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Multiple primary malignant neoplasms in a nonagenarian : Case report and review of literature

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Abstract: *Multiple primary malignant neoplasms are uncommon, but the incidence is increasing owing to increased long term survival amongst cancer patients, longer life expectancy and better diagnostic techniques. They may be metachronous (i.e. occurrence 6 months or more after detection of primary malignancy) or synchronous (occurrence within 6 months of detection of primary malignancy). Here, we present a case of a 94 year old male, diagnosed to have follicular carcinoma of thyroid in 2004 and undergone left hemi thyroidectomy for the same, with metachronous primary Chondrosarcoma involving the left hip bone in 2015 & Ewing's sarcoma of right clavicle in 2017 with metastatic bilateral diffuse pulmonary infiltrates. The tumours were histologically distinct from the primary thyroid neoplasm, hence careful evaluation of the secondary primary malignancies is essential to treat them accordingly without dismissing them as metastases. Although surgery was advisable in this patient, he refused to undergo further surgical interventions and died of respiratory distress & carcinomatous cachexia in early 2018. Very scant data and studies are available on the development of multiple primary malignant neoplasms especially in the elderly population and the possibility of older cancer patients being at higher risk for developing second primaries.*

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I. Introduction

Billroth first described multiple primary malignant neoplasms(MPMN) in 1889[1]. Single or multiple organs may be involved and they may be synchronous or metachronous. The current criteria for the diagnosis of MPMNs, which were established by Warren and Gates[2], are as follows: i) Each of the lesions must be malignant; ii) each of the lesions must exhibit distinctively different pathology; iii) and metastases from the prior malignancies must be excluded. Amongst patients diagnosed to have MPMN, dual cancers are most common, triple primaries in 0.5% of cases and quadruple or quintuple primaries occur in less than 0.1% of patients[3]. The relative risk of developing a second primary malignancy increases by 1.111-fold every month from the detection of the first primary malignancy in any individual[4]. The present study reports a rare case of a patient exhibiting three MPMNs and the final diagnosis was established based on histopathology. Written, informed consent was obtained from the patient.

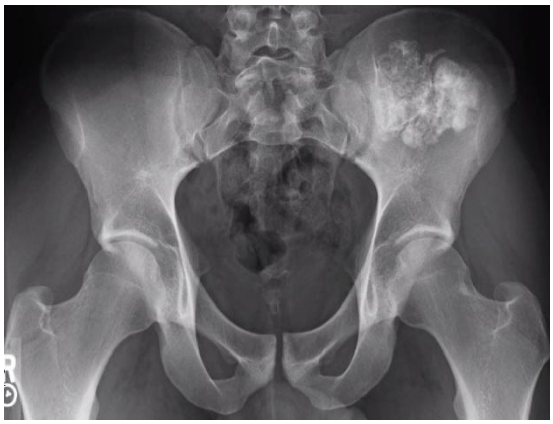
II. Case History

Presenting complaints & Family history:A 94 year old male, resident of western India presented to our hospital with complaints of intermittent fever, giddiness, malaise, difficulty breathing while performing activities of daily living since six months and a large, painless, hard, non-tender swelling on the right side of neck with gradual increment in size over a 10 month period. He denied any tobacco use or alcohol consumption in the past and had a negative family history for thyroid disorders or neoplastic diseases. He had no significant past medical history for co-morbidities.

First tumour:the first tumour to be identified was Follicular carcinoma (CA) involving the left lobe of thyroid in November 2004. The patient presented to a primary care hospital with complaints of palpable neck swelling over left side of neck with associated dysphagia, hoarseness of voice and generalized weakness. Ultrasound of the neck was suggestive of asymmetric enlargement of left lobe of thyroid with multiple nodules of different sizes varying from entirely cystic to solid nodules with involvement of level II & III cervical lymph nodes. Thyroid function tests revealed Total triiodothyronine (T3) level - 129ng/dL [Normal range: 60-181], Total thyroxine (T4) – 6.30 µg/dL [Normal range: 4.5-10.9]& Thyroid stimulating hormone (TSH) – 0.87 µIU/mL [Normal range: 0.35-5.5], all within normal limits.Patient was diagnosed to have follicular carcinoma of thyroid by fine needle aspiration cytology (FNAC)& according to tumour, node, metastasis (TNM) system was classified as $T_3N_{1b}M_0$, Stage III[5]. The tumour was successfully resected in November 2004 (left hemi-thyroidectomywith both left parathyroid resection) and subsequent histopathological examination revealed

minimally invasive differentiated follicular CA with capsular and vascular invasion. Patient was asymptomatic since &discontinued regular follow-up and received no further treatment for the same.

