

Case Report

An Autopsy Case of Granulocyte-Colony-Stimulating-Factor Producing Pulmonary Pleomorphic Carcinoma

Motohisa Kuwahara¹, Nao Kubota², Nakayama Masamichi², Sakiko Sanada², Hirohisa Yano², Hiromoto Kitajima³, Mamoru Nishiyama³, Yoshiko Sueyasu³, Chieko Souda⁴, Akinori Iwasaki⁵

¹Department of Chest Surgery, Takagi Hospital 141-11 Sakami, Okawa-shi, Fukuoka, Japan

²Division of Department of Pathology, School of medicine, Kurume University, Saiseikai Futsukaichi Hospital, Japan

³Division of Respiriology, School of medicine, Fukuoka University, Japan

⁴Division of Nurse, School of medicine, Kurume University, Saiseikai Futsukaichi Hospital, Japan

⁵Department of Chest Surgery, School of medicine, Fukuoka University, Japan

***Corresponding author:** Motohisa Kuwahara M.D., Department of Chest Surgery, Takagi Hospital 141-11 Sakami, Okawa-shi, Fukuoka, Japan, 831-0016. Tel: +81-944-87-0001; Fax: +81-944-87-9310; E-mail: KHC03152@nifty.com

Citation: Kuwahara M, Kubota N, Masamichi N, Sanada S, Yano H, et al. (2017) An Autopsy Case of Granulocyte-Colony-Stimulating-Factor Producing Pulmonary Pleomorphic Carcinoma. Ann Case Rep 2017: J139.

Received Date: 14 February, 2017; **Accepted Date:** 18 February, 2017; **Published Date:** 24 February, 2017

Abstract

A 61-year-old man called an ambulance for general fatigue and astasia, chest roentgenography showed huge mass in the left upper lung fields. At the time of admission, the white blood cell count was 42600 cells/ μ L (neutrophils, 91.5% (38979 cells/ μ L) and red blood cell count was 29100 cells/ μ L (hemoglobin, 7.9 g/dl, hematocrit, 24.8%). The computed tomography (CT) revealed well enhanced huge mass in the left upper thoracic cavity.

The radiologist diagnosed the chronic expanding hematoma or huge solitary fibrous tumor. The patient moved to a university hospital with transfusion of the red blood cells, aspiration cytology was performed and was diagnosed malignancy tumor. The head magnetic resonance imaging showed brain metastasis. Then the patient returned to our hospital, the needle biopsy of the tumor of left upper thoracic cavity under the fluoroscope was performed. The specimens were diagnosed non-small cell lung cancer with spindle cell and giant cell carcinoma, probably sarcomatoid carcinoma. In addition, serum granulocyte colony-stimulating factor (G-CSF) was elevated 226 pg/ml (~39). But the patient's fatigue and loss weight had progressed, the patient died 3 weeks later. An autopsy showed a left lung pleomorphic carcinoma, 775 g weight with duodenum, lymph nodes belong pancreas, intestine and bilateral adrenal metastasis. The cancer cells showed positive immunohistochemical staining for anti-G-CSF antibody. Since G-CSF-producing carcinoma and lung pleomorphic carcinoma leads to poor prognosis, early diagnosis and treatment are needed. The granulocytosis when infection is ruled out, the G-CSF in serum should be examined.

Keywords: Granulocytosis; Granulocyte Colony-Stimulating Factor (G-CSF); G-CSF-Producing Carcinoma; Pulmonary Pleomorphic Carcinoma

Introduction

Granulocyte colony-stimulating factor (G-CSF) produced in some cancers is thought to be an autocrine growth factor [1,2].

Therefore, patients with G-CSF-producing cancer generally have a poor prognosis, and early diagnosis and treatment are required.

This report describes a case of pleomorphic carcinoma that produced G-CSF, autopsy showed multiple organ metastasis.

Case Report

A 61-year-old man called an ambulance by general fatigue,

chest pain and astasia for two weeks. The patient worked for a driver of a home delivery service and had a smoking history of 30 cigarettes/day for 40 years. The patient was pointed out a left lung abnormal shadow by the medical examination at the job, but the patient had not saw a doctor before half year. The patient could not work by the fatigue before a month, could not go outside by general fatigue and astasia for two weeks. Then the patient could not eat a little and become very skinny, left hemiplegia, having a little decubitus ulcer at the sacrum, the body temperature at 36.5°C and the palpebral conjunctives were anemic. The portable chest roentgenography showed huge mass in the left upper lung fields [Figure 1].

