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A Metastatic Granulocyte Colony-Stimulating Factor Producing Sarcomatoid Carcinoma of the Lung Causing Jejunal Intussusception – Report of a Case –

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A 75-year-old man was referred to our hospital with intestinal obstruction caused by intussusception. Abdominal computed tomography (CT) revealed seven polypoid masses in the small intestine, while chest CT revealed a mass in the right lower lobe. Preoperative laboratory tests showed white blood cell (WBC) and neutrophil differential counts of 63,630/mm^3 and 95%, respectively. The serum granulocyte colony-stimulating factor (G-CSF) was 114 pg/mL, which was elevated (normal range, <18.1 pg/mL). After resection of the small bowel, the WBC count decreased to 20,510/mm^3. The pathology showed a poorly differentiated carcinoma with sarcomatous components confirmed by positive immunostaining of cytokeratin (AE1/AE3) and vimentin in the small intestine. Furthermore, immunohistochemistry with specific monoclonal antibodies against G-CSF was positive. A lung biopsy revealed the same histological findings as the small intestine lesion. Therefore, the patient was diagnosed as having a G-CSF producing sarcomatoid carcinoma of the lung with metastasis to the small intestine.

Key Words: Carcinosarcoma; Granulocyte colony-stimulating factor; Metastasis; Intussusception

Granulocyte colony-stimulating factor (G-CSF) producing lung cancer, first described by Asano *et al.*[1] in 1977, is a well known highly malignant cancer with poor prognosis. Among the G-CSF producing lung cancer types, two thirds are large cell carcinomas followed by squamous cell carcinoma.[2,3] Sarcomatoid carcinoma of the lung is a rare histological type of lung cancer with a mixture of biphasic epithelial and stromal tumor cells.[4] It may be difficult to histologically identify the two components. Currently, it is necessary to confirm the components using immunohistochemistry, electron microscopy, and molecular assays. Metastatic sites associated with sarcomatoid carcinoma are similar to the more common non-small cell lung carcinoma, with unusual metastatic sites such as the esophagus, jejunum, and kidneys having been reported.[5] To the best of our knowledge, there are no prior reports of a patient with multiple small bowel metastases from a sarcomatoid carcinoma producing G-CSF and resulting in an intestinal intussusception.

CASE REPORT

A 75-year-old male heavy smoker was admitted to the hospital with epigastric pain, nausea, and vomiting. The physical examination revealed epigastric tenderness and hyperactive bowel sounds. Body temperature was 37.3℃, white blood cell (WBC) counts were 63,630/mm^3 (neutrophil 95%), and chest X-ray revealed a mass in the right lower lung field. The C-reactive protein was measured at 30.07 mg/mL and there was no evidence of infection on routine examination. Follow-up diagnostic tests with chest and abdominal dynamic computed tomography (CT) imaging revealed a homogeneous mass measuring 9 cm in diameter in the right lower lobe of the lung (Fig. 1), in addition to a jejuno-jejunal intussusception (Fig. 2). An emergency small bowel resection was performed for the reduction of the intussusception. Pathology displayed seven ulcero-fungating masses in the duodenum and jejunum. The size of the masses ranged from 7.0×4.0×1.0 cm to 4.0×3.8×0.8 cm. The cut surface of the tumors was whitish and firm. The microscopic

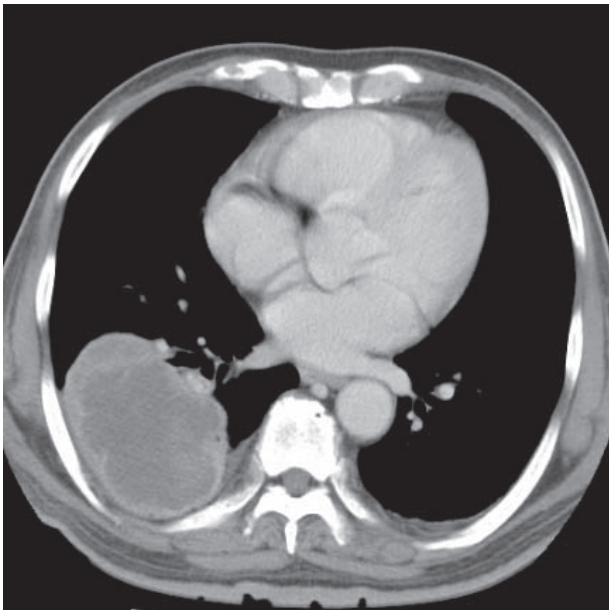

Fig. 1. Computed tomographic scan of the chest shows a 9 cm-sized mass in the right lower lobe.

