

CASE REPORT

Small cell lung cancer associated small bowel obstruction, a diagnostic conundrum: A case report

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Key clinical message

Small cell lung cancer (SCLC), a neuroendocrine aggressive subtype of lung cancer, is associated with paraneoplastic disorders in about 9% of patients. In this report, we describe a middle-aged man who presented with chronic bowel obstruction caused by chronic intestinal pseudo-obstruction (CIPO) due to SCLC.

KEYWORDS

bowel obstruction, chronic intestinal pseudo-obstruction, lung cancer, paraneoplastic, SCLC

1 | BACKGROUND

Small cell lung cancer (SCLC), a subtype of lung carcinoma, is characterized by its histological features of small, round to oval-shaped cells with scant cytoplasm and densely packed chromatin. It typically originates from neuroendocrine cells within the bronchial epithelium. SCLC is distinguished by its aggressive nature, rapid growth, early metastasis, and strong association with cigarette smoking. It comprises approximately 10%–15% of all lung cancers and is notable for its high propensity to spread to distant sites, often leading to widespread metastases at the time of diagnosis. SCLC demonstrates a

high responsiveness to initial chemotherapy and radiation therapy, although relapse is common, necessitating ongoing research efforts to improve treatment strategies and patient outcomes.^{1–3} SCLC is also known to present with a wide range of paraneoplastic syndromes, that can precede its clinical and radiological manifestation.⁴ Among its rare paraneoplastic syndromes is chronic intestinal pseudo-obstruction (CIPO).

The diagnosis and identifying the etiology of CIPO in adults can be challenging.⁵ CIPO can be due to a dysfunction in coordinated propulsive activity in the gastrointestinal tract, with clinical features of mechanical small bowel obstruction.⁶ This condition can affect any part of

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the gastrointestinal tract, including the esophagus, stomach, small intestine, and colon. Symptoms may include abdominal pain, bloating, nausea, vomiting, constipation, diarrhea, and malnutrition due to malabsorption. Diagnosis often involves a combination of clinical evaluation, imaging studies, and in some cases specialized tests to assess intestinal motility.^{7,8}

It is postulated that SCLC-associated CIPO originates from the neuroendocrine activity of cancer cells that results in formation of autoantibodies against neuroreceptors required for normal peristalsis of small intestine.⁹

2 | CASE HISTORY

A 55-year-old man presented to the emergency department with history of nausea, vomiting, abdominal pain and constipation for the past 3 days. It transpired that the patient had similar presentations, albeit less severe, in the previous weeks to the emergency room. Past medical history included obesity and prediabetes. Past social history included a 30-pack-year history of smoking. Upon examination the patient had normal vitals apart from tachycardia. Abdominal examination showed diffusely distended, mildly tender abdomen with no rebound tenderness, and overactive bowel sounds.

3 | METHODS

3.1 | Investigations

Blood investigations including liver and renal function tests, lipase, and calcium were within normal range. There were mildly elevated inflammatory markers with white blood cell count of 14.9 (normal range 4.5 to 11.0×10^9 /uL) and C reactive protein of 15 mg/L (normal <5 mg/L). Stool

tests for occult blood and calprotectin (a marker of bowel inflammation) were negative. *QuantiFERON-TB Gold* test was negative.

The patient received computed tomography (CT) scan with contrast of abdomen and pelvis which revealed features suggestive of small bowel obstruction (Figure 1).

Subsequently, the patient underwent upper and lower gastrointestinal endoscopies which were essentially unremarkable. Conservative management was offered to the patient, which had a relatively well response. Four days later, the patient was discharged home with a follow-up magnetic resonance imaging (MR) enterography (Figure 2). As a noninvasive imaging technique, MR enterography provides detailed views of the small bowel from various angles. This radiological technique enhances the ability to detect abnormalities and assess the extent of disease. It shows excellent soft tissue contrast, thereby making it easier to distinguish among normal and abnormal bowel wall thickening, inflammation, strictures, tumors, and other pathologies.^{10,11}

The results from MR enterography raised concerns of a possible underlying systemic pathology. Consequently, CT scans with contrast of the chest (Figure 3), abdomen, and pelvis were ordered.

