Sweet's syndrome with adenocarcinoma of lung: a rare case report

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Background: Sweet's syndrome is a rare inflammatory disease of unknown etiology, and its relationship with tumors is unknown at present. Sweet's syndrome in patients with solid tumors, especially adenocarcinoma of the lung, is extremely rare. At present, only 1 case of an operative patient has been reported in the literature. Diagnosing lung cancer with Sweet's syndrome is not easy, when there is a fever with an unknown cause and erythemas, especially when the erythemas do not disappear after antibiotic treatment, a skin biopsy is much important. Although the exact mechanism of the disease and its link to lung cancer are unknown, our case shows that the active surgical treatment of the primary disease and appropriate glucocorticoid therapy are effective means.

Case Description: We report the first case of a patient with Sweet's syndrome and lung adenocarcinoma with a decrease in peripheral whole blood cells. A 66-year-old male patient presented, who had been suffering from a fever for >10 days and had multiple tender erythemas, erythemas were mainly on the limbs and upper chest. He was treated with a variety of antibiotics, but his symptoms did not improve significantly. The routine blood tests results show a decline in peripheral blood cells, a chest computed tomography (CT) examination showed a space occupying lesion in the middle lobe of the right lung, which was considered peripheral lung cancer. Sweet's syndrome was diagnosed after a skin biopsy, a pathological examination showed that a large number of neutrophils were infiltrating. The patient then underwent video-assisted thoracoscopic lobectomy associated with the systematic dissection of the mediastinal lymph node, and glucocorticoids were administered. After the operation, the tender erythemas and fever disappeared, at the 1-month follow-up, the chest CT showed no obvious tumor recurrence or metastasis.

Conclusions: To the best of our knowledge, this is the first report of Sweet's syndrome in a patient with lung adenocarcinoma with 3 cell lines reduced. The active surgical treatment of the primary disease and appropriate glucocorticoid therapy proved to be an effective treatment for this syndrome.

Keywords: Sweet syndrome; lung adenocarcinoma; whole blood cells; case report

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Introduction

Sweet's syndrome is a rare disease that usually manifests as acute pain erythema, fever, joint pain, headache, and so on (1). At present, the following 3 subtypes of Sweet's syndrome have been identified: (I) the classic or idiopathic type; (II) the malignant tumor-related type (the most common type is blood tumor-related, but it may also be observed in solid tumor malignancies); and (III) the drug-related adverse type (2,3). The pathogenesis of Sweet's syndrome is not yet known. Studies have shown that Sweet's syndrome may be related to various cytokines and signaling molecules [including granulocyte-colony stimulating factor, interleukin (IL)-1, IL-2, IL-6] (4). In addition, disorders of neutrophil level and function are also important causes of Sweet's syndrome (5).

Currently, Sweet's syndrome is thought to be a group of autoinflammatory skin lesions or neutrophilic dermatoses caused by autoimmune, inflammatory disorders, or malignancies (6). The relationship between lung cancer and Sweet's syndrome is complex, and case reports are very rare. Its onset may be drug-induced (including by erlotinib and other drugs) or paraneoplastic (7,8). No research on the relevant mechanism study of relationship between Sweet's syndrome and lung cancer appears to have been conducted; however, a previous case (7) has shown that the active treatment of primary tumors and glucocorticoid therapy can effectively improve the prognosis of tumors. Laboratory examinations of Sweet's syndrome have shown that most patients have increased peripheral blood leukocytes and erythrocyte sedimentation rates (1), but not all patients have increased leukocytes. Some patients with malignances may have anemia, neutropenia, and thrombocytopenia. This phenomenon is commonly observed in hematological malignancies but has not been reported in Sweet's syndrome associated with lung cancer. The etiology of lung cancer complicated with fever and rash may be various, including infection, antitumor drug use, paraneoplastic syndrome, etc. Since the use of antibiotics and glucocorticoids may mask the symptoms, the diagnosis of lung cancer complicated with Sweet's syndrome is very difficult, and premature skin biopsy may also lead to the wrong direction of treatment.

In this article, we report the case of an elderly male patient who was admitted with fever and multiple tender erythemas. After admission, the laboratory examination showed that his peripheral whole blood cells were decreased, and a chest computed tomography (CT) examination revealed a space occupying lesion in the middle lobe of the right lung. The use of standard antibiotics was ineffective at first. Sweet's syndrome was later confirmed by skin biopsy. After adequate preoperative preparation, the patient underwent radical surgery for lung cancer and perioperative glucocorticoid therapy, and the tender erythemas disappeared after surgery. Our case suggests that timely skin biopsy is very important in clinical cases of lung cancer complicated with fever and rash of unknown etiology, which will provide us with the correct treatment direction for lung cancer complicated with Sweet's syndrome. We present the following case in accordance with the CARE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5934/rc).