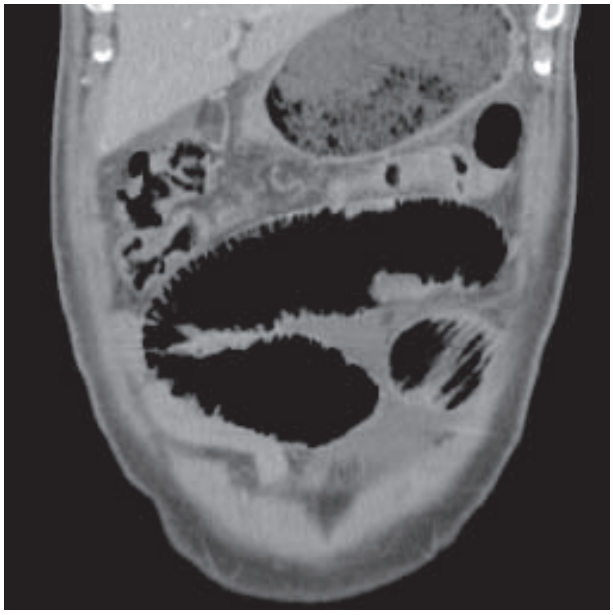

Fig. 2. Abdominal computed tomography shows jejuno-jejunal intussusception with obstruction at the distal end. Several intraluminal mass-forming lesions are noted in the distended small bowel loops.

findings of the tumor showed atypical spindle cells with giant cell formation, as well as a scarce stromal component between the tumor cells. Many polymorphous leukocytes were scattered in and around the tumor cells (Fig. 3A). The tumor cells showed positive immunostaining for cytokeratin (AE1/AE3) and vimentin (Fig. 3B, C), as well as being negative for CD117 and smooth muscle actin. In addition, strong positive immunoreactivity for G-CSF was noted in the tumor cells (Fig. 3D) and the serum level of G-CSF was 114 pg/mL, which was elevated (normal, < 18.1 pg/mL). On the basis of these findings, a pathological diagnosis of a G-CSF producing sarcomatoid carcinoma was established. A transbronchial lung biopsy revealed the same microscopic and immunohistochemical staining patterns as the small bowel lesions. Based on these results, we diagnosed the small bowel lesions as metastatic sarcomatoid carcinoma from the lungs. Postoperatively, the WBC count (20,510/mm^3) and serum levels of G-CSF (81 pg/mL) decreased. At the three-month postoperative follow-up, a surge in the WBC count to 84,390/mm^3 was detected. A repeat CT scan of the chest and abdominal area showed an increased size of the lung mass and evidence of multiple metastatic lesions in the para-aortic lymph nodes and spleen. The patient died one week later after readmission to the hospital.

DISCUSSION

Pulmonary sarcomatoid carcinoma is a rare malignant tumor which constitutes 0.3-1.3% of all lung malignancies.[5] In the past 10 years, 10 cases of pulmonary sarcomatoid and two cases of paraneoplastic leukocytosis in non-small cell carcinoma were reported in Korea over the last 10 years.[6-8] However, there have been no reported case of pulmonary sarcomatoid carcinoma in a patient with accompanying severe leukocytosis.

The CSF has four factors; G-CSF, granulocyte/macrophage-CSF, interleukin-3, and macrophage-CSF.[9] Generally, G-CSF producing tumors are histologically characterized as poorly differentiated, and on a clinical level, can rapidly progress. Survival from the time of diagnosis is reported to be only about 4.7 ± 3.1 months (mean ± standard deviation).[10] Many have speculated that G-CSF released by tumor cells might bind G-CSF receptors to the tumor cells, triggering proliferation, invasion, and migration via autocrine and paracrine mechanisms. Others have postulated that G-CSF promotes angiogenic activity indirectly, while direct or indirect immunosuppression of G-CSF tumor immunity has also been reported.[11,12] In addition, G-CSF inhibits apoptosis of both leukocytes and tumor cells.[13]

Histologically, marked neutrophilic infiltration in and around the tumor cells, and an increased leukocyte count, suggested a G-CSF producing cancer in our patient. The elevation of the se-

