CASE REPORT

Immoderate perfume use leading to non-keratinising sinonasal squamous cell carcinoma with bone and lung metastases

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Abstract

Squamous cell carcinoma (SCC) of the sinonasal tract (SNSCC) is a cancerous epithelial tumour which originates from the epithelium surface lining the nasal cavity and paranasal sinuses and shows squamous differentiation. Here, we report the case of a patient who had the habit of soaking cotton cloth at night with perfume and spreading it over his face and sleeping for around eight hours in this position. The patient had been doing this for 30 years without any gap and presented with complaints of nose bleed and difficulty in breathing since three to four months. Upon scanning of the face, a polypoidal lesion was seen in the left nasal cavity causing partial obstruction of the nasal cavity. Biopsy of the nasal mass confirmed the presence of neoplastic lesions positive for cytokeratin 5/6 diagnosed as non-keratinising SCC. Upon further evaluation of symptoms, metastases in bones and lungs were also confirmed.

Keywords: Nasal cavity, Paranasal sinuses, Perfume, Carcinoma, Keratin-5.

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Introduction

Sinonasal squamous cell carcinoma (SNSCC) presents in two primary forms: keratinising (KSCC) and non-keratinising (NKSCC). NKSCC is an uncommon malignancy affecting the nasal cavity and paranasal sinuses, distinguished by its characteristic anastomosing ribbon-like growth pattern and minimal to absent keratinisation or cellular maturation. The World Health Organisation (WHO) classifies several previously used terms—such as Schneidrian carcinoma, transitional cell carcinoma, cylindrical cell carcinoma, Ringertz carcinoma, and respiratory epithelial carcinoma—as outdated synonyms for NKSCC. At present, tumour grading for NKSCC lacks standardisation, and it remains uncertain whether its clinical outcomes differ significantly from those of KSCC.[1] Approximately 20% of SNSCC cases are made up of distinct histological variants, each with unique morphological features. The five primary subtypes include adenosquamous, spindle cell (also known as sarcomatoid), basaloid, papillary, and verrucous carcinoma, with reported five-year disease-specific survival (DSS) rates of 15%, 32%, 56%, 62%, and 70%, respectively. In contrast, the five-year DSS rate for conventional SNSCC (encompassing both KSCC and NKSCC) is around 45%. NKSCC specifically accounts for an estimated 10–27% of SNSCC cases. According to the WHO Global Cancer Observatory 2, 129,079 new cases of nasopharyngeal cancer were diagnosed in 2018, with 72,987 related deaths. The highest prevalence rates are observed in Eastern and South-eastern Asia, with 64,304 and 34,681 new cases, respectively. In Southern China, the prevalence reaches as high as 20 per 100,000 individuals, compared to just 0.5 to 1 per 100,000 in regions like Europe and North America. Over the past two decades, prevalence rates have been declining with global reductions ranging from 1% to 5% per year. Despite these trends, the total number of new cases is expected to rise due to global population growth. Projections for 2030 estimate approximately 158,558 new cases and 93,338 deaths from nasopharyngeal cancer worldwide.[2]

Identified risk factors for SNSCC include exposure to substances such as nickel, chlorophenols, textile dust, chromium, isopropyl alcohol, radium, and tobacco smoke. Additionally, it is estimated that between 36% and 58% of NKSCC cases in the sinonasal region are associated with human papillomavirus (HPV) infection. Common presenting symptoms include nasal blockage, discharge, nosebleeds (epistaxis), facial pain or pressure, and ocular symptoms in cases where the tumour invades the orbit. In more advanced stages, NKSCC may extend into the oral cavity, leading to symptoms such as ulceration, mobile teeth, and referred pain. The maxillary sinus is the most frequently involved site in SNSCC, accounting for around 60% of the cases, followed by the nasal cavity (approximately 25%) and ethmoid sinuses (around 15%).[3] Tumours originating from the maxillary sinus tend to behave differently than those arising from the naso-ethmoidal complex. Notably, although regional lymph node metastases are generally rare in SNSCC, lesions in the

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maxillary sinus exhibit a higher likelihood of nodal spread, likely due to distinct lymphatic drainage patterns compared to tumours of the naso-ethmoidal area.[4] The presented report details a case of an old male patient with non-keratinising SCC with bone and lungs metastases.

