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# FRIGHTENING LOOK OF SECONDARIES OF AN UNDETECTED PRIMARY MALIGNANCY-A CASE REPORT

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**ABSTRACT**
Cancers of unknown primary site (CUPs) present a heterogeneous group of metastatic tumors, for which all standard methods of diagnostic work-up fail as far as identifying the site of origin at the time of diagnosis is concerned.3-5% of all malignancies comprised by the CUP's. Patient's profile, gender, the position of the secondary cancer in the body and detailed clinical workup and laboratory workup of the tumor gives important clues in the diagnosis of CUP's. Cancers with unknown primary present a common diagnostic dilemma to the clinicians, as the biggest problem is in tracing the primary in such patients. These cancers are a result of an untraceable occult primary somewhere in the body which present as secondaries, giving a hint of their existence. The tact is in using these secondaries as a guide to the primary lesion. In the present case report we describe a 60 yr old female who presented to the surgery OPD as a case of multiple unusually large and frightening swellings over the face and back and raised a suspicion of secondary metastasis on presentation.

## INTRODUCTION

The exact incidence of a Cancer of unknown primary [CUP] is not known. However an estimated incidence worldwide is taken as 3-5% while its diagnosis during postmortem is taken upto 12-15% [1].Patients presenting with a CUP are invariably considered as being in stage IV of their disease. The five year survival of such cancer patients is a poor 11% [2].

Due to its aggressive presentation and lack of proper diagnosis in such cases early management is of great importance. Inspite of the routine diagnostic workup & specific tests for cancer like PET scans and tumor markers these tumors remain untraceable to a clinician and herein comes the role of a pathologist who can by minimally invasive procedures like FNAC throw some light on the tumor origin of such secondaries by diagnosing on the basis of the malignant cell morphology and pattern.

## CASE REPORT

A 60 years old female who was apparently asymptomatic 6 months back visited the surgery OPD with complains of large swellings in the buccal cavity bilaterally, forehead and lower back on the right side. The swellings were initially small in size but grew progressively in the past six months, largest measuring up to 7x5 cms on presentation. The swellings in the buccal cavity were discharging blood and pus every time she chewed and were accompanied with intense pain in the teeth and were associated with marked halitosis. The swelling on the back was more recent and was painful measuring up to 6x5 cms. The swelling on the forehead measured up to 4x3 cms. On examination all the swellings were firm to hard, warm to touch, fixed and hypopigmented spots present over the skin surrounding the swellings on the back and forehead. There was no discharge from the swellings.

The patient had undergone hysterectomy with bilateral salpingo-opherectomy 2 yrs back for fibroid uterus and had been asymptomatic since then. The patient has no history of tobacco chewing or any other form of addiction.

**INVESTIGATION**

The patient was investigated for her complains, her hemoglobin was-7.2gm/dl, TLC-10, 500, DLC-N62, L30, E8, Platelet count-3.5 lakh.

**KFT and LFT within normal limits**

Her CT showed soft tissue attenuation lesion involving mandibles and scalp on both sides. An MRI of the face and neck performed in the hospital revealed heterogeneous soft tissue lesion eroding the mandibles on one side and showing soft tissue extension on one.

She was sent to the pathology department for FNAC of the swellings FNAC was done taking all aseptic precautions, from all the four swellings. Blood mixed material was aspirated. On microscopy all smears revealed, a hemorrhagic background with sheets of as well as singly lying cells which had hyperchromatic nuclei and minimal cytoplasm. These cells were mildly pleomorphic, with increased nucleo-cytoplasmic ratio. However at places bizarre forms were seen with very large nuclei. The microscopic picture gave a positive impression for malignancy. However the tumor was so poorly differentiated that no definitive diagnosis could be made and a search for primary lesion by biopsy was advised to the patient. The patient was on chemotherapy in the department of surgery, Eras Lucknow medical college and hospital but was lost to follow-up after two rounds of chemotherapy.