Second tumour: In November 2015, patient presented to our hospital with complaints of left dull-aching hip pain. Plain radiograph of left hip revealed a large mass arising from left iliac bone with sclerotic areas and hazy cortical irregularities with periosteal new bone formation suggestive of chondrosarcoma. Diagnosis was confirmed by FNAC and using the Enneking staging system6 was classified as Stage Ib (i.e. low grade tumour). Patient was advised surgical excision of the tumour, but did not give consent for the same and was managed conservatively. Patient was scanned for regional metastasis and was negative for the same.



Third tumour: In December 2017, patient presented with a palpable mass over the right side of neck in supra-clavicular region. Ultrasound of neck revealed a large heterogenous solid cystic lesion in right supra-clavicular region with internal vascularity, displacing carotid artery and internal jugular vein, with underlying right clavicle appearing irregular. Origin of the mass could not be traced, hence a Computerised tomographic (CT) scan of neck was done which showed a malignant mass sized 6.7 x 8.8 x 7.6cm arising from medial part of right clavicle with right supra-clavicular lymph nodal involvement. Diagnosis of metastatic metachronous Ewing's sarcoma was established following FNAC. Chest radiograph & screening CT scan showed right apical pneumothorax with bilateral ill-defined non-homogenous opacities suggestive of multiple metastases. According to the American Joint Committee on Cancer (AJCC)staging system[7], patient was classified as having $T_2N_1M_{1a}$, Stage IVb, Grade 3. Although, Fluorodeoxyglucose positron emission tomography (FDG-PET) scanning and surgery was considered necessary, negative consent was given by the patient for any form of further intervention & was managed palliatively. Patient died consecutively following respiratory distress and carcinomatous cachexia in January 2018.

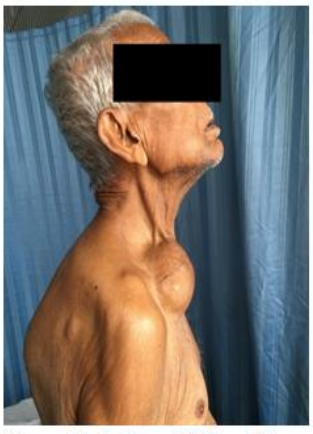


Figure: 1(Lateral view) Neck swelling.

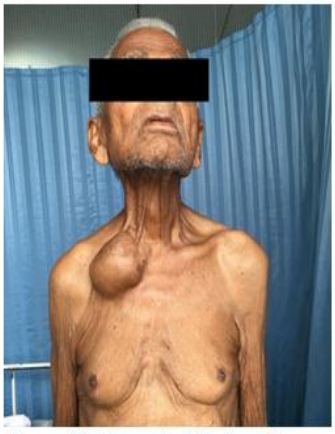


Figure: 2(Anterior view) Neck swelling

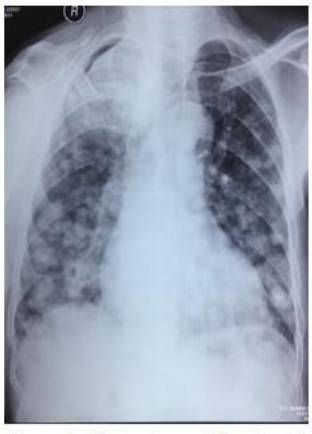
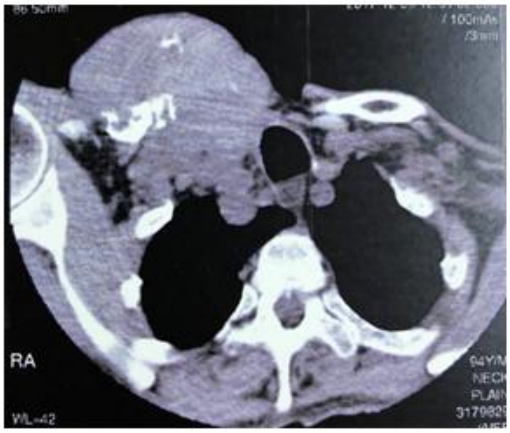


Figure: 3 ;Chest radiograph showing right upper zone pneumothorax with bilateral lung fields ill-defined homogenous opacities giving it a cannon-ball appearance suggestive of multiple lung metastases.



