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Small Cell Lung Carcinoma and Synchronous Rectal Adenocarcinoma and Jejunal Gastrointestinal Stromal Tumor Present in a Patient With History of Laryngeal Squamous Cell Carcinoma

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Abstract. *Background: The synchronous diagnosis of two or more primary malignancies in a patient is overall rare. Case Report: We report such a case of a 67-year-old male smoker with a history of laryngeal squamous cell carcinoma. He was incidentally identified through follow up computed tomography to have three masses in the lung, rectum and jejunum, respectively. Biopsies were performed and demonstrated synchronous lung small cell carcinoma (pT1bN0) and rectal adenocarcinoma. The patient underwent fractionated stereotactic radiation (FSRT) to the pulmonary tumor and chemotherapy with cisplatin and etoposide followed by laparoscopic rectum low anterior resection and small bowel segmental resection. Final pathology diagnoses confirmed synchronous microsatellite stable (MMS) moderately differentiated adenocarcinoma of the rectum (pT3N1b) and jejunal gastrointestinal stromal tumor (GIST), spindle cell type (pT2N0). At 8 months follow up post-surgery, the patient was doing well and no tumor recurrences were identified. Conclusion: To the best of our knowledge, this is the first documented case of synchronous primary small cell lung carcinoma, rectal adenocarcinoma, and GIST in the English literature. The rarity, diagnosis and treatment challenges of these entities are discussed.*

Lung cancer is the leading cause of cancer death and colorectal cancer is the fourth leading cause of cancer death in the United States (1). Small cell Lung carcinoma (SCLC) originates from neuroendocrine cells (2) and is a high grade malignant epithelial tumor. Colorectal carcinoma (CRC) arising from the mucosal epithelium is the most common type of colorectal malignancy (3). Gastrointestinal stromal tumor (GIST) is a mesenchymal neoplasm with variable clinical behavior characterized by differentiation of the interstitial cells of Cajal in the gastrointestinal wall. Synchronous cancers are defined as two or more primary neoplasms diagnosed in a single patient within six months (3). Sparse literature reviews estimate the occurrence of CRC with another primary tumor to be around 3.5% (4). Synchronous SCLC and adenocarcinoma of the rectum is exceedingly rare and only one case has been reported in the English literature through PubMed search (2). Herein, we report a case of a 67-year-old man with a history of laryngeal squamous cell carcinoma. Through his routine follow up, we found that he had synchronous primary SCLC, rectal adenocarcinoma, and jejunal GIST. To the best of our knowledge, this is the first documented case of such three synchronous primary neoplasms present in follow up for prior history of cancer. The rarity, diagnosis and treatment challenges of these entities are discussed.

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Case Report

A 67-year-old male current smoker (one pack of cigarettes daily for 37 years) with a history of laryngeal squamous cell carcinoma treated by chemoradiation presented for twenty years follow up post therapy. He had a family history of heart disease and lung cancer. He was in a good state of health and had an episode of diverticulitis, which brought above a CT scan of the abdomen and pelvis that identified an incidental 2 cm jejunal mass suspicious for neuroendocrine tumor. A colonoscopy was done for the evaluation of the diverticular disease that identified a rectosigmoid junction adenocarcinoma