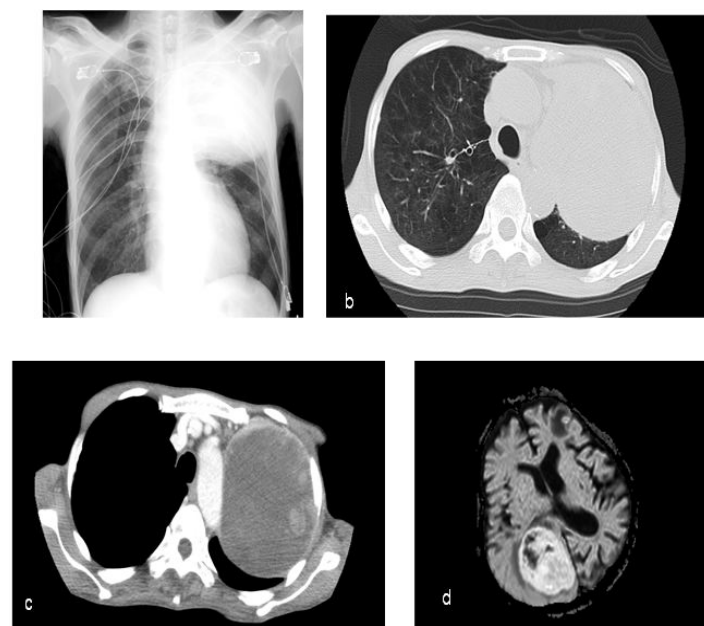


Figure 1: a) Chest roentgenography showed huge mass in the left upper lung fields. (b, c) The computed tomography (CT) revealed well enhanced huge mass 11.6 cm in size at the left upper thoracic cavity and peripheral mass was very enhanced and inside mass was homogenous faintly enhanced. (d) The head magnetic resonance imaging showed two brain metastasis.

At the time of admission, emergency laboratory data showed an increase in the following: white blood cell count (WBC) 42600 cells/ μ L (neutrophils, 91.5% (38979 cells/ μ L)), Platelet 53.3×10^4 cells/ μ L, alkaline phosphatase 467 IU/L, C-reactive protein 24.2 mg/dL and a decrease red blood cell count was 29100 cells/ μ L (hemoglobin, 7.9 g/dl, hematocrit, 24.8%), mean corpuscular volume 85.2 fl, sodium 132 mEq/l, Chlorine 90 mEq/l, serum-amylase 21 IU/l, creatine kinase 36 IU/l. The computed tomography (CT) revealed well enhanced huge mass 11.6 cm in size at the left upper thoracic cavity and peripheral mass was very enhanced and

inside mass was homogenous faintly enhanced (Figure 1b, c). The left under lobe and lingual segment look like normal and probably compressed upper segment was seemed, then we considered the extrapulmonary mass. The radiologist diagnosed the chronic expanding hematoma or huge solitary fibrous tumor. The patient had serious anemia then we feared the chronic expanding hematoma. The patient moved to a university hospital with transfusion of two packs of the red blood cells, an aspiration cytology was performed and was diagnosed malignancy tumor. The head magnetic resonance imaging showed two brain metastasis (Figure 1d). Because surgical indication were none, then the patient returned to our hospital. The bronchoscopy was performed but left upper segmental bronchus was compressed obstruction and could not insert biopsy forceps. The needle biopsy of the tumor of left upper thoracic cavity under the fluoroscope was performed. The specimens were diagnosed non-small cell lung cancer with spindle cell and giant cell carcinoma, probably sarcomatoid carcinoma. In addition, serum granulocyte colony-stimulating factor (G-CSF) was elevated 226 pg/ml (~ 39). The tumor makers were elevated cytokeratin-19 fragment 3.7 ng/ml, Pro-gastrin-releasing peptide 118 pg/ml, Neuron-specific enolase 38.8 ng/ml. But the patient's fatigue, chest pain and weight loss had progressed, we treated best supportive care with administered 40 mg morphine and midazolam 40 mg/daily, the patient died 3 weeks later and underwent an autopsy without craniotomy. An autopsy showed a huge mass originated left upper lobe lung, 11 \times 10 \times 6 cm in size, and 775 g weight, with necrosis and invaded to chest wall. The grayish-gelatinous nodules, 1 cm in size were revealed at duodenum, lymph nodes belong pancreas, small intestine at oral 110 cm and bilateral adrenal glands. Histopathologically, the giant and spindle cell elements of the tumor are admixed with components of adenocarcinoma. Carcinomas composed of mixture of spindle and giant cell carcinoma qualify as pleomorphic carcinoma. Giant tumor cells show abundant, eosinophilic, granular cytoplasm, and contain eosinophilic globules. The nuclei are large, irregular and multilobated with coarse chromatin and prominent nucleoli. Immunohistochemistry, Mucicarmine stain was slightly positive, TTF-1 and Calretinin were negative, Vimentin and CAM 5.2 were positive. The vascular invasions were positive on the EVG stain and lymphatic vessel invasions were positive on the D2-40 stain. Then tumor was diagnosed pleomorphic carcinoma admixed with component as adenocarcinoma with vascular invasion. The tumors of duodenum, lymph nodes belong pancreas, intestine and bilateral adrenal glands were same futures and then the tumors were diagnosed distant metastasis of the pleomorphic carcinoma. The cancer cells showed positive immunohistochemical staining for anti-G-CSF antibody (CALBIO-CHEM®, USA). [Figure 2]