**Figure 1. Clinical presentation of swelling over forehead and buccal cavity**

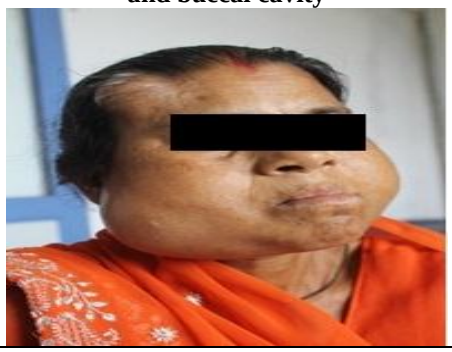


**Figure 2. The swellings over back**

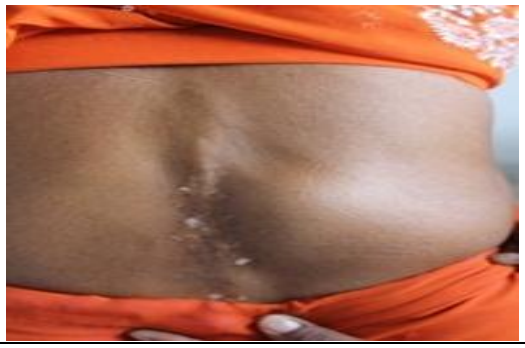
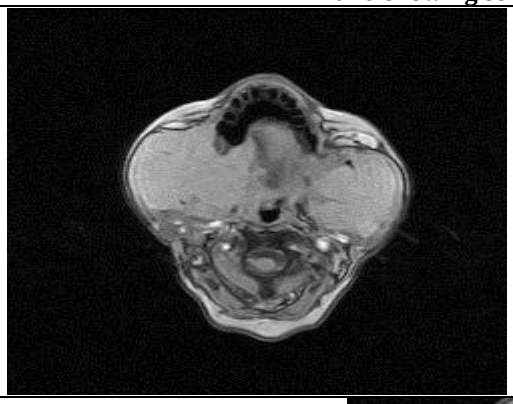
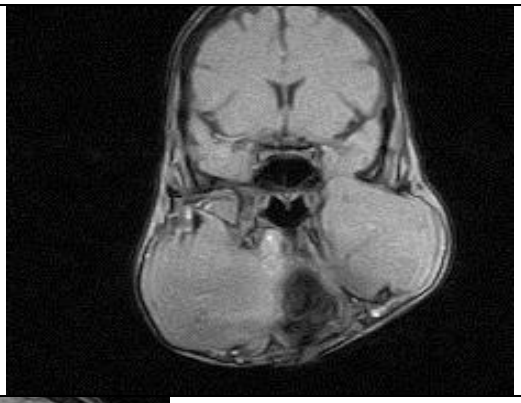


**Figure 3,4,5. MRI of the head and neck revealed heterogeneous soft tissue lesion eroding the mandibles on one side and showing soft tissue extension on other side**





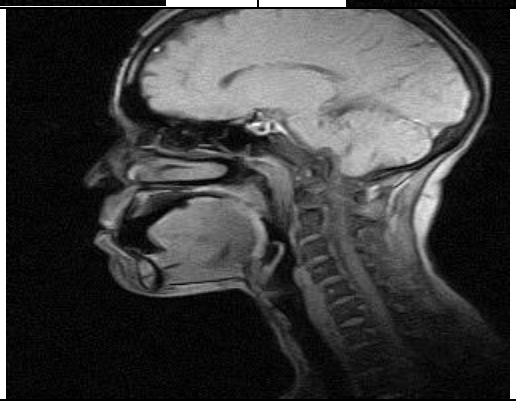


**Figure 6. Low power view of FNAC of swellings .Smear shows singly lying cells which had hyperchromatic nuclei and minimal cytoplasm. These cells were mildly pleomorphic, with increased nucleo-cytoplasmic ratio**

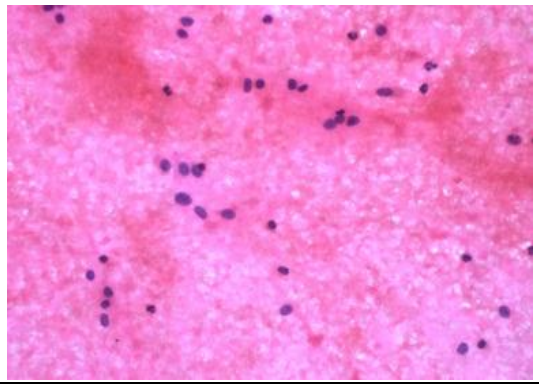


**Figure 7. Smears show singly lying as well as clusters of atypical cells with hyperchromatic nuclei and minimal cytoplasm. These cells were mildly pleomorphic, with increased nucleo-cytoplasmic ratio,on a haemorrhagic background**