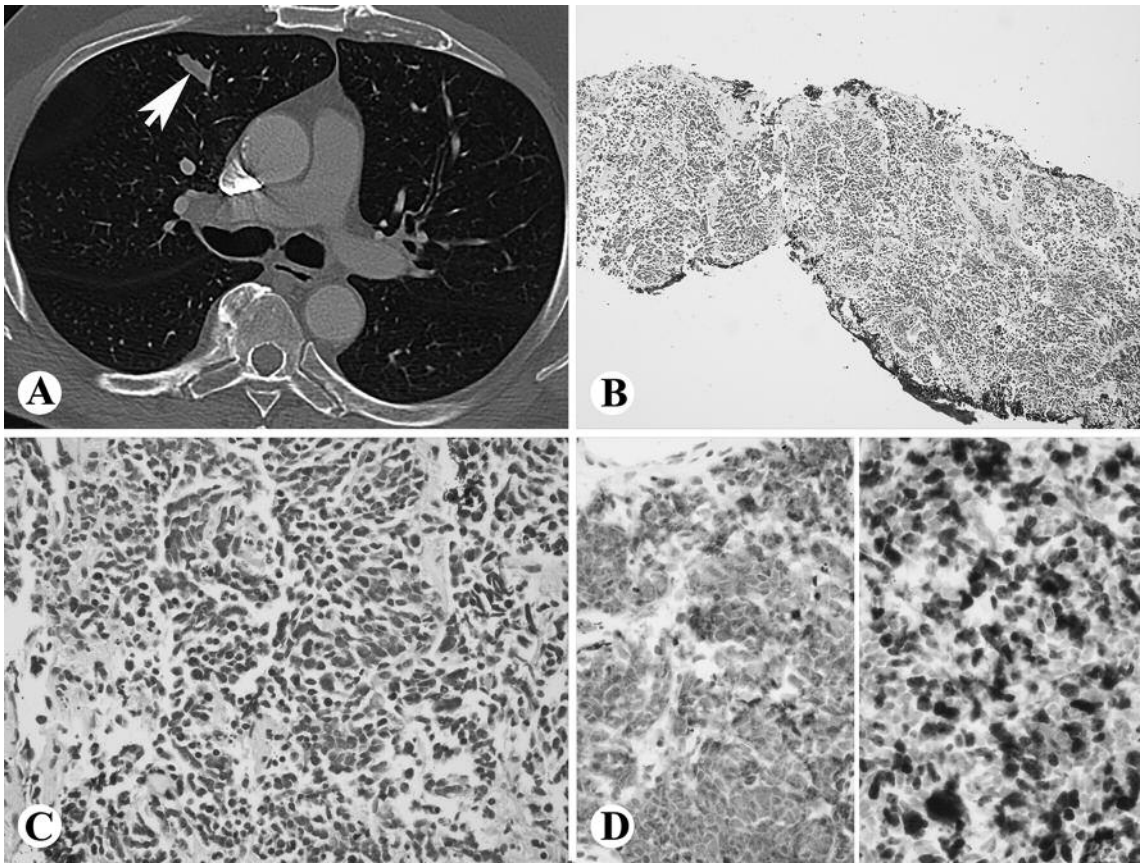

Figure 1. *Lung small cell carcinoma. A) CT scan showing a lung nodule (arrow); B-D) Fine needle biopsy showing histological features diagnostic of neuroendocrine carcinoma, small cell type (B and C, H&E stain), positive synaptophysin immunoreactivity (D, left) and 80% of Ki-67 index (D, right) (B, 100×; C-D, 400×).*

not amendable for endoscopic resection. A computed tomography (CT) scan of the chest was performed as part of the rectal cancer work up, which identified new lung lobular branching opacity resulting from obstruction of a subsegmental anterior right upper lobe segment bronchus (Figure 1A). Positron emission tomography (PET) scan revealed a fluorodeoxyglucose (FDG)-avid anterior right upper lobe 1.3 cm nodule that was worrisome for malignancy, possibly being metastasis of the laryngeal squamous cell carcinoma. Right upper lobe lung CT guided fine needle core biopsy was performed. Histologically, the neoplastic cells showed a morphology of small cell carcinoma (Figure 1B and C). The tumor cells were positive for synaptophysin (Figure 1D, left), chromogranin, and TTF1, with a high Ki-67 index (90%) (Figure 1D, right); negative for p40 and CDX2. The pathologic diagnosis was lung small cell carcinoma (p T1b). Histologically, the rectal mass (Figure 2A) showed morphology of invasive adenocarcinoma, moderately differentiated, intestinal type (Figure 2B) arising in a tubular adenoma with high grade dysplasia. The rectal adenocarcinoma was microsatellite stable (MMS) with intact nuclear expression of the DNA mismatch repair (MMR) proteins including MLH1, MSH2, MSH6 and PMS2; suggesting a very low possibility of Lynch Syndrome.

Multidisciplinary tumor board discussions were performed to coordinate care of the three primary tumors. Since there were low risks for bleeding and obstruction from the rectal adenocarcinoma or the jejunal mass, treatment for the SCLC was prioritized. Patient was deemed medically inoperable for SCLC, thus, three fractionated stereotactic radiation (FSRT) and chemotherapy with cisplatin and etoposide were initiated. Although the patient was not tolerating the chemoradiation therapy well, there was a good disease response. The patient underwent laparoscopic low anterior sigmoid-rectal resection and small intestinal segmental resection. Multiple specimens were sent for pathological evaluation.

Pathological assessment of the rectal resection revealed a 3.0×2.7×0.5 cm mass below the peritoneal reflection. Three of thirty-four lymph nodes were positive for carcinoma. Margins were uninvolved. The tumor stage was pT3N1b.

