A tale of synchronous lung carcinoma and diffuse large B-cell lymphoma of ileum: A rare combination

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ABSTRACT

The occurrence of multiple malignancies in the same patient being synchronous or metachronous is a rare event. The incidence of multiple malignancies varies with age, sex, geographic origin, and site and type of tumors. The pathogenetic etiology may be multifactorial and include genetic predisposition, immunodeficiency, radiation therapy, chemotherapy and various infectious agents. It is crucial to recognize synchronous malignancies because course of treatment and management is difficult. The synchronous occurrence of pulmonary squamous cell carcinoma and ileal diffuse large B-cell lymphoma (DLBCL) is not reported in the Indian medical literature until today; hence, we publish this case for its rarity.

KEY WORDS: Diffuse large B-cell lymphoma, synchronous malignancies, squamous cell carcinoma

INTRODUCTION

Multiple malignancies in the same patient can present within 6 months of diagnosis of primary when it is considered to be synchronous occurrence. The second malignancy may also occur after 6 months of diagnosis or treatment of the primary when it is cited to be metachronous. The incidence of multiple malignancies is rare and the etiology is multifactorial. Diagnosis of the same is challenging with respect to characterizing the tumors as two independent primary malignancies with exclusion of metastasis. Treatment and prognosis is also variable.

Here we present a unique case with two tumors presenting synchronously.

CASE REPORT

A 68-year-old male, known smoker, alcoholic and hypertensive on regular medication, presented with history of cough, shortness of breath, wheezing of 6 months duration associated with occasional bouts of hemoptysis. He had no past or family history of malignancies. No history of generalized lymphadenopathy. The results of the laboratory tests were within normal limits except for a mild normocytic anemia. Clinical and radiological findings favored the diagnosis of carcinoma lung stage T1N0M0. A whole body PET-CT was performed which showed a hypermetabolic cavitating spiculated mass lesion in the upper lobe of right lung measuring 3.6 × 2.5 cm suggestive of primary lung neoplasm and a hypermetabolic eccentric wall thickening in short segment of distal ileal loop of uncertain nature [Figures 1 and 2]. Prior to resection of small bowel mass a contrast-enhanced CT enteroclysis was performed on a 64-slice scanner with axial and coronal reformations which showed an eccentric soft tissue lesion towards terminal ileum measuring 18 mm in length and 10 mm in thickness. The patient underwent VATS for right upper and middle lobectomy with mediastinal nodal clearance and laparoscopy-assisted ileal loop resection and anastomosis.

The ileal mass was subjected to frozen section examination to ascertain its nature. Segment of ileum measured 8 cm in length and showed a relatively well circumscribed polypoidal grey white submucosal nodule measuring 4 × 2.5 × 2 cm. A provisional diagnosis of poorly differentiated malignancy was rendered.
FFPE sections from ileal mass showed diffuse expansion of lamina propria, submucosa as well as the muscle layer by sheets of large cells. These neoplastic cells possessed moderate to abundant amount of cytoplasm with vesicular nuclei and prominent nucleoli. Some of these cells exhibited irregular, cleaved, lobated nuclei. Numerous mitotic figures were identified. However, there was no evidence of squamoid or glandular differentiation [Figure 3a and b]. The overlying mucosa showed partial villous atrophy. The mesenteric lymph nodes identified showed reactive changes. Immunohistochemically, the neoplastic cells were positive for LCA, CD20 and CD79a. There was no expression of CK20, CK5, CK7, TTF-1, CD3, CD5, CD30, EMA and ALK1. Ki 67 index was 75%, thus confirming a diagnosis of diffuse large B-cell lymphoma (DLBCL) (anaplastic features) [Figure 4] and not metastatic squamous cell carcinoma. A bone marrow aspiration and biopsy was performed which showed no marrow involvement.

Subsequently, the lobectomy specimen consisted of upper and middle lobe of lung together measuring 15 × 13 × 3 cm. Cut section exhibited a grey white tumor in apical region of right upper lobe measuring 3 × 2 × 2 cm. The histopathologic examination of lung tumor revealed a moderately differentiated invasive squamous cell carcinoma [Figure 5]. There was no evidence of metastasis in the hilar nodes. The bronchial resected margins and pleural surface were free of tumor.

Following surgery, the patient received six cycles of CHOP chemotherapy at standard doses and his follow up over 18 months remains uneventful.

