCCs by Alvarez Marcos et al yielded distant metastasis in lung in 58% of patients, bone in 22%, liver in 9%, soft tissue in 9%, and others in 2%.¹³

Vulvar metastasis is usually an isolated recurrence, being associated with other metastatic sites in 3 of 18 (16.7%) patients. Vulvar metastases usually arose on labia majora as asymptomatic nodules/masses; however painful bleeding exophytic/ulcerated/papular lesions were also reported. Vulvar metastases were diagnosed within 2 years from primary treatment (median time: 10 months). Vulvar metastases occurred most frequently in postmenopausal women, frequently representing a worrisome prognostic event: the median survival after vulvar metastasis is 20 months.⁵

As the incidence of vulvar cancer has been rising over the past decades, increased clinical and scientific interest has emerged to improve therapeutic options. Treatment options range from ultra-radical surgery in form of pelvic exenteration to multimodal treatment including neoadjuvant or definitive chemo radiation. In surgically unresectable metastatic vulvar cancer, therapeutic options are extremely limited and generally experimental due to the absence of established clinical data. Furthermore, patients with metastatic disease are often heavily pretreated. Even though neoadjuvant chemotherapy has shown promising results in primary disease, much lower activity can therefore be expected in recurrent or metastatic settings. This reflects in a 1-year survival rate of 31% in patients with recurrent or metastatic vulvar carcinoma. Over the past decade a few small prospective studies for advanced or metastatic vulvar cancer have been initiated. To improve treatment for metastatic vulvar cancer, the level of information regarding incidence and localization of metastases has to be improved. So far, very few publications included patients with metastatic vulvar cancer.⁶

Gandhi AK et al presented an almost similar case of vulvar metastasis where a 76-year-old female (with a 15-year history of breast cancer) presented with a non healing ulcer in the vulvar region. The patient was given standard treatment for the primary cancer and was on tablet Letrozole 2.5 mg since then. There was significant improvement of the vulvar lesion at 6 months of follow up.⁷

The treatment offered in advanced cases of head and neck malignancy is often palliative. As our patient was in stage IVB, he was started on palliative radiotherapy. In our patient, although palliative radiotherapy did not induce response, but it provided subjective relief in symptoms to the patient.

Conclusion

Metastatic carcinoma from oropharynx can virtually involve any organ of the body. Vulvar involvement is very rare in metastatic oropharyngeal carcinoma. The goal of treatment includes disease control, palliation of symptoms and better quality of life. The case report showed that palliative radiotherapy can yield a good symptomatic response in vulvar metastasis. Awareness of this unusual pattern of metastasis would help in early diagnosis and also systemic work up with deciphering of further distant metastasis and early institution of the therapy. Advanced cases of oropharyngeal carcinoma can be very aggressive and metastatic spread to vulva should be considered as a possibility though it is rare, especially when patient presents swelling over perineal region. More case reports and studies are required to standardize an approach to manage such patients.

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