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Secondary Immune Thrombocytopenic Purpura in malignant peritoneal mesothelioma: A Paraneoplastic Syndrome

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Abstract: Thrombocytopenia is a common manifestation of tumors, which is usually caused by myelosuppression caused by bone marrow involvement of malignant tumor cells or radiotherapy. Immune thrombocytopenia (ITP), as a paraneoplastic syndrome, is more common in lymphatic proliferative neoplasms and rheumatic diseases, less common in solid neoplasms, and has not been reported in peritoneal epithelioid mesothelioma. Herein, we report a 45-year-old patient with peritoneal epithelioid mesothelioma who received remission of thrombocytopenia after treatment with hormones, intravenous human immunoglobulin, and thrombopoietin receptor agonists, as well as subsequent surgery and chemotherapy for the tumor.

Keywords: Thrombocytopenia; Paraneoplastic syndrome; Immunoglobulin; Thrombopoietin; Chemotherapy

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1 Introduction

Immune thrombocytopenia is an acquired autoimmune hemorrhagic disorder characterized by an isolated decrease in peripheral blood platelet count without a clear cause. The annual incidence of adult ITP reported abroad is (2 ~ 10) / 10^5[1]. The main manifestation of this disease is hemorrhage. The main pathogenesis of ITP is the loss of immune tolerance to platelet autoantigen, which leads to abnormal activation of humoral and cellular immunity, and jointly mediates accelerated platelet destruction and platelet insufficiency caused by the disorder of megakyotic cell maturation[2].

There are many reports in lung cancer breast cancer and renal cancer. There is no mature treatment strategy for the treatment of immune thrombocytopenia secondary to peritoneal epithelioid mesothelioma, and more cases need to be accumulated for summary[3-4].

2 Case introduction

The 45-year-old female patient was admitted to the hospital on December 08, 2019 due to "systemic bleeding points and oral blisters for 3 days". She was in good health and denied the history of hypertension; diabetes; liver disease; rheumatic disease; thyroid disease and other diseases. No history of drinking or smoking; no similar family history; denied the history of food and drug allergy. Not taking drugs or vaccinating recently. Physical examination: scattered bleeding spots of the size of rice grains, several soy-sized vesicles in the oral cavity. There was no systemic superficial lymph node enlargement. Breath sound in both lungs is clear, dry and wet rales are not heard, heart rate is 65 beats/min, rhythm is consistent, dry and wet rales are not heard, liver, spleen and subcostal is not touched. No edema in both lower extremities. Blood routine showed leukocyte count of 8.71×10^9/L, hemoglobin concentration of 139.00g/L↓, platelet count of 12.00×10^9/L, no naive cells were observed in peripheral blood. The tumor markers AFP, CEA, CA125 and CA153 were not abnormal, and the thyroid function indexes FT3, FT4 and TSH were not abnormal. Liver function, kidney function and blood sugar are normal. Antinuclear antibody test showed no abnormality, anti-phospholipid antibody showed no abnormality. CT examination of chest and abdomen showed no abnormality. Helicobacter pylori

C14 breath test was normal. Thrombocytopenia caused by rheumatic diseases, thyroid diseases, drugs, infections, liver diseases and neoplastic diseases were excluded, and initially diagnosed as immune thrombocytopenia. Dexamethasone was given 40mg/d×4 days, and recombinant human thrombopoietin 15,000 units/day were given. Hemostatic drugs and platelet infusion were used for supportive treatment. The number of platelets in blood routine monitoring was always less than 10×10^9/L, with intermittent bleeding of skin and gingiva. Later, bone marrow examination was performed on December 20, 2019. Bone marrow cytology showed active hyperplasia, no pathological hematopoiesis, 83 megakaryocytes, and maturation disorder of megakaryocytes. Bone marrow flow and chromosome karyotype analysis showed no abnormality. Bone marrow pathological examination: the degree of hyperplasia is generally normal, no pathological hematopoiesis, no myelofibrosis. Platelet autoantibody test: platelet dispersive fluid GPIIb/IIIa positive, platelet dispersive fluid GPIa/IIa positive, platelet dispersive fluid GPIa/IIa positive. Based on the above tests, immune thrombocytopenia was still diagnosed. Dexamethasone was given 40mg/d×4 days again, and recombinant human thrombopoietin was discontinued. In the following 10 days, blood routine monitoring showed that the platelet level was still less than 10×10^9/L, indicating poor therapeutic effect. After 5 days of intravenous administration of human immunoglobulin (0.4g/kg/d), no increase of platelets was observed. After 10 days of treatment, the patient's platelets gradually began to rise to normal without bleeding. She continued to take Etripopa after discharge. Two weeks after discharge, the patient gradually developed dull abdominal pain and discomfort. On February 15, 2020, the patient was admitted to the hospital due to abdominal pain. After admission, the patient was given chest and abdominal CT: the examination showed no abnormalities in chest CT, thickened gastric antrum wall, ascites, enlarged retroperitoneal lymph nodes, multiple nodules in bilateral adnexa, peritoneal and omentum. Gastroscopy showed non-atrophic gastritis, and gastric horn mucosal biopsy showed moderate chronic mucosal inflammation, mild intestinal metaplasia, and moderate atrophy .Peritoneal nodule pathology combined with immunohistochemistry, epithelioid mesothelioma considered, immunohistochemistry:WT-1 positive, CK7 positive, CR positive, CK5/6 positive, P53 partial weak positive, CA125 positive, CK8 positive, CKLMW positive, D2-40 positive, Ki-67 proliferation index about 15%, ER negative, PR negative, PAX-8 negative, CK20 negative, CDX-2 negative, SATB2 negative, Villin was negative, TTF-1 negative, P63 negative, GATA3 negative, CD31 negative, and ERG negative. The patient underwent surgery for abdominal epithelioid mesothelioma on February 25, 2020. After surgery, the patient's platelets remained in the normal range, and the patient was gradually discontinued from ettripopa, followed by 6 courses of chemotherapy. After that, the patient maintained a normal platelet level. At follow-up, the patient's platelets remained in the normal range.