Case Report

A 64-year-old male patient was seen at the OPD of Noor-e-Zia consultant clinic, in Karachi, on July 10, 2024. He had a history of soaking cotton cloth in perfume, spreading it over his face, and sleeping for almost eight hours since 30 years. The patient used eau de toilette that contains alcohol, water, fragrant oils, fixatives, essential oils, perfume extracts, and colorants. He had complaints of nose bleed without pain from the left nostril and difficulty in breathing for three to four months with dry mouth. There was involuntary weight loss of around 15kg during the past six months. The patient's immune system was normal. He was a known case of hypertension for the past 10 years, maintained on Angiotensin converting enzyme (ACE) inhibitors. Initially, the patient consulted a general practitioner who diagnosed him with nasal septum deviation but due to the worsening of symptoms he consulted an ENT surgeon where he was advised to have multi-slice computerised tomography (CT) scan of the face, both with and without IV contrast. CT scan revealed polypoidal mass lesion in the left nasal cavity which was causing partial obstruction. This lesion projected through posterior nasal space into nasopharynx and damaged the inferior nasal turbinate with right sided nasal septum deviation. The maxillary infundibulum was expanded, blocking the ostiomeatal complex; there was mucosal thickening and retained secretion in the left maxillary sinus. Mucosal thickening was also noted in ethmoid sinuses along with extraconal retrobulbar fat of the left orbit along the lamina-papyracea. It showed heterogeneous enhancement after IV contrast. These findings could be due to sinonasal polyposis with superadded fungal infection, though the possibility of inverted papilloma cannot be ruled out. Clinical correlation and biopsy of the mass was suggested for further evaluation. The right nasal cavity appeared normal with mild hypertrophy (Figure 1). Histopathology of the left nasal mass was confirmed through punch biopsy. Specimen consisting of two, irregular, light brown, soft tissue pieces, collectively measuring 2 x 0.8 x 0.7 cm, was received in formalin in a single cassette. Sections examined revealed fragments of a neoplastic lesion composed of nests, aggregates, and trabeculae of neoplastic cells. Individual neoplastic cells were polygonal in shape containing moderate to abundant amount of eosinophilic cytoplasm and nuclei with open chromatin. A panel of immunohistochemical staining were performed that showed the reactivity pattern as follows: Cytokeratin 5/6: positive in the neoplastic cells and P16: negative for human papilloma virus concluded as non-keratinising squamous cell carcinoma. As per CT scan of the paranasal sinuses, histopathology, and immunohistochemistry, the patient was diagnosed with non-keratinising SCC. The ENT surgeon then advised the patient to have radionuclide whole body skeletal survey (bone scintigraphy) done for metastatic work-up for left nasal neoplastic mass. Skeletal scintigraphy was performed with 740 Megabecquerel (MBq) of Technetium (Tc) -99m injected intravenously and whole body static images were acquired three hours after injection. Delayed static images showed abnormally increased radiotracer uptake over the skull with left nasal and maxillary bone (primary lesion site), sternum, multiple ribs, multilevel cervical dorsal and lumbar vertebrae, sacrum, pelvic bones, and proximal end

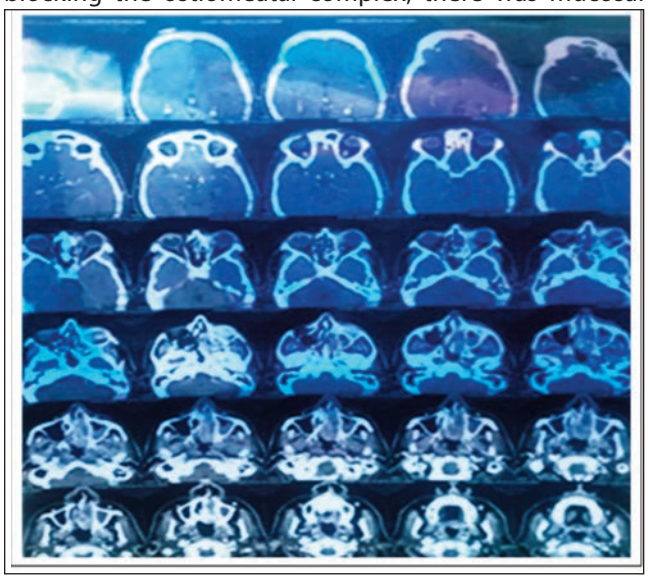

Figure-1: CT scan of Paranasal Sinus.

**Right ostiometal complex appears normal. *Mild hypertrophy of the nasal turbinates noted on the right side. *Left frontal, right ethmoid, maxillary and the right sphenoid sinuses appear normal and show no mucosal thickening, retained secretion or cyst formation.*

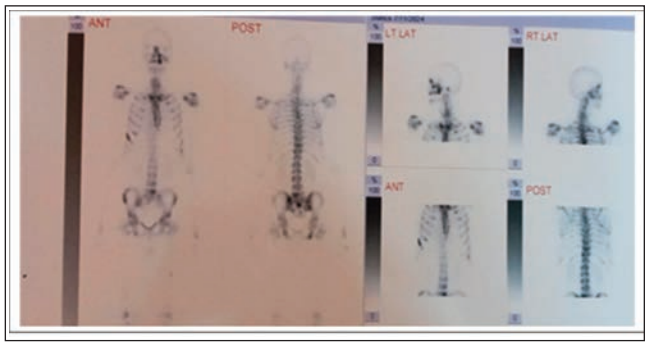

Figure-2: Radionuclide whole body skeletal survey showing bone metastases (bone scintigraphy).

