A Case Report on Paraneoplastic Pemphigus Associated Colonic Carcinoma

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Paraneoplastic pemphigus (PNP), an acantholytic mucocutaneous syndrome, has a universal association with malignancy and a poor prognosis.[1] The clinical picture is characterized by painful mucosal erosions, ulcerations, and polymorphous skin lesions that progress to blistering eruptions on the trunk and extremities. In the reviews of all PNP, hematologic malignancies such as non-Hodgkin's lymphoma, chronic lymphocytic leukemia, and Castleman's disease account for the most part; nonhematologic malignancies are very seldom especially adenocarcinoma of colon.[2] These will be illustrated in the following paper on the basis of a case report of a patient with colonic adenocarcinoma who presented with PNP.

A 68-year-old male presented to the emergency room with progressive bullous and erosive skin lesions involving the whole body for 13 days, associated with dysphagia. The patient had been operated on for moderately differentiated sigmoid colonic adenocarcinoma 3 weeks ago [Figure 1a–1c]. He suffered hypertension 20 years and occurred cerebral infarction 10 years ago. He did not smoke and addict to drink. On clinical examination, he had ulcerated and bullous lesions on the palate, cheek mucosa and lip, flaccid blisters, exfoliated skin, and crusted erosions involving trunk and back especially around the incision were observed [Figure 1d and 1e]. Laboratory tests showed hypoproteinemia: white blood count 5.4×10^9/L, hemoglobin 160 mg/L, and platelets 286×10^9/L. Skin biopsy was performed on the abdominal skin lesion and the histology showed suprabasal acantholysis with bullous cleft formation, which was compatible with PNP [Figure 1f]. Prednisone 100 mg/d was started for treatment of pemphigus, and 1 week later with a maintenance dose 60 mg/d. In order to prevent infection at the beginning 2 weeks of the treatment, cefmetazole 4 g/day was given. Maintaining treatment, he enjoyed an important improvement in pain and no new lesions. The dermatic and mucosal lesion recovered 4 weeks later [Figure 1g and 1h]. Before and after the skin lesions, we did not find a clear recurrence and metastatic lesions.

PNP is a life-threatening autoimmune disease characterized by cutaneous blister and erosions with mucosal involvement. It is mostly seen in association with lymphoproliferative disorders but is very rare in colorectal cancer.[2] PNP commonly parallel with the malignancy and will be retrieved after the primary tumor removed. About 17% of PNP cases without a previous diagnosis of a neoplasm.[3] The clinical findings include incurable stomatitis and polymorphic skin lesions. Mucosal involvement is almost always present, ocular, oral, pharyngeal, laryngeal, anus, and/or vulvar lesions; skin manifestations range from papules and plaques similar to erythema multiforme, vesicles, and blisters that resemble pemphigus vulgaris or even pruritic plaques similar to lichen planus. Some patients also have respiratory complications such as bronchiolitis obliterans, with the potential risk of respiratory failure. The diagnosis is based on clinical appearances, histopathology, the detection of tissue bound and circulating autoantibodies, and the underlying neoplasm. The diagnostic criteria can be divided into major and minor ones.[4] The major criteria include polymorphous skin eruption, concurrent internal neoplasia, antibodies with an