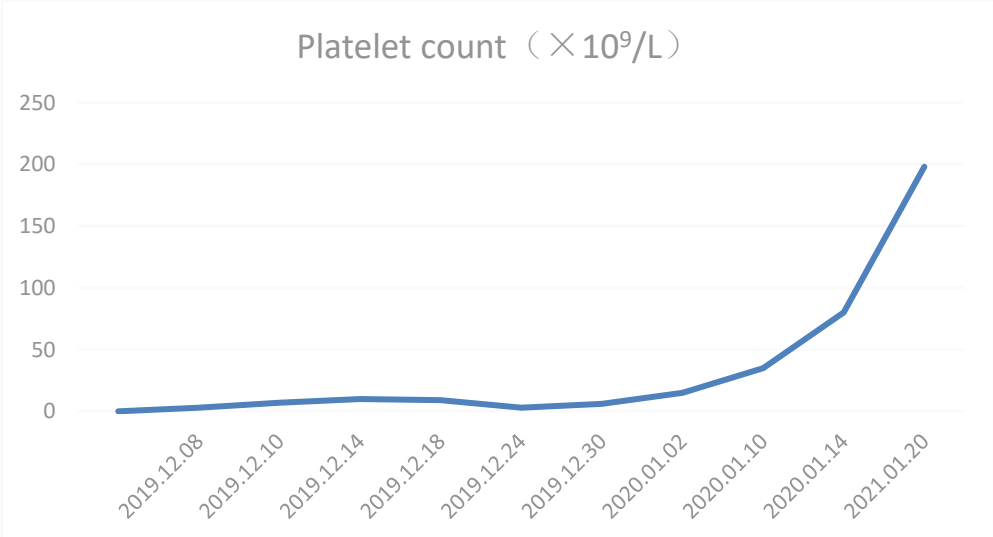

Figure 1. Platelet count

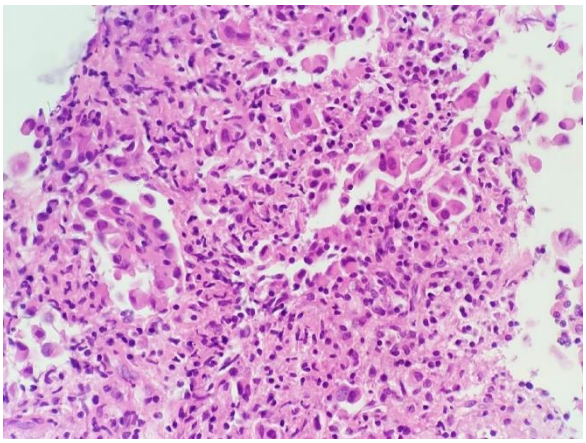

Figure 2. The neoplastic cells were arranged in small nests with epithelioid appearance, red cytoplasm and anomalous nuclei. HE staining at 400 times magnification）

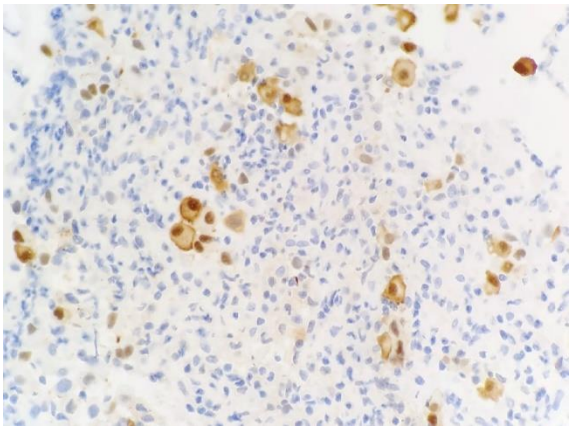

Figure 3. Immunohistochemical staining with Calretinin showed positive tumor cells at 400 times magnification