Further investigation included bronchoscopy with endobronchial washing and brushing and endobronchial biopsy of the anterior segment of the right upper lobe that results from which were inconclusive. Therefore, the patient underwent endobronchial ultrasound-guided fine needle aspiration (EBUS-FNA) of right hilar and subcarinal lymph node which confirmed a cytological diagnosis of metastatic SCLC. Malignant cells staining was positive for neuroendocrine markers CD56 and synaptophysin (Figure 4).

Positron emission tomography CT scan (PET-CT) was ordered to assess the staging of the disease for further management and advise on prognosis. The findings were suggestive of extensive stage SCLC (Figure 5).

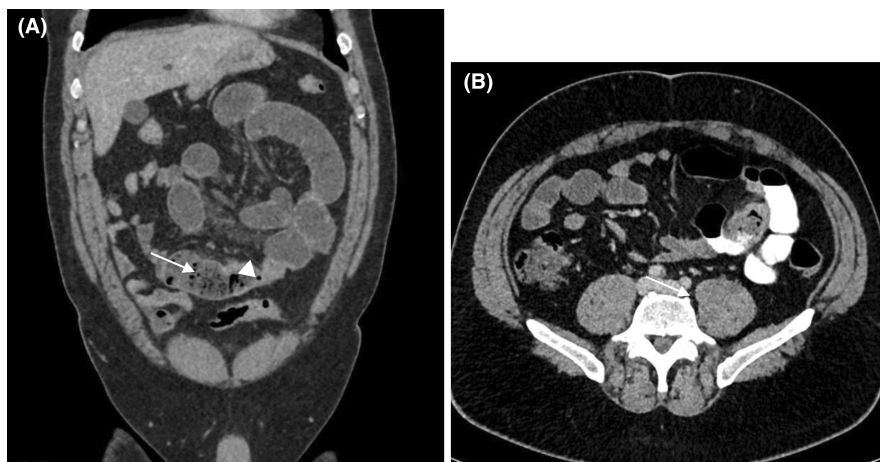


FIGURE 1 CT scan with contrast of abdomen and pelvis. (A) coronal view showing fecalization of the small bowel and dilated proximal segments (arrow), irregular wall thickening of the short segment distal ileum (arrowhead). (B) cross sectional view showing redemonstration of the irregular wall thickening of the short segment distal ileum with only partial narrowing of the lumen (arrow).

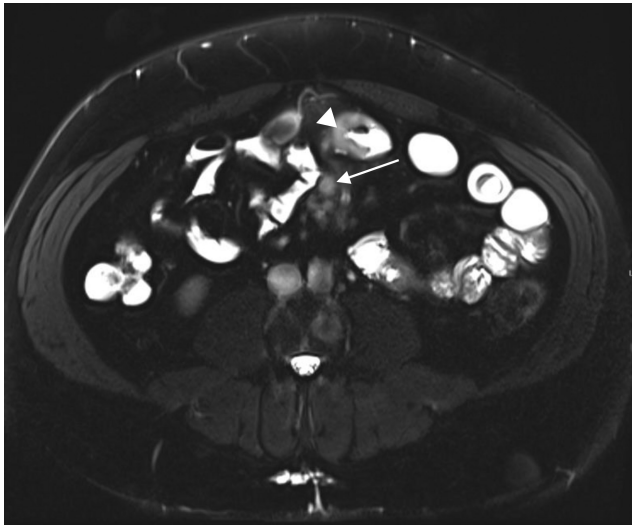


FIGURE 2 Axial T2 fat saturated image from the MR enterography study shows asymmetrical small bowel wall thickening (arrowhead) and adjacent mesenteric lymphadenopathy (arrow) with no significant mechanical cause for intestinal obstruction.

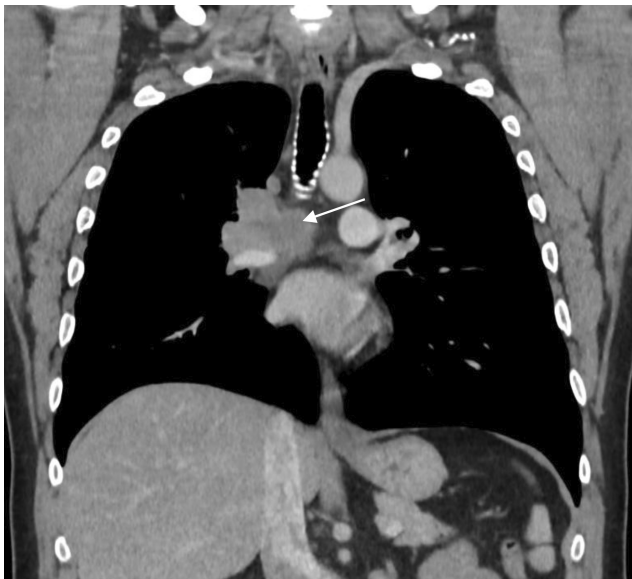


FIGURE 3 Coronal reformatted image of a contrast CT study of the chest shows a solid infiltrative right hilar soft tissue density mass invading the mediastinum (arrow).

