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ABOUT COVER

Editorial board member of *World Journal of Clinical Cases*, Dr. Li is a Professor at the Nanjing University Medical School in Nanjing, China. Having received his Bachelor's degree from Xuzhou Medical College in 1997, Dr. Li undertook his postgraduate training first at Nanjing Medical University, receiving his Master's degree in 2004, and then at Fudan University, receiving his PhD in 2007. He advanced to Chief Physician in the Department of Anesthesiology at The Affiliated Hospital of Nanjing University Medical School in 2017 and has held the position since. His ongoing research interests involve ultrasound (transthoracic echo and transesophageal echo) in clinical anesthesia and ultrasound-guided limb and trunk nerve block in postoperative pain management. (L-Editor: Filipodia)

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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Sweet syndrome as a paraneoplastic manifestation of cholangiocarcinoma: A case report

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Abstract

BACKGROUND

Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, is a rare skin disorder that may be associated with cancer.

CASE SUMMARY

A 58-year-old female presented with a cholestatic syndrome and significant

The authors read the CARE checklist (2016) and the case report was prepared and revised in accordance with the CARE checklist (2016).

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weight loss three months before admission. Five months earlier, she had abruptly developed skin lesions with erythematous papules that evolved to erythematous blisters. Clinical evaluation and laboratory tests confirmed hepatic cholangiocarcinoma. Skin lesions histopathological findings showed neutrophilic dermatosis, massive edema, fibrin, necrosis, and elastosis. These results, in association with the macroscopic aspects of the findings, led to the diagnosis of paraneoplastic Sweet's syndrome due to cholangiocarcinoma. As staging was consistent with an advanced tumor without a cure perspective, we opted to perform percutaneous biliary drainage, and subsequently, palliative care. Eventually, after a few weeks, the patient died.

CONCLUSION

In conclusion, the diagnosis of the underlying disease-causing Sweet's syndrome must be accurate, and patients need to be followed-up, as neoplasia such as cholangiocarcinoma may be a later manifestation.

Key Words: Cholangiocarcinoma; Paraneoplastic syndrome; Sweet syndrome; Case report; Bullous lesions; Cholestasis

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Core Tip: Sweet's syndrome preceding solid neoplasia, especially cholangiocarcinoma, is a rare condition. Only two cases of Sweet's syndrome associated with cholangiocarcinoma have been reported. Bullous skin lesions should be evaluated with a broad differential diagnosis, including the possibility of preceding the diagnosis of neoplasia. The evaluation and follow-up of patients with this condition is essential, seeking diagnosis and treatment in early stages of the neoplastic lesion.

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INTRODUCTION

Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, is a rare inflammatory disorder characterized by the abrupt appearance of painful, edematous, and erythematous papules, plaques, or nodules on the skin. Fever and leukocytosis frequently accompany the cutaneous lesions. It may be clinically divided into three types: Classical or idiopathic, malignancy-associated, and drug-induced^[1]. The malignancy-associated form was described in approximately 20% of Sweet's syndrome cases^[2]. Within these cases, the most common reported association has been with hematopoietic neoplasia (nearly in 85%), while fewer cases were associated with solid tumors, as was our described case^[3]. It is interesting to note that there is a scarcity of case reports about the association between Sweet's syndrome and cholangiocarcinoma. Therefore, we describe the case of a patient who was diagnosed with the paraneoplastic Sweet's syndrome and had this malignant biliary tumor, to remind physicians about this possible association.

CASE PRESENTATION

Chief complaints

A 58-year-old female presented at our service on March 21st of 2018, with a three-month history of cholestasis symptoms, as well as significant weight loss (about 20 kg). She reported jaundice, choloria, acholia, and itching.

History of present illness

Two months before the development of the gastrointestinal symptoms, she had suddenly progressed with skin lesions (erythematous papules) that evolved to erythematous blisters.

History of past illness

She denied other comorbidities, fever, and diarrhea.

Physical examination

On physical examination, she was malnourished, pale, afebrile, and presented significant jaundice. The abdominal exam was remarkable for a mild diffuse abdominal tenderness to deep palpation, as well as for an enlarged nontender, firm, and irregular liver. There were also blistering and crusted skin lesions, simulating pemphigus, throughout the scalp, hands, and feet (Figure 1).

