Case report

Rare case of peristomal pemphigus vulgaris in an operated case of carcinoma of the rectum

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SUMMARY

Pemphigus vulgaris (PV), in association with malignancy of the rectum, is a very rare presentation. We present here a case of a 58-year-old woman presenting with atypical skin eruptions in the peristomal area, which gradually progressed to her entire body. These lesions were later diagnosed to be PV. She developed these lesions in her postoperative period following an anterior resection with a covering ileostomy for her rectal malignancy. She had received neoadjuvant chemo+radiotherapy for her malignancy.

BACKGROUND

Pemphigus vulgaris (PV) is a rare autoimmune disorder causing severe blistering of skin and of the mucous membranes lining the mouth, nose, throat and genitals. Blisters have thin roofs and break easily to leave raw areas that can be extensive and painful. It is caused by antibodies against desmoglein 1 and desmoglein 3, present in desmosomes (type II hypersensitivity reaction). Loss of desmosomes results in loss of cohesion between keratinocytes in the epidermis and a disruption of barrier function served by intact skin.

CASE PRESENTATION

A 58-year-old, highly anxious female patient was diagnosed to have a moderately differentiated adenocarcinoma of the rectum through endoscopy and biopsy. She also suffered from diabetes mellitus, hypertension and hypothyroidism. Her contrast-enhanced imaging of the abdomen and pelvis was suggestive of a locally advanced disease, for which she received neoadjuvant chemotherapy (capecitabine tablet)+radiotherapy (200 cGy for 28 days). She was then referred to us for the definitive treatment. We found her to be highly anxious and under undue emotional stress on account of her disease, its prognosis and her family obligations. She underwent an anterior colonic resection with primary anastomosis with a covering ileostomy after her neoadjuvant treatment. Postoperative recovery was uneventful, and she was discharged on the seventh postoperative day on full orals with good ileostomy output. Two weeks after the procedure, she noticed an excoriation of the skin with burning sensation around the ileostomy site and the laparotomy incision site. She came for follow-up with us 2 weeks after that with excoriation extending onto the adjacent abdominal wall ([figure 1](#)). On local examination, the stoma was healthy and

functioning well with semisolid content. There was no leak of the contents of the bag. Skin around the stoma and suture line showed excoriation. No other stoma-related complications such as retraction, prolapse, parastomal hernia or necrosis were seen. The patient was started on conservative management and was advised to use various alcohol-free barrier creams containing a combination of lanolin oil, magnesium citrate, methyl paraben, cyclomethicone, glyceryl oleate and mineral oils. She was also advised to use broad-spectrum antifungal and antibiotic creams and to keep the affected area dry with various zinc oxide dusting powders. Care was taken to avoid colostomy bag leak, and a specialised in-house stoma care nurse was also involved in her care. Various antibiotic creams and commercially available placental extracts were also used as topical agents. In spite of these conservative measures, the skin lesions continued to increase in size and number and gradually spread over the patient's entire abdominal wall. Hence, decision was taken to reverse the stoma earlier so as to prevent further contact dermatitis, which was our initial diagnosis. The stoma was reversed on day 48 after primary surgery. Even after the reversal, the skin lesions showed no signs of abating ([figure 2](#)). There were new lesions appearing daily, and gradually, the entire anterior abdominal wall and the back and trunk also started developing blistering painful lesions ([figures 3 and 4](#)). We consulted a dermatologist for the same.

We did not consider a diagnosis of paraneoplastic pemphigus while sending the skin biopsy specimen since there was no evidence of concurrent residual internal malignancy. Hence, we did not do immunofluorescence testing and also did not test the antidesmoglein titres. After arriving at the diagnosis of pemphigus, the patient was started on methylprednisolone and she had an initial improvement; hence, no further tests were carried out. Later, when there was a recurrence of the skin lesions, she was started on rituximab. In hindsight, this was probably the time that we should have ruled out paraneoplastic syndrome, but again the patient responded very well to the rituximab treatment; hence, we did not pursue any further diagnostic modalities.

INVESTIGATIONS

The consultant dermatologist found Nikolsky's sign to be positive; a punch biopsy was taken from the skin lesions and the result was sent for histopathology. The histopathology revealed

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Figure 1 Skin lesions after anterior resection with loop ileostomy.

intraepidermal suprabasal acantholytic blistering dermatitis. The blisters showed a tombstone pattern with occasional acantholytic cells. There was also neutrophilic spongiosis at the periphery of the blister. This was suggestive of PV (figure 5).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of peristomal skin lesions commonly include contact irritation, allergic dermatitis, pre-existing skin diseases like psoriasis, eczema, seborrheic dermatitis and, rarely, squamous carcinomas, as well as PV.

TREATMENT

After we arrived at a diagnosis of PV, the patient was started on prednisolone tablets 40mg once a day on postoperative day 7.

Figure 2 Persistent skin lesions after stoma closure.

Figure 3 Blistering skin lesion

The dosage was kept on the lower side of the therapeutic limit in view of recent bowel anastomosis. She gradually responded to the same and was discharged on oral steroids. Since there was clinical improvement, her steroid dosage was gradually reduced, but this led to a recurrence of her skin lesions. Hence, a decision was taken to start her on rituximab injection, a monoclonal chimeric IgG1 antibody targeting the B cell-specific cell-surface antigen CD20. Rituximab was given according to the rheumatoid arthritis protocol, where 1 g is given in intravenous infusion at 15 days' interval.^{1,2} She was given two doses of the same.