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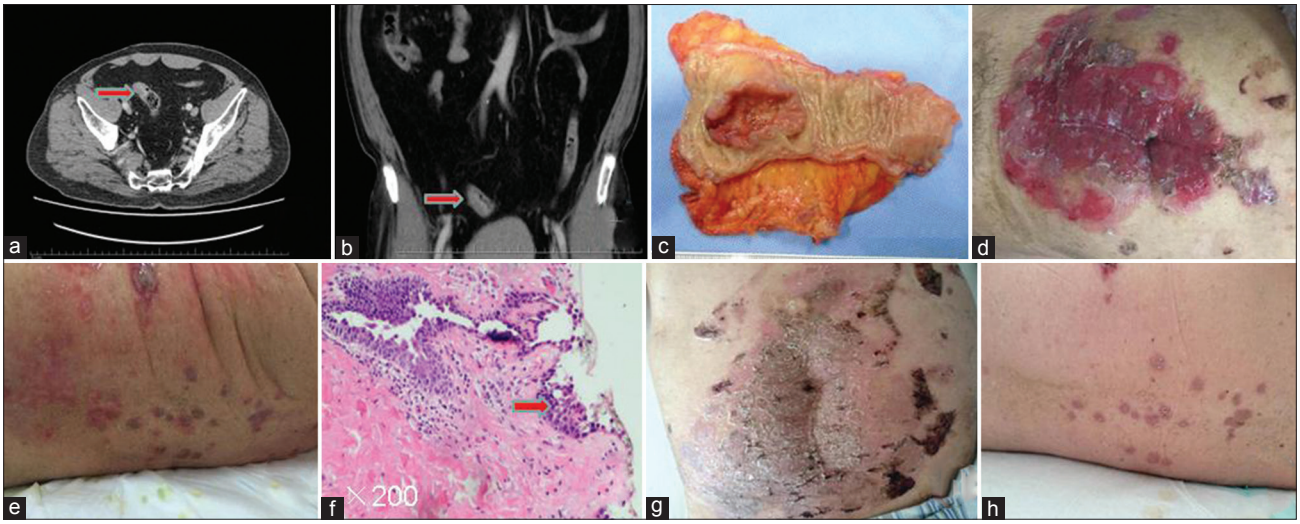

Figure 1: Paraneoplastic pemphigus associated with colonic cancer. (a and b) Abdomen CT before operation of the sigmoid colonic cancer. Where the arrows indicated the sigmoid colonic cancer shown in the abdomen CT. (c) Radical excision sample of the sigmoid colonic cancer. (d and e) Ulcerated and bullous lesions in the skin 3 weeks after operation, suggested the paraneoplastic pemphigus. (f) Skin biopsy pathology (HE, original magnification ×200), where the arrow showed suprabasal split with an intense lichenoid infiltrate. (g and h) After prednisone treatment, the dermatic lesions recovered 4 weeks later. CT: Computed tomography.

immunoprecipitation specific standard, and the minor criteria include histological evidence of intraepithelial acantholysis, direct immunofluorescence (DIF) showing a linear pattern in an area of the basement membrane with immunoglobulin G (IgG) and complement 3 (C3) deposition, and in DIF using rat bladder epithelium as a substrate. The histopathologic hallmark of PNP is a predominant interface reaction pattern, characterized by basal cell vacuolar degeneration, dyskeratotic and necrotic keratinocytes, and lymphocytic inflammation characterized by lymphocytic exocytosis with either as sprinkling of lymphocytes at the basement membrane zone or a band-like infiltrate in the upper dermis.[3] However, sometimes acantholysis might be minimal or absent. In DIF, there is a deposit of IgG (with or without C3) in the intercellular spaces of the epidermis and/or basement membrane, and IIF shows antibodies of the IgG type.[4] If there are three major criteria, or two major and one minor criteria, PNP can be sure.

Due to the rarity of the condition and the high rates of treatment failure, there was no consensus on consistently efficacy treatment.[5] The efficacy ones has been gained from individual case reports, small case series, and expert recommendations.[5] As the common causes of death include sepsis, pain, undernourish, gastrointestinal bleeding, and bronchiolitis obliterans, etc., therefore, management of associated complications is needed. Moreover, if PNP is suspected as a diagnosis, the below 6 steps should be given: (1) stabilization of the patient, (2) investigation for the presence of malignancy, (3) establishment of a definitive diagnosis of PNP, (4) removal of the underlying neoplasm where feasible, (5) medical treatment of the underlying neoplasm, and (6) treatment of the disease itself (individualized for the patient) through either: (a) immunosuppression, (b) immunomodulation, and (c) removal of pathogenic autoantibodies.[5] Among all the above treatment strategies, the most widely suggested are combine prednisone (0.5–1.0 mg/kg) with cyclosporine (5 mg/kg) and might also include cyclophosphamide (2 mg/kg). However, commonly the responses to treatment were poor, and the mortality rate was about 90%.

Our case was quite unusual concerning the major criteria. Commonly, PNP is parallel with the malignancy, but our case delayed. Another peculiarity was the good response to the treatment. As a life-threaten autoimmune syndrome, PNP deserves keen understanding and attention by the dermatologist and surgeon. Great diagnostic and management should been made in order to depress the morbidity rate and improve the life quality for these chronically ill patients.

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Conflicts of interest

There are no conflicts of interest.

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