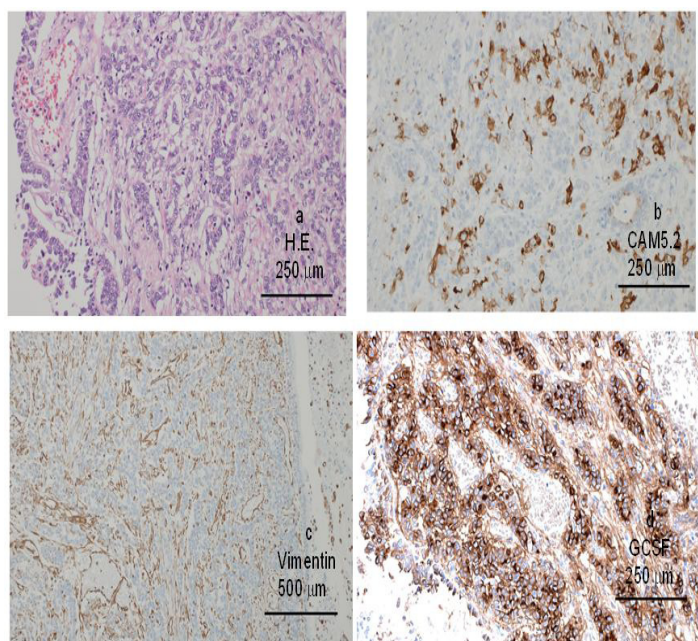


Figure 2: (a) Hematoxylin-eosin stain: The giant and spindle cell elements of the tumor are admixed with components of adenocarcinoma. Carcinomas composed of mixture of spindle and giant cell carcinoma qualify as pleomorphic carcinoma. (b) CAM5.2 (c) Vimentin (d) G-CSF200 were positive.

Discussion

Pleomorphic Carcinoma is a poorly differentiated non-small cell lung carcinoma namely a squamous cell carcinoma, adenocarcinoma, or undifferentiated non-small cell carcinoma that contains at least 10% spindle and/or giant cells or a carcinoma consisting only of spindle and giant cells are classified by WHO classification [5]. Because definite diagnosis may only be made on a resected tumor or an autopsy case. The specific histological components should be mentioned in the diagnosis. By definition, in small biopsy samples, sarcomatoid elements may be described as our case. These tumors account for 2-3% of cancer cases in surgical series, but for

< 1% epidemiological studies [6]. Most cases of these carcinoma arise in tobacco smokers [7]. These are aggressive tumors, with spread similar to that of other non-small cell carcinomas. Distant metastasis commonly found, including in unusual location about gastrointestinal tract and retroperitoneal space. Pleomorphic carcinoma are often peripherally located, favoring the upper lobe [8].

Granulocytosis is the presence in peripheral blood of an increased number of granulocytes, a category of white blood cells. Often, the word refers to an increased neutrophil granulocyte count, as neutrophils are the main granulocytes. Almost of granulocytosis caused by viral or/and non-viral infection, a small cases of tumors related.

We encountered a rare patient with a pleomorphic carcinoma and huge tumor shadow in upper lesion of the left thoracic cavity. This patient presented with marked inflammatory responses. The excised tumor consisted of a carcinomatous lesion in the university hospital, MRI was presenting brain metastasis then treated best supportive care with administered morphine and midazolam. In addition to no fever, granulocytosis, and elevated serum CRP concentration, our patient presented with elevated serum concentrations of G-CSF

In addition, immunohistochemical examination showed that the cancer cells were positive for G-CSF. Probably granulocyte macrophage colony-stimulating factor, interleukin-6, other stimulating factors and other cytokines elevated in the patient, but we measured G-CSF only for the cost [9].