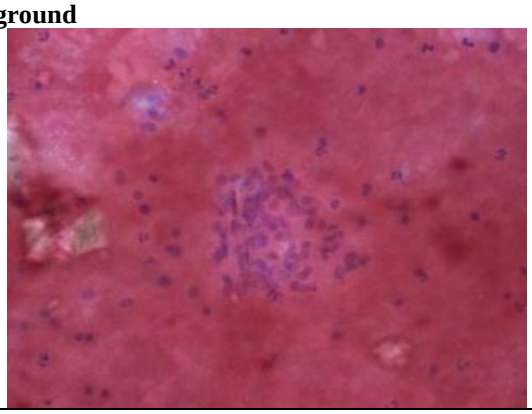


**Figure 8. Smear reveals sheets of atypical cells**

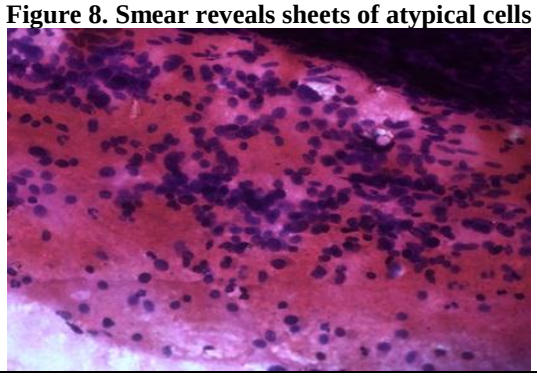
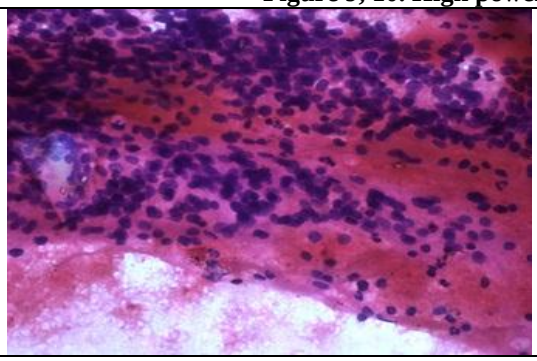
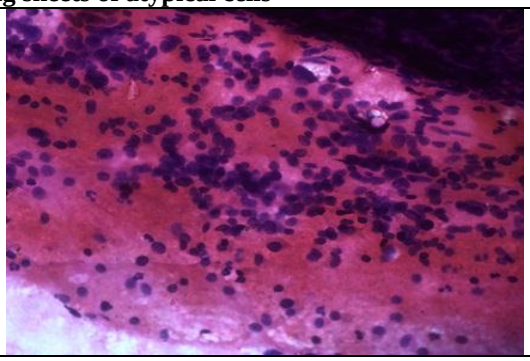


**Figure 9, 10. High power view showing sheets of atypical cells**





## DISCUSSION

The worldwide incidence of Cancer of unkown primary origin is 2-6% [3]. The problem lies in the inability to identify a primary site of cancer. The primary site of cancer is important as the treatment, expected outcome, and overall prognosis of the cancer depends on it. The diagnosis of carcinoma of unknown primary generates a lot of anxiety among patients and doctors alike, who feel that there is need of better evaluation and modalities for such cases. The origin of cancer depends on chromosomal mutations affecting the cell signaling pathway leading to abnormal cell proliferation [4,5]. In CUP's the original tumor remains small or undetectable at the time of metastasis, leading to the clinical presentation of cancer of unknown primary origin. Whether a specific genetic or mutational factor plays a role in cancer of unknown primary origin remains uncertain. The median survival range of patients suffering from CUP's is from 11 weeks to 11 months [6]. The 5-year overall survival of such patients is approximately 11% [7]. Equal male:female ratio is seen in most cases of CUP. 59-66 years is the median age of presentation in both men and women [8, 9]. Lab studies for metastatic cancer with an unknown primary site should include routine investigations such as complete blood count (iron deficiency may point toward an occult gastrointestinal malignancy leading to chronic blood loss), urinalysis (microscopic hematuria may be a sign of occult genitourinary malignancy), liver and renal function tests,

stool examination for occult blood, and measurement of Prostate specific antigen [PSA] in males. Imaging studies should include chest radiograph, computed tomography of abdomen and pelvis, and mammography in women [9,10]. Positron emission tomography with 18F-fluoro-2-deoxy-D-glucose (18F-FDG-PET) is increasingly being used in the evaluation of metastatic malignancies. This may be especially the case in suspected head and neck malignancies. However, this testing lacks specificity and may only be useful to identify promising sites for biopsy [11]. Although the ancillary investigations are useful they pose a problem of high false positive rate but the combination of PET/CT may reduce the false-positive rate to a great degree.

Depending on the clinical situation, further imaging studies may include computed tomography of the chest or breast magnetic resonance imaging .The therapy in CUP's should be tailored on an individual basis according to the diagnosis and prognosis of the disease. . Patients with poor prognosis CUP have just a 8 month survival rate hence better diagnostic and treatment modalities are needed [13]. The 10–15% cases of CUP patients who are of the favorable risk group should be treated similar to patients with equivalent known primary tumors with metastatic disease [11]. The patients with poor-risk CUP have a dismal prognosis despite all the therapeutic assistance available in clinical studies [11, 12]. Hence although a CUP has bad prognosis in general, if somehow an early clue to its origin can be obtained, by minimally invasive procedures like FNAC, the clinician can get a direction to pursue the patients treatment and to save his life.

## CONCLUSION

Cancers with unknown primary form a minimal but significant part of the routine OPD cases needing thorough investigation and follow-up. Invasive investigation modality like FNAC plays a very important role in giving an idea about the origin of the tumor when both clinical suspicion and radiological investigations fail. Even after commencement of chemotherapy the prognosis of such tumors is not very good, hence modalities for earlier detection and targeted treatment are the need of the hour.

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