Highlight box

Key findings

- This is the first report of Sweet's syndrome in a patient with lung adenocarcinoma with 3 cell lines reduced.

What is known and what is new?

- Sweet's syndrome in patients with solid tumors, especially adenocarcinoma of the lung, is extremely rare.
- This is the first report of a case of patient with lung adenocarcinoma with a decline in peripheral blood cells combined with Sweet's syndrome.

What is the implication, and what should change now?

- We should pay attention to Sweet's syndrome in patients with lung adenocarcinoma, and appropriate glucocorticoid therapy proved to be an effective treatment for this syndrome.

Case presentation

A 66-year-old male patient was admitted to Gaozhou People's Hospital on September 20, 2019, who had been suffering from a fever for >10 days. He was admitted to the Respiratory Department of our hospital. The patient had a history of type II diabetes, coronary heart disease, and hypertension. On admission, a CT examination revealed a space occupying lesion in the middle lobe of the right lung, and a diagnosis of peripheral lung cancer was considered (*Figure 1*). The patient underwent a careful physical examination on admission with the following results: body temperature, 37.6 ℃; heart rate, 103 beats/min; and blood pressure, 159/91 mmHg. The patient had an emaciated physique, and erythemas on many parts of the body, mainly including the limbs and upper chest, which were painful when touched (*Figure 2*). The superficial lymph nodes of the whole body were not palpable or swollen. The respiratory

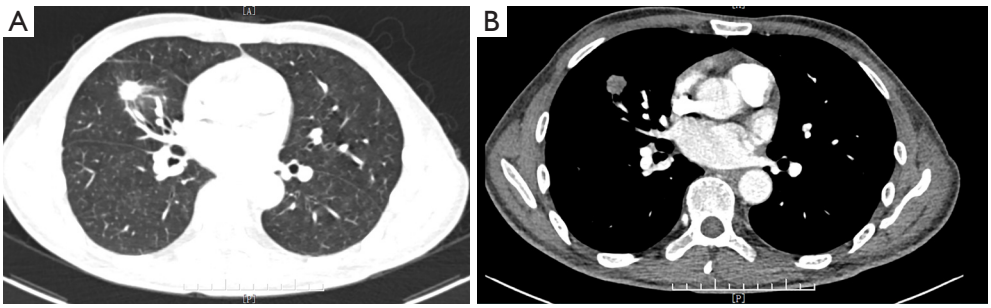

Figure 1 Chest CT scan showing the space occupying lesion in the middle lobe of the right lung. (A) Mediastinal window; (B) pulmonary window. Scale bar =10 cm. A, anterior; P, posterior; CT, computed tomography.

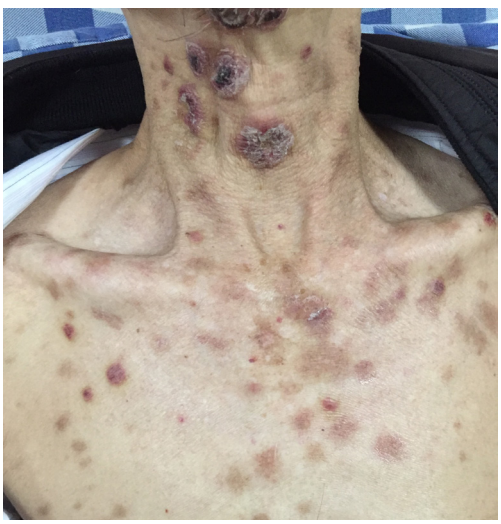

Figure 2 Multiple tender erythemas on the limbs and upper chest preoperatively.

sounds of both lungs were rough, but not dry, and moist rales were heard.

The patient underwent a further blood sampling–related examination after admission. The routine blood tests results were as follows: white blood cell count, 3.46×10^9/L ↓; lymphocytes, 0.50×10^9/L ↓; neutrophil ratio, 77.2%; lymphocytes ratio, 14.4%; hemoglobin, 85 g/L, red blood cell count, 2.91×10^{12}/L ↓; antinuclear antibodies spectrum, negative. Widal agglutination test results, both serum 1,3-β-D-glucan and galactomannan (GM) were negative.

The patient was initially diagnosed with: (I) a right middle lung space occupying lesion; (II) lung infection; (III) coronary heart disease; (IV) hypertension; (V) type II diabetes; (VI) erythemas; and (VII) moderate anemia.

The patient had repeated fever after admission, and no obvious improvement was observed after anti-infection treatment with different kinds of antibiotics. After consultation with the Dermatology Department, a skin biopsy was performed of a lesion on the upper chest area, and a pathological examination showed that the epidermis was normal with hematoxylin and eosin (H&E) staining, the dermal vessels were dilated, a large number of neutrophils were infiltrating, and a small amount of red blood cells were overflowing; there was no evidence of vasculitis (*Figure 3*). Sweet's syndrome was confirmed.