OUTCOME AND FOLLOW-UP

After the treatment with rituximab, the patient showed improvement in her disease status, and gradually the lesions healed with hyperpigmentation (figure 6). She continues to remain in remission 14 months after the second dose of rituximab (figure 7).

DISCUSSION

Pemphigus is defined as a rare group of autoimmune life-threatening blistering disorders characterised by acantholysis (loss of keratinocyte to keratinocyte adhesion) that results in the formation of intraepithelial blisters in mucous membranes

Figure 4 Skin lesion involving the back .

Figure 5 Histopathology H&E staining: intraepidermal suprabasal acantholytic blistering dermatitis. The blister shows a tombstone pattern with occasional acantholytic cells. Neutrophilic spongiosis is shown at the periphery of the blister.

and the skin. Peristomal skin reactions are mostly irritant reactions, particularly from leakage of urine or faeces (42%). A few other pre-existing skin diseases like psoriasis, seborrhoeic dermatitis, eczema (20%); infections (6%); allergic contact dermatitis (0.7%); and pyoderma gangrenosum 0.6% may show a flare-up after the creation of a stoma.³ Bullous pemphigoid and PV skin lesions are very rare and so far have only been reported in peristomal location in patients with inflammatory bowel disorders.⁴⁻⁶ Paraneoplastic pemphigus is also a known entity, with the most frequently reported associated malignancies to be lymphomatoid and haematological in origin.⁷ This makes the presence of peristomal PV in our case of carcinoma of the rectum very rare. The triggering factors of PV are still unclear. Pemphigus is known to be multifactorial and involves interaction between genetic predisposition and environmental factors. Our

patient did not give any previous history of autoimmune diseases or any mucosal lesions in the past. She did not have a positive family history for the same. There was no history or indication of allergy to any topical ointments or cosmetics or medicines. Medications, thermal burns, ultraviolet light, ionising radiation, viral infection, surgery, cosmetic and contact allergens, and even emotional stress have been known to act as triggers for pemphigus. Reichert-Penetrat *et al* reported a case of PV over a 40-year-old surgical scar in an elderly man with oral ulceration.⁸ Mehregan *et al* also reported a case of pemphigus arising in areas of surgical manipulation after rhinoplasty and hair transplantation between 3 months and 1 year after surgery, respectively.⁹ Rashid *et al* reported a case of skin lesions in and around the appendectomy wound 2 weeks after surgery.¹⁰ These reports suggest a temporal association between surgery and pemphigus, in our case also, our patient developed the skin lesions nearly 2 weeks after her surgery. Various published studies suggest that there is some role of psychological stress in triggering PV. The role of psychogenic factors in the induction of pemphigus foliaceus was first reported by Perry and Brunsting in 1965.¹¹ Brenner and Bar-Nathan in 1984 described two patients who had developed PV under emotional stress.¹² Our patient was a highly anxious person. She did not exhibit any personality disorders, but she was under great emotional stress due to her disease and its prognosis. Matias *et al* have reviewed the literature until August 2013 and published their findings on psychological stress leading to pemphigus.¹³ Since there was no past history of any autoimmune disease or skin disorders in our case and we could

Figure 6 Post-treatment status 1 month after rituximab.

Figure 7 Post-treatment status 14 months after rituximab.

not find any other triggering factor after a detailed study, we concluded that emotional stress was the likely triggering factor for the development of PV in our patient. That, coupled with the presence of PV in the stoma, created a malignancy of the rectum, which makes our case very rare. We did not consider a diagnosis of paraneoplastic pemphigus while sending the skin biopsy specimen since there was no evidence of concurrent residual internal malignancy. Hence, we did not do immunofluorescence testing and also did not test the antidesmoglein titres. After arriving at the diagnosis of pemphigus, the patient was started on methylprednisolone and she had initial improvement; hence no further tests were carried out. Later, when there was a recurrence of the skin lesions, she was started on rituximab. In hindsight, this was probably the time that we should have ruled out paraneoplastic syndrome, but again the patient responded very well to the rituximab treatment; hence, we did not pursue any further diagnostic modalities.

Learning points

- The differential diagnosis of peristomal skin lesions commonly include contact irritation, allergic dermatitis, pre-existing skin diseases like psoriasis, eczema, seborrheic dermatitis and, rarely, squamous carcinomas as well. However, it is essential to also entertain a differential of pemphigoid lesions.
- The importance of severe emotional stress as a trigger for various autoimmune and skin disorders, especially in postoperative patients after a major surgery, should also be kept in mind.
- Treatment of the underlying stress might help to alleviate symptoms to some degree.
- A high index of suspicion and low threshold to biopsy-suspected skin lesions will help in increasing the number of cases diagnosed and might be able to define standards of care in the future.

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Research Centre, Peddar Road, Mumbai; and UA is a general surgery resident at the Department of Surgery, Jaslok Hospital & Research Centre, Peddar Road, Mumbai. All the authors have made significant contributions towards the making of this paper. The entire concept and design was arrived at by consensus. Each of them has contributed to variable degrees. SAB and MB take responsibility for the integrity of the work as a whole from inception to published article, and both of them should be designed as the 'guarantor'. SAB, the lead author, along with coauthors, certify that they have seen and approved the final version of the manuscript and all subsequent versions. They have made substantial contribution to the conception, design and acquisition of data. They have drafted the article and revised it critically for important intellectual content.

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