3.2 | Treatment and progress

The treatment of this case involved a combination of immune check point inhibitors and platinum-based chemotherapy doublet which is the current first line therapy standard of care for SCLC with extensive stage.¹²⁻¹⁴ The intervention included a combination of carboplatin, etoposide, and atezolizumab. After three cycles of the intervention, PET scan showed good response to treatment

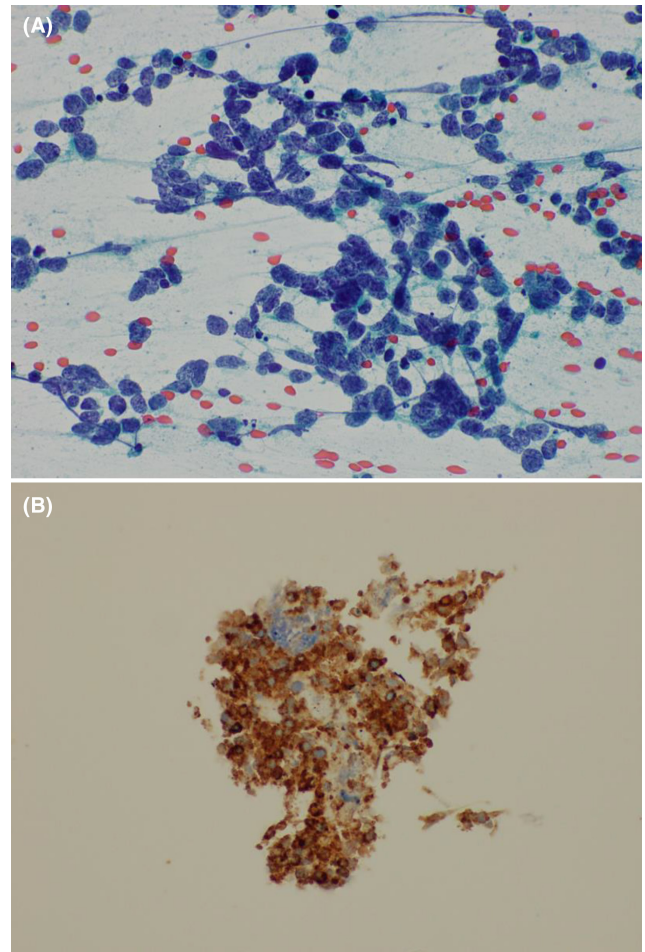


FIGURE 4 EBUS-FNA of mediastinal lymph node. (A) smear of small cell carcinoma cells admixed with small lymphocytes (Pap stain) at $\times 800$ magnification. (B) cell block from the sample showing strong and extensive staining with Synaptophysin (immunohistochemical stain with diaminobenzidine end product) at $\times 400$ magnification.

in comparison with the previous metabolic activities seen in the thoracic and the adrenal glands. Of note, there was also a resolution of the previously seen intense segmental small bowel uptake. Additionally, there was a 1 cm sized residual uptake at one of the involved organs (Figure 6). In addition to the pleasant radiological findings, there was significant improvement in the patient's symptoms of small bowel obstruction associated and a general improvement in overall health and wellbeing.

4 | DISCUSSION

CIPO carries a high morbidity and mortality and can be difficult to diagnose since it can present with recurrent episodes of intestinal obstruction in the absence of an obstructive lesion that causes complete bowel blockage.¹⁵