*Three-hour delayed static images shows abnormally increased radiotracer uptake over: Skull with left nasal and maxillary bone (primary lesion site), sternum, multiple ribs, multiple cervical dorsal and lumbar vertebrae, sacrum, pelvic bones, and proximal end of both femurs with left femoral shaft. Scan shows bilaterally symmetrical tracer distribution in both axial and appendicular skeleton.

of both the femurs with left femoral shaft. Degenerative changes were noted on bilateral shoulders, elbows, wrist, hip, knee, ankle representing arthritis. Whole body bone scan scintigraphic findings were consistent with bone metastases (Figure 2). A CT scan of the chest and whole abdomen was also performed. Axial and coronal images were obtained after IV contrast injection. Diffused sclerotic metastatic deposits in the axial and appendicular skeleton were suggestive of metastatic SCC of the nasal cavity. Atelectasis was seen in the lungs bilaterally with peribronchial thickening in the right lung. Patchy areas of consolidation were also seen in the anterior segment and lingular segments of the left upper lobe along with multiple small nodules in the lungs. Findings suggested infective aetiology and required follow-up. The patient was advised surgical removal of the primary lesion followed by chemotherapy and radiotherapy.

Discussion

SCC is recognised as the most prevalent histological type, representing approximately 50% to 60% of all head and neck cancers in the United States.[5] Neoplasms of the maxillary sinus are the most frequently encountered among sinonasal malignancies, accounting for nearly 80% of these cases.[6] This report presents a considerably high risk of SNC due to exposure to organic solvents and a significant dose-response relationship with solvents. In a research related to sinonasal inverted papilloma (IP), a noteworthy link and a dose-response association between exposure to organic solvents and occurrence of SNC was observed which supports the possible link between solvents and IP.[7] One more study revealed the risk of sinonasal cancer with considerably increased odds ratios (OR 2:11) due to persistent exposure to fumes generated from welding involving organic solvents. The odds ratio (OR) in case-control studies aid in identifying the probability of association of exposure with the occurrence; a value less than one suggests that the exposure is linked with reduced odds of exposure occurrence.[8] SCC of the sinonasal tract are a highly aggressive cancer that often invades nearby structures. Approximately 15% of the cases go on to develop distant metastases and most commonly affects the lungs, mediastinum, liver, or bones. Bone is the second most frequent site of distant metastasis after the lungs, accounting for approximately 15–39% of such cases. The axial skeleton is most affected, while the bones of the limbs are involved far less often, appearing in only about 17% of the cases. The presence of bone metastases at the time of diagnosis of primary tumour suggests a more aggressive tumour behaviour. Most of the affected bones were from the appendicular skeleton and showed bilateral involvement, which is quite uncommon. Degenerative changes consistent with arthritis were observed in both the shoulders, elbows, wrists, hips, knees, and ankles. Bone metastases often lead to pain and reduced mobility, significantly impacting the quality of life.[9] Patients with tumours originating in the nasal cavity tend to seek medical attention earlier and generally have a better prognosis compared to those with tumours in the maxillary sinus. The overall five-year survival rate is about 60% for nasal squamous cell carcinoma, compared to roughly 42% for maxillary sinus tumours. Prognosis is typically linked to the tumour stage and presence of lymph node metastases. NKSCC usually carries a more favourable outcome than the keratinising form. Additionally, tumours exhibiting a cohesive or pushing invasion pattern are associated with a better prognosis than those with a diffuse or single-cell invasive pattern.[10] Hence, early detection allows for timely treatment, improving patient outcomes and enhancing the quality of life.

Conclusion

This case report highlights a possible association between heavy perfume use and the development of SCC, suggesting a potential role in the carcinogenesis that merits further toxicological research. It is relatively uncommon for facial SCC to directly invade bone as compared to other malignancies. The rarity of direct bone involvement may be due to the limited blood flow and lymphatic drainage in the superficial facial tissues and underlying bones. Nevertheless, SCC is still capable of reaching bone structures through alternative pathways, such as perineural spread or distant metastasis. Hence, further research is required for prospective investigations.

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MS: Literature search, study design, concept and writing.
MK: Literature search, writing and data collection.
FS: Editing.
EB: Editing and review.