After the diagnosis of Sweet's syndrome, the patient was treated with dexamethasone (10 mg/day), and the fever disappeared; the rash also improved in the hospital, and the patient's condition improved. After adequate preparations before the operation, the patient was placed under general anesthesia and underwent video-assisted thoracoscopic lobectomy of the right middle lobe and the systematic dissection of the mediastinal lymph node on November 14, 2019. The postoperative pathology revealed that the lung lesion was composed of a proliferation of infiltrating dysplastic epithelial cells with glandular structures. The patient was diagnosed with adenocarcinoma (in the right middle lung). The patient was received a small dose of dexamethasone after the operation. At the 1-week follow-up, the rash had subsided (*Figure 4*), and 1 month later, the chest CT showed no obvious tumor recurrence or metastasis. The patient was then treated with prednisolone at 10 mg/day orally after his discharge from the hospital. The rash disappeared 3 months after surgery and no definite sign of tumor recurrence. The diagnosis, treatment, progression, and follow-up timeline of this patient since diagnosis is summarized in *Figure 5*.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the

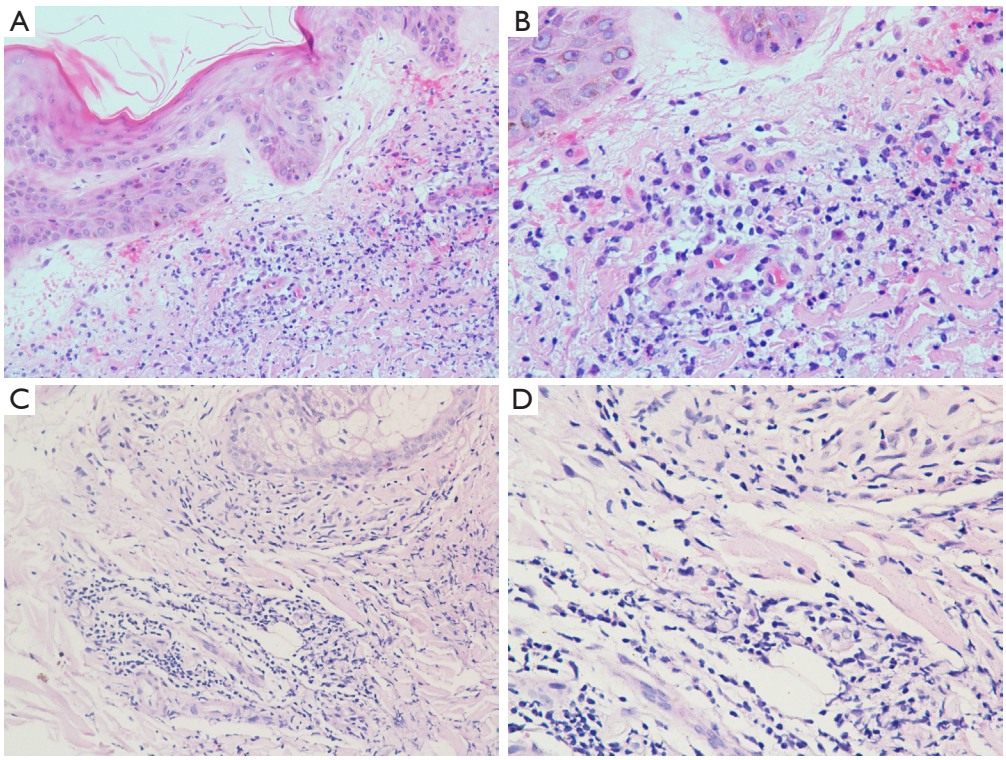

Figure 3 Histopathological findings: the dermal vessels were dilated; a large number of neutrophils were infiltrated; a small amount of red blood cells were overflowing. These findings were consistent with the features of Sweet's syndrome. H&E staining: (A) 200×; (B) 400×. Acid-fast stain: (C) 200×; (D) 400×. H&E, hematoxylin and eosin.

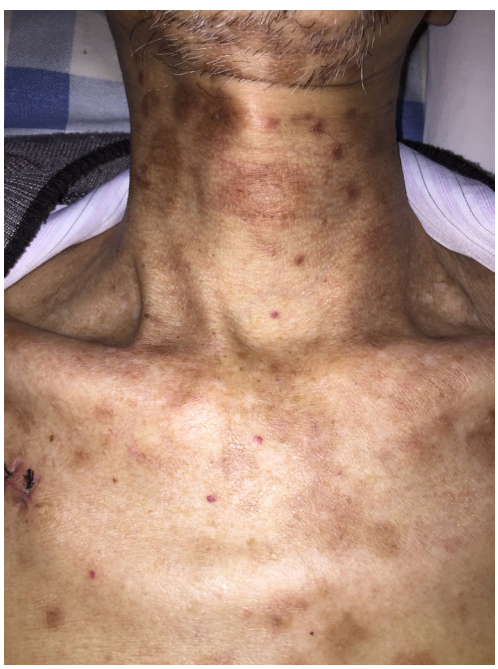

Figure 4 Multiple tender erythemas on the limbs and upper chest postoperatively.

Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, is a rare inflammatory disease of unknown etiology. Its main characteristics are fever, and painful erythema of the face, neck and extremities (9). The main pathological change in a skin biopsy is diffuse neutrophil infiltration in the dermis, and generally there is no evidence of leukocyte rupture vasculitis (10). It was first described in 1964 by Robert Douglas Sweet (11), after which, successive relevant cases were reported, scattered around the world. The main cause of the disease is unknown, and its etiology is very complex. Current research suggests that it is related to infection, autoimmune diseases, malignances, and drugs. It may be an atypical hypersensitivity reaction mediated by

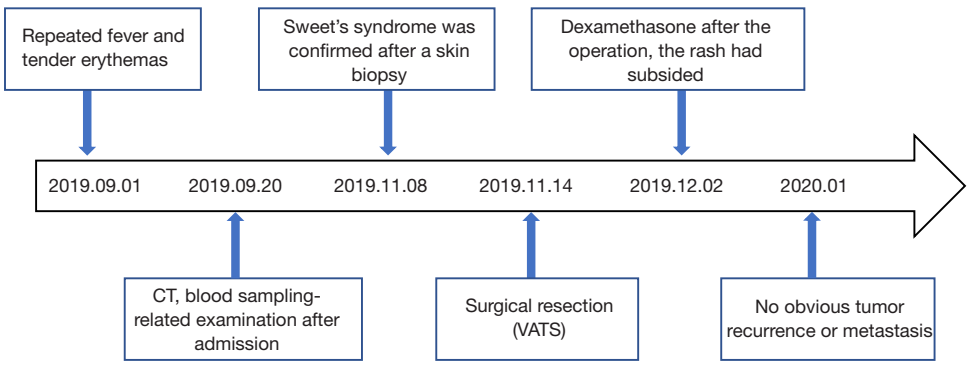

Figure 5 Timeline of the diagnosis, treatment, progression, and follow-up of the patient. VATS, video-assisted thoracoscopic surgery; CT, computed tomography.

cytokines. Immune complexes and leukocyte chemotaxis are thought to be factors leading to the onset of the syndrome (12). At present, the main types of Sweet's syndrome are classic, malignant tumor–related, and drug-induced. In Sweet's syndrome related to a malignant tumor, the malignancies are mainly hematological, and reports of solid tumors in patients with Sweet's syndrome are rare (13).

At present, reports of lung cancer related to Sweet's syndrome are extremely rare. The first case of lung adenocarcinoma-related Sweet's syndrome was reported in 1993 (14), and only a few other cases have been reported worldwide. In addition to the symptoms of fever, tender erythemas, patients may show a decline in peripheral blood cells, which often occurs in hematological malignancies. This is the first report of a case of patient with lung adenocarcinoma with a decline in peripheral blood cells combined with Sweet's syndrome. The patient had repeated fever and tender erythemas, the cause of which was unknown. Sweet's syndrome was confirmed by skin biopsy pathology.

At present, the main treatment method for this disease is to actively treat the primary disease (e.g., by administering surgery, radiotherapy, or chemotherapy to treat the lung cancer). Proper glucocorticoid therapy is also important (7). This patient had a recurrent fever, which was treated by conventional antibiotic treatment. After glucocorticoid treatment, the patient's symptoms improved significantly. After lung cancer surgery, the patient was discharged shortly after surgery. After surgery, he continued glucocorticoid maintenance treatment. At present, no significant tumor recurrence has been found in the postoperative checks. Some scholars have suggested that when there is a fever with an unknown cause and erythemas, especially when the erythemas do not disappear after antibiotic treatment, a diagnosis of Sweet's syndrome should be considered (15). Skin biopsy is very important in the diagnosis and treatment of lung cancer with a fever of unknown cause, especially if a patient has painful erythema and peripheral blood cell decline. Skin biopsy plays a positive role in diagnosing Sweet's syndrome and improving the prognosis of patients.

Conclusions

Lung cancer patients with recurrent fever and painful rash may have Sweet's syndrome. This disease is very rare in clinical practice and is easily misdiagnosed as infectious diseases, which delays the treatment process. Our case shows that the active surgical treatment of the primary disease and appropriate glucocorticoid therapy are effective means for treating Sweet's syndrome, but further research needs to be conducted to examine the relationship between them and their potential mechanism of action.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://atm.amegroups.

com/article/view/10.21037/atm-22-5934/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5934/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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