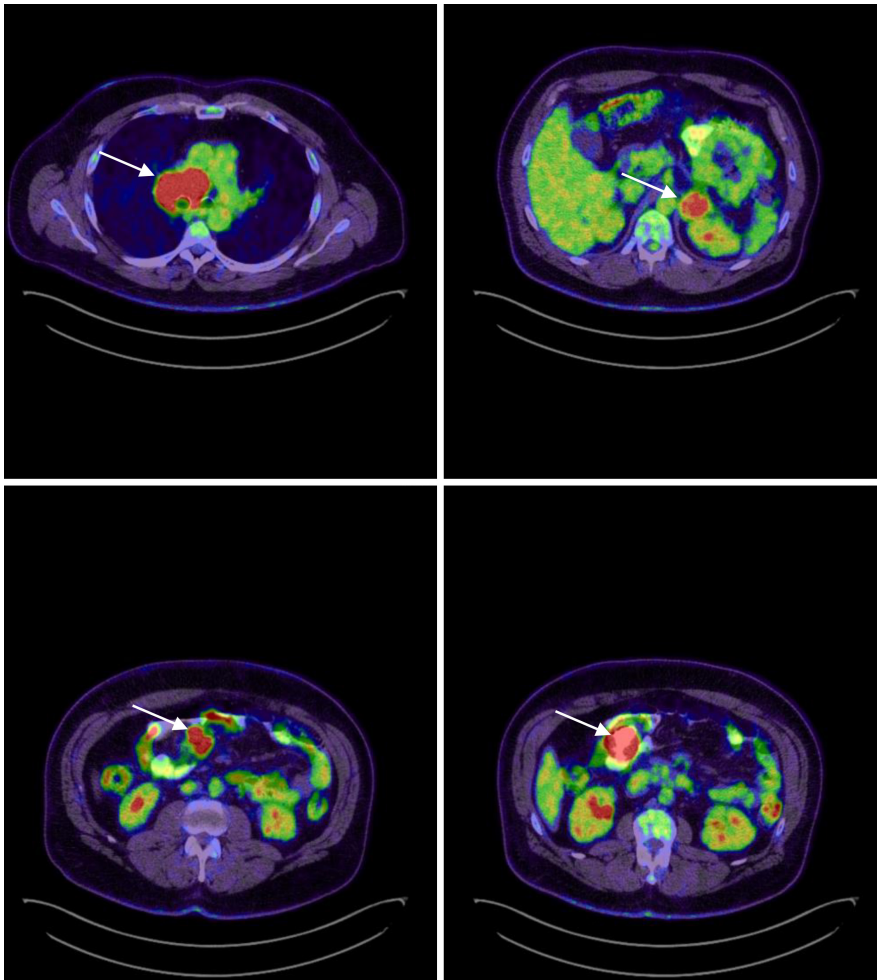


FIGURE 5 PET-CT scan showing hot uptake in different organs. Top left: Right hilar mass. Top right: Left adrenal mass. Bottom left: Mesenteric lymph nodes. Bottom right: Bowel mass.

Due to the wide range of aetiologies associated with bowel obstruction, particularly CIPO, a significant proportion of patients end up with unnecessary investigations including laparoscopy and laparotomy.^{16–18}

Nevertheless, there is growing awareness among clinicians that paraneoplastic syndromes of SCLC might present with CIPO, hence it must be included in the list of differential diagnosis and diagnostic work ups.^{18,19} Differentials of SCLC include pulmonary hamartoma, chronic eosinophilic pneumonia, actinomycosis, aspergillosis, carcinoid tumorlet, cryptococcosis, parasitosis, inflammatory myofibroblastic tumor, and others.²⁰ It is postulated that almost 50% of CIPO cases are resulted from systemic diseases of neurological, paraneoplastic, autoimmune, metabolic, or infectious origins.²¹ The paraneoplastic activity of SCLC arises from the neuroendocrine nature and the significant genomic activity of this type of malignancy. Neurologically mediated CIPO caused by SCLC can be due to the production of specific antibodies, namely anti-Hu or type 1 antineuronal nuclear antibody (ANNA-1), that have been frequently demonstrated in preclinical models and patients with SCLC-associated CIPO.^{21–23} It is hypothesized that these antibodies along with lymphoplasmacytic