3 Discussion

Thrombocytopenia is associated with 5% to 10% of solid tumors at initial diagnosis, and the incidence of thrombocytopenia increases during disease progression and treatment, including immune thrombocytopenia (ITP), cancer-associated thrombotic microangiopathy (CatM), and myelosuppression after chemotherapy. Many reports suggest that immune-mediated thrombocytopenia is a manifestation of paraneoplastic syndrome[5-6]. Paraneoplastic syndrome is a disease that has no direct relationship with the growth, invasion, or metastasis of tumors. It is caused by the autonomous secretion of hormones and cytokines by tumors. To date, no paraneoplastic ITP has been reported in patients presented with peritoneal epithelioid mesothelioma. In this case, the patient showed no signs of infection、 DIC or hypersplenism. No drugs、 vaccines or blood transfusions were used before hospitalization. No tumor bone marrow infiltration was found in the bone marrow, HIV and hepatitis virus infection were excluded, and no connective tissue disease evidence was found. We were initially unable to determine whether immune thrombocytopenia was primary IT or secondary ITP. However, with the diagnosis of peritoneal epithelioid mesothelioma and surgical treatment, the rapid recovery of the patient's thrombocytopenia further supports the diagnosis of para-neoplastic immune thrombocytopenia.

A 2012 review of 68 published cases of ITP associated with solid tumor-related immune thrombocytopenia found that 35 patients (53%) were diagnosed with immune thrombocytopenia at the same time as the tumor, and 1 patient had complete remission of immune thrombocytopenia after surgical treatment of the tumor. One patient had complete remission of immune thrombocytopenia after chemotherapy[7]. Epithelioid mesothelioma with immune thrombocytopenia has not been reported. There is also insufficient evidence to support the improvement of immune thrombocytopenia after surgery or chemoradiotherapy for solid tumors. At present, the main pathogenesis of solid tumor complicated with immune thrombocytopenia is as follows: the dysregulation of immune function in tumor patients produces platelet antibodies; Some haptens produced by tumors have the same antigenicity as the surface molecules of megakaryotic cells, resulting in cross immune reaction. Some active metabolites of tumor inhibit the differentiation and maturation of megakaryocytes[8]. Treatment of paraneoplastic ITP associated with solid tumors includes corticosteroids、 splenectomy、 IVIG and TPO receptor agonists、 platelet infusion and surgery、chemotherapy、and/or radiation therapy for underlying malignancies. Our patients after surgical treatment of peritoneal mesothelioma platelet gradually returned to normal, this may be due to the immune regulating environmental change and tumor antigen and the disappearance of the metabolites, leading to antibody disappear and remove interference of megakaryocyte differentiation, suggests that the malignant tumour of the potential for this kind of secondary ITP treatment is essential. This case supports the relationship between peritoneal mesothelioma and immune disease. We suggest that removal of the tumor leads to remission of ITP and partial remission of thrombocytopenia once the antigens that trigger the immune response are removed. This article emphasizes the importance of treating primary tumors to improve the clinical process of ITP, and also contributes to the smooth progress of

epithelial tumor chemotherapy. The normal platelet count can ensure the smooth progress of chemotherapy.

In addition, current guidelines do not recommend screening for solid tumors in patients with ITP without a clear cause and recommend screening for solid tumors. The relationship between ITP and epithelioma needs to be further studied.

4 Declaration of interest

The authors declare that there is no conflict of interest that would prejudice the impartiality of this scientific work.

References

[1] Moulis G, Palmaro A, Montastruc JL, et al. Epidemiology of incident immune thrombocytopenia: a nationwide opulation based study in France[J]. Blood, 2014, 124(22): 3308- 3315. DOI: 10.1182/blood-2014-05-578336.

[2] Zufferey A, Kapur R, Semple JW. Pathogenesis and therapeutic mechanisms in immune thrombocytopenia （ITP） [J]. J Clin Med, 2017, 6(2):16. DOI: 10.3390/jcm6020016.

[3]Krauth MT, Puthenparambil J, Lechner K. Paraneoplastic autoimmune thrombocytopenia in solid tumors. Crit Rev Oncol Hematol. 2012 Jan;81(1):75–81.

[4]Dillon C. Cockrell， Raj S. Kasthuri， Ersan Altun， Secondary Immune Thrombocytopenia in Metastatic Renal Cell Carcinoma: A Case Report and Discussion of the Literature[J]. Case Rep Oncol 2020;13:1349–1356.DOI: 10.1159/000511067

[5]K. Yang, T. Zhang, J. Chen et al., “Immune thrombocytopenia as a paraneoplastic syndrome in patients with asopharyngeal cancer,” Head and Neck, vol. 34, no. 1, pp. 127–130, 2012.

[6]S. Zheng, H. Chan, R. J. Epstein, and J. E. Joseph, “Resolution of paraneoplastic immune thrombocytopenia following everolimus treatment for metastatic renal cell carcinoma,” Internal Medicine Journal, vol. 45, no. 6, pp. 666–669, 2015.

[7] Krauth MT, Puthenparambil J, Lechner K. Paraneoplastic autoimmune thrombocytopenia in solid tumors. Crit Rev Oncol Hematol. 2012; 81: 75-81.

[8] Yang Boyan. Identification and management of solid tumor-associated thrombocytopenia. Chinese Medical Journal, 2019, 99(8): 561-565.