These cytokines have been reportedly produced by lung cancers, especially by large cell inflammatory cells. To analyze this mechanism, we assessed the expression of several chemokines using immunohistochemistry.

Conclusions

We encountered a patient with a pleomorphic carcinoma of the lung. This tumor produced G-CSF resulting in several systemic responses. [Table: 1]

| | | | | | | | |
|-------|-----|-------|------|-----|-------|-------|--------|
| TP | 6.6 | T-bil | 0.6 | CK | 36 | WBC | 42.6 |
| ALB | 3.0 | BUN | 18.5 | CRP | 24.2 | (Neut | 91.5%) |
| GOT | 20 | CRE | 0.77 | BS | 24.16 | RBC | 29.1 |
| GPT | 21 | Na | 132 | | | Hb | 7.9 |
| LDH | 325 | K | 3.6 | | | Ht | 24.8 |
| ALP | 467 | Cl | 90 | | | MCV | 85.2 |
| γ-GTP | 33 | S-Amy | 21 | | | PLT | 53.3 |

Table 1: Laboratory findings on admitted to hospital.

Citation: Kuwahara M, Kubota N, Masamichi N, Sanada S, Yano H, et al. (2017) An Autopsy Case of Granulocyte-Colony-Stimulating-Factor Producing Pulmonary Pleomorphic Carcinoma. Ann Case Rep 2017: J139.

[Table: 2]

| | | |
|----------------------|-------------------|---------|
| <u>NSE</u> | <u>38.8 ng/ml</u> | (~10) |
| <u>CK19f</u> | <u>3.7 ng/ml</u> | (~3.5) |
| <u>SCC</u> | 0.8 ng/ml | (~1.5) |
| <u>ProGRP</u> | <u>118 pg/ml</u> | (~69.9) |
| <u>CEA</u> | 2.7 pg/ml | (~5.0) |
| <u>GCSF</u> | <u>226 pg/ml</u> | (~39) |

Table 2: Abnormal values indicated underline.

References

1. Matsuyama S, Shimonishi T, Yoshimura H, Higaki K, Nasu K, et al. (2008) An autopsy case of granulocyte-colony-stimulating-factor-producing extrahepatic bile duct carcinoma. World J Gastroenterol 14: 2924-2927.
2. Clark LH, Moll S, Houghton D, O'Connor S, Soper JT (2017) Leukocytosis due to markedly elevated granulocyte-colony stimulating factor levels in a patient with endometrial cancer: Case report and literature review. Gynecol Oncol Rep 20: 5-8.
3. Takagi Y, Nakamura H, Miwa K, Adachi Y, Fujioka S, et al. (2010) A case of G-CSF-producing invasive apical cancer resected following preoperative adjuvant therapy. Thorac Cardiovasc Surg 58: 304-306
4. Nonami Y, Yamamoto M, Sasaguri S (2005) G-CSF producing giant tumor in the lung. J Cardiovasc Surg 46: 313-314.
5. Travis WD, Brambilla E, Burke AP, Marx A (2015) Nicholson AG "WHO Classification of tumours of the Lung, Pleura, Thymus and Heart". Switzerland: WHO Press 7.
6. Yendamuri S, Caty L, Pine M, Adem S, Bogner P, et al. (2012) Outcomes of sarcomatoid carcinoma of the lung: a Surveillance, Epidemiology and End Results Database analysis. Surgery 152: 397-402.
7. Fishback NF, Travis WD, Moran CA, Guinee DG Jr, McCarthy WF, et al. (1994) Pleomorphic (spindle/giant cell) carcinoma of the lung. A clinicopathologic correlation of 78 cases. Cancer 73: 2936-2945.
8. Raveglia F, Mezzetti M, Panigalli T, Furia S, Giuliani L et al. (2004) Personal experience in surgical management of pulmonary pleomorphic carcinoma. Ann Thorac Surg 78: 1742-1747.
9. Watanabe M, Ono K, Ozeki Y, Tanaka S, Aida S, Okuno Y (1998) Production of granulocyte-macrophage colony-stimulating factor in a patient with metastatic chest wall large cell carcinoma. Jpn J Clin Oncol 28: 559-562.