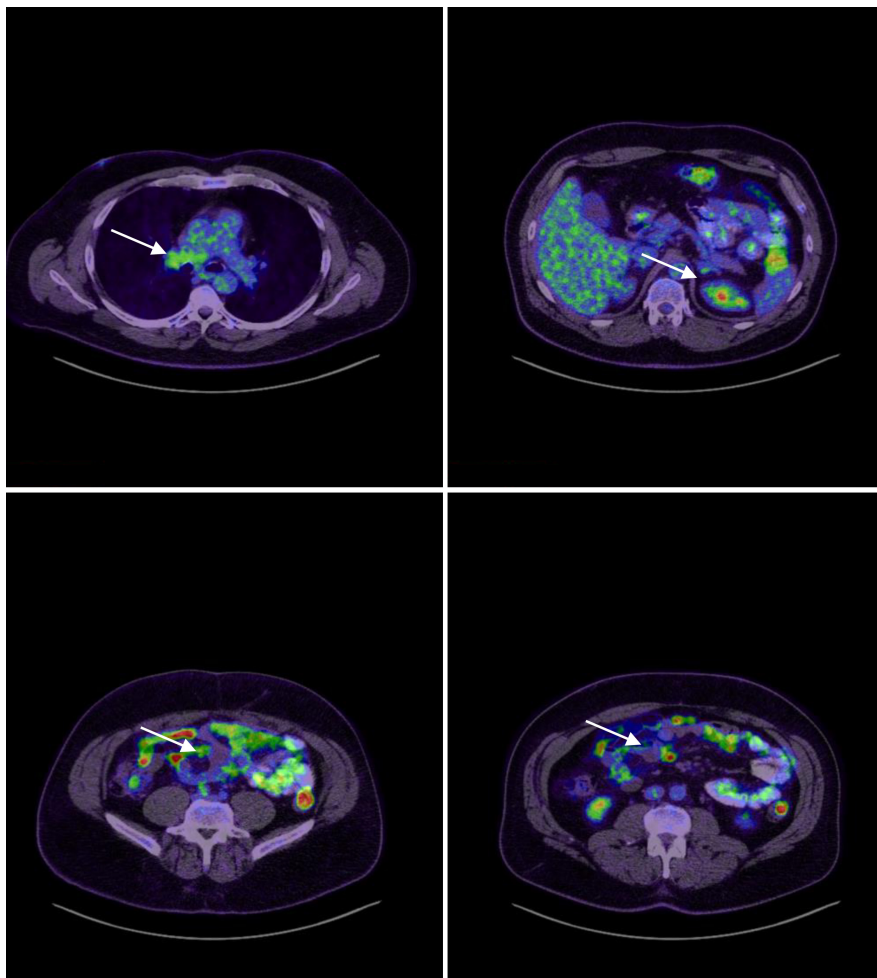
infiltrations are involved in interactions with the enteric plexus; disrupting its function and subsequently may lead to irreversible altered gut motility.²⁴

Further investigations may have been considered if the CIPO was not primarily due to SCLC. Our investigations lacked further autoimmune profiling which could potentially play a significant role in CIPO.^{22,25} An anorectal manometry or rectal biopsy would have been appropriate, if indicated clinically, to rule out Hirschsprung disease. Autonomic function tests could have been ordered to rule out autonomic dysfunctions, amyloidosis, multisystem atrophy, and other diseases that may manifest with similar presentation.²⁵ Genetic counseling and testing may be ordered in the future to check for affected genes that are involved in the disease pathogenesis. The diagnostic flowchart in adult patients with CIPO has been described elsewhere.²⁵

5 | CONCLUSION

This report presented the case of a middle-aged patient with a history of recurrent bowel obstruction and the

FIGURE 6 PET CT scan showing post-chemotherapy metabolic resolution in different organs. Top left: Right hilar mass. Top right: Left adrenal mass. Bottom left: Mesenteric lymph nodes. Bottom right: Bowel mass.



journey SCLC-associated CIPO diagnosis. The case report involved good clinical and radiological response to systemic anticancer therapy in form of combination of chemoimmunotherapy. This case demonstrated the conundrum in the diagnosis of CIPO and at times a prolonged diagnostic pathway to identify the underlying etiology. Clinicians are expected to recognize a growing range of paraneoplastic presentations in patients presented to general medical and surgical specialities, mainly due to the acceleration of newly diagnosed cancers worldwide and the rising incidence of cancer diagnoses reflecting population growth, aging populations, lifestyle changes, environmental exposures, and improvement of anticancer treatment that result in reducing mortality rates.²⁶

AUTHOR CONTRIBUTIONS

Mohammad Ayoub: Conceptualization; data curation; formal analysis; writing – original draft; writing – review and editing. **Mohammad Natheef AbuHaweeleh:** Data curation; writing – review and editing. **Nabil Mahmood:**

Formal analysis. **Colin Clelland:** Formal analysis. **Malak Mohammad Ayoub:** Data curation. **Harman Saman:** Conceptualization; data curation; formal analysis; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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