**DISCUSSION**

Gluckmann classified second malignancies as synchronous, when two malignancies are present simultaneously or occur within a 6 month period of diagnosis of first tumor and metachronous when second malignancy is diagnosed beyond 6 months interval. Whole body PET-CT detects new unexpected 18 F-FDG avid primary malignant tumors in at least 1.2% of patients with cancers.[1] Extensive search of the literature revealed few cases showing coexistence of different types of lung carcinomas and malignant lymphomas as listed in Table 1.

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**Figure 1:** Fused sagittal PET/CT images shows a hypermetabolic centrally necrotic mass lesion in apical segment of right upper lobe

**Figure 2:** Fused sagittal PET/CT images show intensely hypermetabolic short segment small bowel thickening in terminal ileum

**Figure 3:** (a) Sections showing ileum with lamina propria showing involvement by neoplastic cells (H and E, ×10). (b) High power view showing neoplastic cells with large nuclei and irregular nuclear membrane and conspicuous nucleoli (H and E, ×40)

**Figure 4:** Large cells showing diffuse membrane positivity for CD20 (IHC, ×40)
Figure 5: Section from lung showing a moderately differentiated invasive squamous cell carcinoma (H and E, ×40)

Table 1: Synchronous malignancies involving different types of lung cancers and lymphomas

| Authors            | Synchronous Malignancies                                      |
|-------------------|--------------------------------------------------------------|
| Hyeon et al.[3]   | Synchronous double cancer of rectal diffuse large B-cell lymphoma and squamous cell carcinoma of lung (H and E, ×100) |
| Chanel et al.[5]  | Synchronous pulmonary adenocarcinoma and extranodal marginal zone lymphoma of MALT type |
| Rothenburger et al.[6] | Non-Hodgkin’s lymphoma coexisting with NSCLC           |
| Rubiales et al.[9] | Synchronous occurrence of a small-cell lung cancer and a Hodgkin lymphoma |
| Sun et al.[10]    | Synchronous occurrence of pulmonary SCC and MCL of lymph node |

Gastrointestinal tract is the most frequently involved extra-nodal site in non-Hodgkin’s lymphoma. Primary lymphomatous tumors constitute about 9% of all gastrointestinal tract tumors, stomach being the most common (50-60%) followed by small intestine (30%). Most of gastrointestinal lymphomas are non-Hodgkins lymphomas and are commonly derived from B cells from the lymphoid tissue present in the lamina propria and submucosa. Small bowel lymphoma most commonly involves the terminal ileum and can present as circumferential mass, narrowed lumen or aneurysmal dilatation, and cavitary lesions.[4] Pathogenetic factors that can induce synchronous malignancy include genetic predisposition, immunodeficiency, and various infectious agents including EBV. Lifestyle factors such as smoking, alcohol, exercise and diet, clearly play a role in a long list of cancers. Further individuals with genetic predisposition to multiple neoplasms, polymorphism for metabolizing enzymes, radiation and chemotherapy used to treat a primary cancer can be the causative factors. Our patient is a known smoker, alcoholic and had not received prior chemo or radiotherapy. Although many genetic perturbations have been detected to date, the relationship between synchronous tumors remains unclear. We have not studied the genomic alterations between the lung tumor and ileal lymphoma, however, some authors have shown such comparison in other synchronous malignancies. One study described genetic aberrations and the degree of genomic association between 23 synchronous breast cancers from 10 patients using metaphase comparative genomic hybridization and array comparative genomic hybridization (aCGH). The authors showed that genetic abnormalities in synchronous breast cancers, when compared to their matched counterparts, were found to have a common core set of genetic alterations, with additional unique changes present in each tumor.[9] A therapeutic dilemma exists in deciding the course of treatment in patients with synchronous malignancies. More cases should be reported in the literature so as to formulate a definite line of management in such difficult scenarios.

CONCLUSION

Registry on patients with second cancers including treatment received and family history will be a valuable resource for assessment of risk factors and for evaluation of genetic abnormalities in these tumors. This information will be useful for planning clinical trials and to implement targeted therapy.

ACKNOWLEDGEMENTS

We would like to thank Mr. Sudhakar, Mr. Ravinder, Mrs. Ajitha for the technical support extended.

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How to cite this article: Fonseca D, Musthyala B, Ahmed F, Murthy SS, Raju K. A tale of synchronous lung carcinoma and diffuse large B-cell lymphoma of ileum: A rare combination. Lung India 2015;32:398-401.

Source of Support: Nil, Conflict of Interest: None declared.