Laboratory examinations

Tumor markers analysis showed a CA 19.9 of 1281.5 U/mL (upper limit of normal, 37.0 U/mL), alpha-fetoprotein of 2.13 ng/mL (upper limit of normal, 10.0 ng/mL), and CEA of 14.8 ng/mL (upper limit of normal, 4.9 ng/mL). The remaining laboratory tests showed leukocytes count of $8.900/\text{m}^3$ (80%, neutrophils), C-reactive protein of 23 mg/L (upper limit of normal, 10.0 mg/L), marked increased cholestatic liver enzymes, and bilirubin levels. Aminotransferases were mild to moderately elevated.

Imaging examinations

The patient underwent an abdomen computed tomography that revealed an infiltrative mass causing dilatation of the bile ducts, as well as increased mesenteric lymph nodes, and ascites (Figures 2 and 3). Further investigation with a magnetic resonance of the upper abdomen with cholangiopancreatography, confirmed stricture of the common bile and hepatic ducts due to probable neoplasia, and upstream dilatation of the biliary tree.

FINAL DIAGNOSIS

The patient underwent an echo-endoscopy with fine-needle aspiration biopsy of the tumor that confirmed the diagnosis of cholangiocarcinoma. Biopsies of the skin blistering and crusted lesions simulating pemphigus throughout the scalp, hands, and feet, were performed. Microscopy analysis showed neutrophilic dermatosis with massive edema, fibrin, necrosis, and elastosis (Figure 4).

TREATMENT

The aforementioned results, in association with the macroscopic aspects of the lesions, led to the diagnosis of paraneoplastic Sweet's syndrome. The patient was started on steroids and antihistamines to treat the skin lesions without success.

OUTCOME AND FOLLOW-UP

Due to the advanced stage of the tumor, with no cure perspective, we opted to perform percutaneous biliary drainage for symptomatic relief and subsequent palliative care. Figure 5 describes the chronology of the events.

DISCUSSION

We reported the case of a patient diagnosed with Sweet's syndrome as a paraneoplastic manifestation of a cholangiocarcinoma, in which the primary symptoms were cholestatic syndrome and weight loss. The clinical evolution, laboratory tests, and skin lesions biopsy results made it possible to confirm the diagnosis of Sweet's syndrome based on Su and Liu's criteria^[4] (1896) modified by von



Figure 1 Blistering skin lesions suggesting pemphigus on foot (A) and hands (B).



Figure 2 Axial plane image of computed tomography obtained in the portal phase showing significant intrahepatic biliary tract dilatation (orange arrows).



Figure 3 Axial plane image of computed tomography obtained in the portal phase showing an infiltrative aspect of the tumor, with irregular contour and mild contrast enhancement located at the common bile duct (orange arrows) determining biliary tract dilatation.

den Driesch^[5]. Sweet's syndrome is characterized by the sudden appearance of erythematous papules and/or plaques, which can contain vesicular surfaces and usually affect thorax, back, face, neck, and upper extremities^[5]. Our patient presented with abrupt onset of erythematous papules, histopathological evidence of dense neutrophilic infiltrate with no signs of leukocytoclastic vasculitis and had an underlying visceral malignancy. Laboratory values at presentation showed > 8000 leukocytes as well > 70% neutrophils.

There are three possible clinical categorizations for this syndrome based upon etiology: Classical or idiopathic, malignancy-associated, and drug-induced^[1]. Malignancy-associated Sweet's syndrome corresponds to approximately 20% of the cases^[2]. It is most associated with hematological neoplasia (in 85% of the cases), and less frequently, with solid tumors, as was the case of our patient^[3]. The main form of presentation in these cases associated with malignancy is as a paraneoplastic syndrome. The appearance of the skin lesions can precede the primary illness' diagnosis in months to years^[6]. The histopathological and laboratory test results favored the patient's diagnosis of a paraneoplastic Sweet's syndrome in our case.

Gold standard treatment is to administer systemic steroid therapy, which may lead to a fast remission of the symptomatology. Treatment of the primary underlying disease is also related to the chances of patient recovery^[9]. Nevertheless, in our case, corticosteroid and antihistamine therapy were unsuccessful. Another therapeutic approach that we adopted was biliary drainage to proportionate symptomatic relief. There are no current well-established guidelines to treat malignancy-associated Sweet's syndrome^[3].