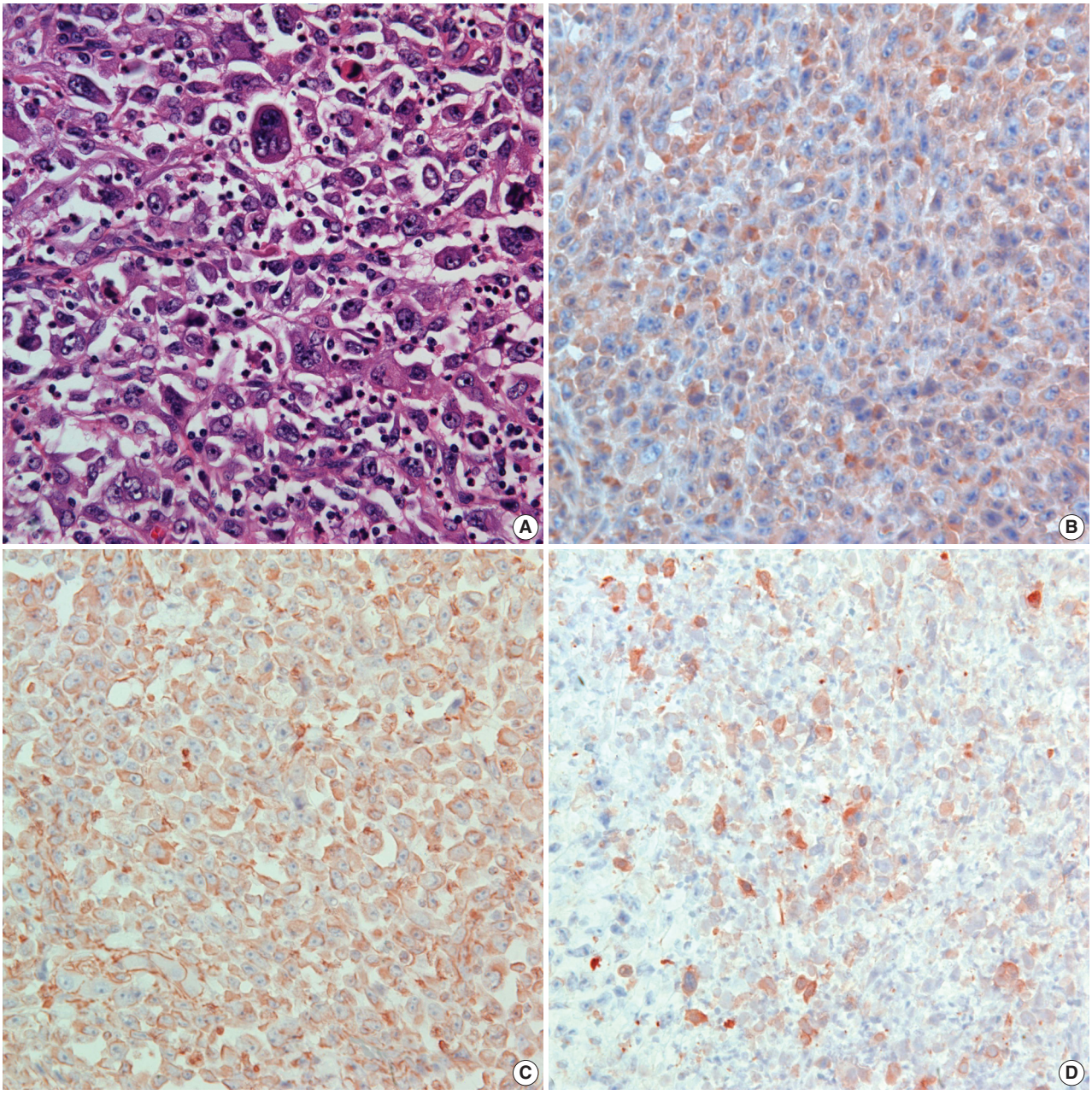

Fig. 3. (A) Microscopic findings show pleomorphic atypical cells with polymorphonuclear leukocytic infiltration. Both tumor and multinucleated giant cells show immunoreactivity for anti-cytokeratin (B), anti-vimentin (C), and anti-granulocyte colony-stimulating factor (D).

rum G-CSF and positive cytoplasm immunohistochemical staining using a monoclonal antibody supported the diagnosis of a G-CSF producing tumor. The downtrend in leukocytes and normalization of serum G-CSF levels after tumor resection was also indicative of G-CSF producing tumors. In our case, the leukocytosis never resolved completely, most likely due to the primary lung carcinoma that was still present.

In conclusion, after resection of a G-CSF producing tumor, tumor progression and surveillance may be easily detected by monitoring increases in the WBC counts. Therefore, following the WBC counts might be a cost effective method for monitoring disease progression and metastasis of G-CSF producing tumors.

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