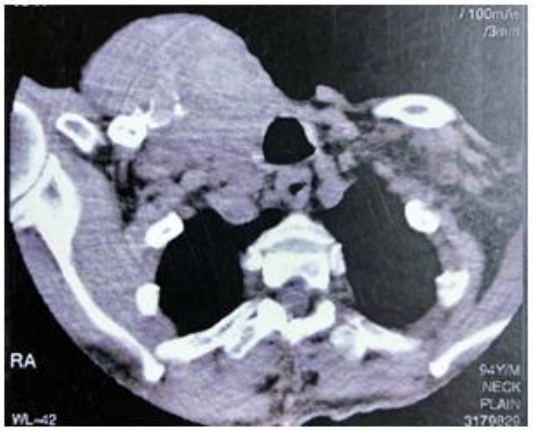


Figure: 4 & 5 ; Computerised tomography (CT) scan of neck plain : Malignant mass arising from medial part of rightclavicle with supraclavicular lymph nodes involved; posteriorly extending into right paratracheal region touching the internal jugular vein & brachiocephalic artery; medially mass is anterior to right border of sternum; inferiorly extendsinto the pectoralis major and superiorly touching the right sternocleidomastoid muscle, mass also touches the right lobeof thyroid and causing mild deviation of trachea to the right.

III. Discussion

The current study presents the case of a patient with three pathologically verified primary tumours, one in the thyroid gland and others in the left iliac and right clavicular bones. All tumours were malignant with extension beyond their organ of origin, consistent with the definition of MPMNs. The prevalence of triple primaries, age of the patient and the unusual organs of origin, make the case academically interesting.Multiple primary malignancies have been increasingly reported in recent years[7-9], however, it remains rare to encounter a patient with three primary malignancies.

The mechanisms responsible for the development of MPMNs are not fully understood; however, frequently implicated factors include genetic susceptibility, immune status and previous intensive exposure to carcinogens, such as chemo- and/or radio-therapy used to treat tumors[8,10]. A number of hereditary conditions are also associated with multiple primary malignant neoplasms; for example, Li-Fraumeni syndrome, a rare disorder that greatly increases the risk of developing various types of cancers. The types of cancer most often associated with this syndrome are breast cancer, osteosarcoma and soft tissue sarcomas, as well as brain tumours, leukemia and adrenocortical carcinoma[11].

Quantitative data on the occurrence of MPMN exists; however, no emphasis has been placed on the presence of MPMN among older-aged cancer patients. Studies and research on MPMN do not address the potential of older cancer patients being at a higher risk of second primaries. The literature regarding MPMNs recommends that secondary primary cancers should be resected as early as possible and states that the probability of successful treatment is similar to that of a single cancer[12]. Also, long-term follow-up and screening strategies are important for patients who have undergone curative resection of malignancies. Healthcare workers should consider that the prevalence of multiple primary malignancies appears to be increasing and, thus, should be considered to differentiate secondary primary cancer from metastatic cancer.

Zhao J et al[13] reviewed a rare case of eight multiple primary malignant neoplasms in a female patient over a >32 year period. The patient was co-operative and attended the hospital frequently, and was therefore diagnosed early, all of the tumours removed and successfully treated. Thus, a poor prognosis is not necessarily indicated in a patient presenting with multiple primary malignancies, provided timely diagnosis and adequate treatment are provided.

IV. Conclusion

Older patients with a malignancy might be at greater risk of developing a second one. In patients presenting with an additional tumour, it is important for healthcare workers to consider the possibility of a metastatic or novel primary malignancy. Ageing increases the incidence of cancer and the occurrence of MPMN. The frequency of persons with multiple cancers will increase owing to prolonged life-span, improved diagnostic modalities and prompt therapeutic management. Multiplicity of neoplasms does not necessarily indicate a poor prognosis. Prolonged follow-up after surgical therapy should be considered. Further investigations on genetic abnormalities are expected to reveal the mechanism of onset of multiple primary cancers and provide a way of predicting malignancies in the future.

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