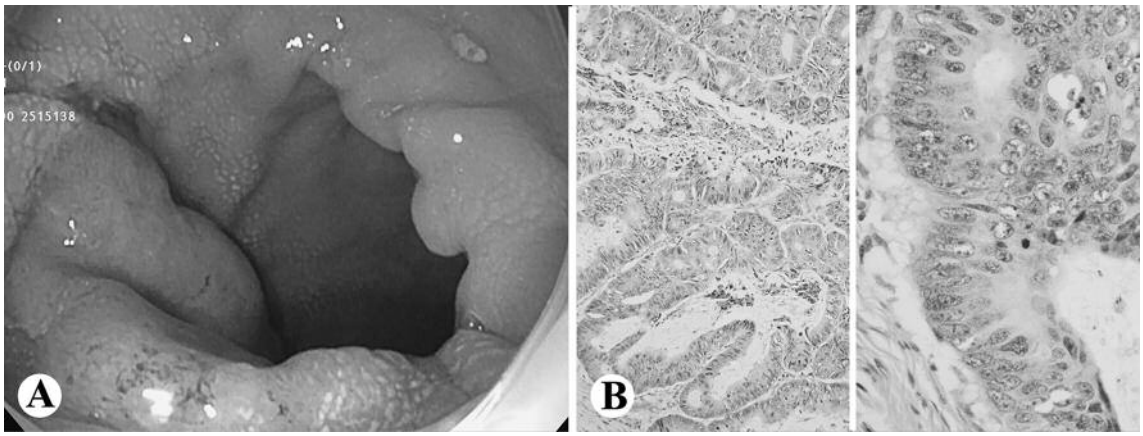

Figure 2. *Rectal adenocarcinoma. A) Colonoscopy showing a rectal mass. B) Biopsy of the rectal mass showing a moderately differentiated, intestinal type adenocarcinoma (H&E stain, left, 100×; right, 400×).*

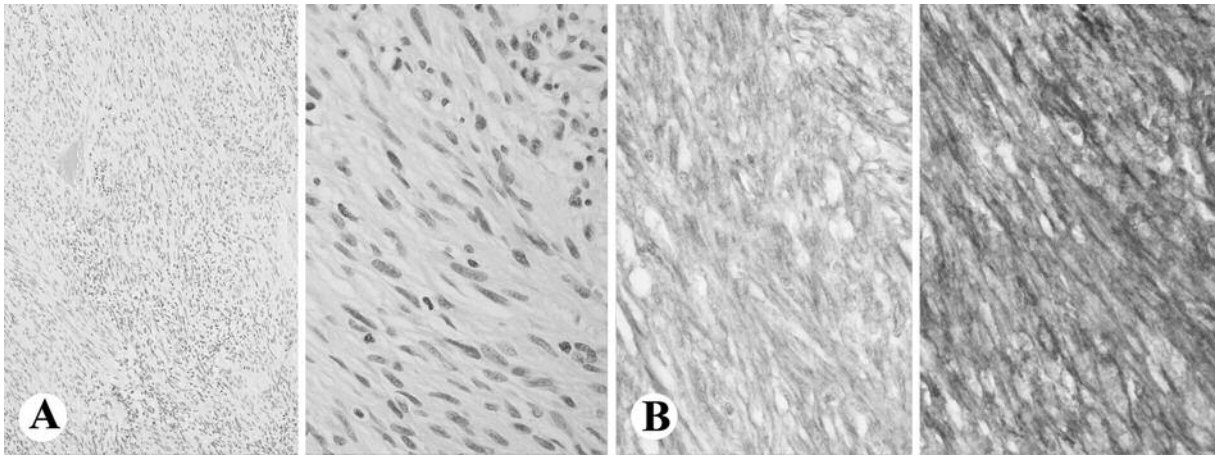

Figure 3. *Jejunal gastrointestinal stromal tumor. A) Histologically, the jejunal tumor showing spindle cell proliferation (A, H&E stain). B) The tumor is positive for DOG1 (left) and CD117 (right) by immunohistochemistry (A, left,100×; A, right and B, 400×).*

Gross examination of the small bowel specimen found a 2.2×1.7×1.3 cm nodule within a portion of the proximal jejunum. In histology, H&E staining revealed a low grade (G1), spindle cell type of gastrointestinal stromal tumor (Figure 3A and B). Immunohistochemical studies showed that the tumor was positive for DOG1 (Figure 3C) and KIT (CD117) (Figure 3D). The tumor stage was pT2N0.