To our knowledge, there are only two reported cases of Sweet's syndrome in association with cholangiocarcinoma. The first case ever describing this association, was published in 2006. In this case of a 68-year-old woman, skin lesions preceded the diagnosis of the malignant tumor, as it occurred with our patient^[7]. The other case report described a 72-year-old man with cholangiocarcinoma in which Sweet's syndrome manifested 3 years after the initial diagnosis, five months after chemotherapy interruption due to a semi-urgent surgery^[8].

CONCLUSION

In conclusion, the diagnosis of the underlying disease-causing Sweet's syndrome must be accurate, and patients need to be followed-up, as neoplasia such as cholangiocarcinoma may be a later manifestation.

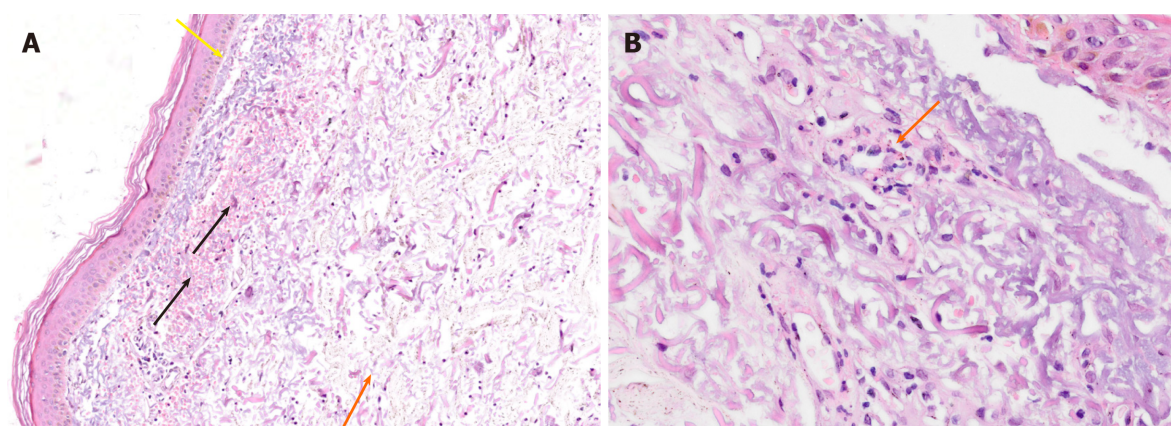


Figure 4 Skin lesions biopsy stained with hematoxylin-eosin showed elastosis (yellow arrow), edema (orange arrow), bleeding focus and red cells extravasation (black arrows) (A) and capillary destruction (B).

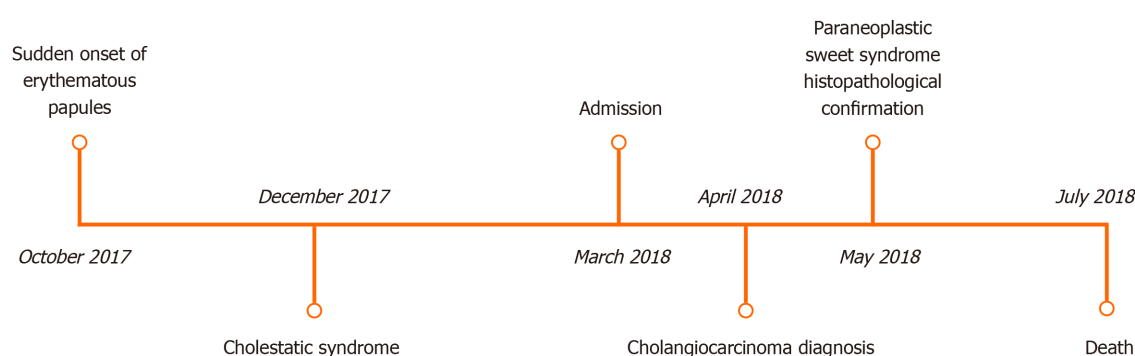


Figure 5 Timeline of events reported in the clinical case.

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