The patient had an uneventful postoperative recovery and was given adjuvant chemotherapy with cisplatin and etoposide for 4 cycles. Capecitabine for the colon cancer was added as the patient declined to receive FOLFOX (folinic acid, fluorouracil, and oxaliplatin) with concerns more toxicity. At 8 months follow up post-surgery, the patient was doing well and regained 75% of his strength. No significant tumor recurrence was identified on CT images.

Discussion

The incidences of distant metastases of primary laryngeal squamous cell carcinoma were reported as 3.7 to 16% (5). Our patient had a history of laryngeal carcinoma for 20 years with no detailed information of the location within his larynx. Interestingly, at 20 years follow up post chemoradiation therapy, no recurrent laryngeal carcinoma or regional metastasis was identified. However, three additional masses were incidentally identified in the lung, rectum, and jejunum, respectively. Through multidisciplinary tumor board discussion, three biopsies were performed and confirmed synchronous SCLC, rectal adenocarcinoma and jejunal gastrointestinal stromal tumor. To the best of our knowledge, cases of synchronous primary rectal adenocarcinoma, SCLC and jejunal

gastrointestinal stromal tumor have not been documented in the English literature through a PubMed search.

Due to the significant differences in tumor morphology of each entities, biopsies with histological assessment are the key to the correct diagnoses. Clinicians and pathologists need to be aware that one or multiple other primary tumors can be seen during a regular follow up of cancer after therapy. In our case, the incidentally identified 1.3 cm nodule in the lung was cytologically and histologically evaluated through CT-guided fine needle aspiration and biopsy. Different to the metastatic squamous cell carcinoma of the larynx, the tumor had a rosetting appearance consisting of small cells with scant cytoplasm, ill-defined cell borders, finely granular nuclear chromatin, with absent or inconspicuous nucleoli. The tumor cells are positive for the neuroendocrine markers including synaptophysin and chromogranin, and positive for TTF1 making the primary lung neuroendocrine carcinoma. The available predictive models for colorectal carcinoma are based on the evaluation of symptoms, and their diagnostic accuracy is limited (3). The diagnosis of rectal adenocarcinoma in our case is mainly based on colonoscopy and biopsy. Metastatic carcinoma is commonly seen in a jejunal mass in adult patients with a history of carcinoma, but our CT imaging findings were more consistent with a neuroendocrine tumor than metastatic carcinoma. However, the morphology of the jejunal mass showed cytologically bland spindle cell proliferation with positive GIST markers including DOG1 and CD117, supporting the diagnosis of GIST (pT2N0), which is consistent with a separate primary tumor.

This is an unusual case, and the treatment is even more challenging. On its own, the SCLC is a highly fatal cancer, the combination of platinum and etoposide with thoracic radiation therapy being the most widely used regimen, with clinical trials consistently achieving median survivals of 18 to 24 months and 40% to 50% 2-year survival rates with less than a 3% treatment-related mortality (6). Colorectal carcinomas (CRC) have a more favorable prognosis, the five-year survival rate of stage IIIB CRC is 72% (7). Lastly, GIST is the most common mesenchymal tumor in the jejunum and at stage I, resection alone is an effective treatment. Through multidisciplinary discussions, the patient underwent FSRT, an effective treatment options for SCLC, in combination with chemotherapy with platinum and etoposide to control the SCLC and then, he underwent laparoscopic resection of the jejunal GIST and rectal cancer. At 8 months follow up post-surgery, the patient was doing well and no significant tumor recurrence was identified on CT images.

In summary, this report documents a rare and unusual case of synchronous primary SCLC, rectal adenocarcinoma and jejunal GIST incidentally identified in a 67-year-old male with previous history of laryngeal squamous cell carcinoma during the regular follow up. Sequential treatment with FSRT and chemotherapy prior to resection of the rectal carcinoma and GIST provided the patient individualized medical care. Overall, this case demonstrates the importance of identifying unique primary malignancies despite the relatively low incidence of occurrence in patients with a history of cancer, as the therapeutic approach and potential patient outcomes can be drastically impacted.

Conflicts of Interest

The Authors declare that they have no conflicts of interest in regard to this case report.

Author's Contributions

BL wrote the article; SS saw the patient and reviewed the article; MMM performed the surgery and reviewed the article; and JL made the diagnoses, collected and analyzed the data, wrote and finalized the article.

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