Cutaneous paraneoplastic syndrome associated with anal squamous cell carcinoma: a rare presentation of an uncommon cancer

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ABSTRACT
Paraneoplastic syndromes associated with anal squamous cell carcinoma (SCC) are rare. Erythema gyratum repens (EGR) is a cutaneous paraneoplastic syndrome with distinctive characteristics. Here, we report the rare case of an 73-year-old woman with a chronic erythematous rash for 11 months associated with intense pruritus. She was treated with prednisone and antihistamines by dermatologists, but did not respond. The patient was subsequently seen in our clinic for unintentional weight loss and anorexia with intermittent nausea and vomiting. During further evaluation with imaging studies, upper endoscopy, and colonoscopy with biopsy, poorly differentiated anal SCC was identified. Biopsies of the skin rash were characteristic of EGR. She was treated using concurrent chemotherapy with 5-fluorouracil and mitomycin C and pelvic radiation (50.4 Gy in 28 fractions) for anal SCC. She tolerated the treatment, and her rash faded, with resolution of the pruritus.

Key Words Paraneoplastic syndrome, anal squamous cell carcinoma, erythema gyratum repens

BACKGROUND
Erythema gyratum repens (EGR) is an uncommon paraneoplastic syndrome involving the skin on a considerable amount of body surface area, sparing the palmar and plantar surfaces. It is characterized by concentric rings of rapidly migrating erythematous eruptive lesions with a “wood grain” appearance and scaling edge. In approximately 70% of cases, the presence of EGR is associated with internal neoplasms. Here, we report a unique case of EGR as a paraneoplastic syndrome in an elderly woman with anal canal squamous cell carcinoma (SCC).

CASE PRESENTATION
A 73-year-old woman presented with a complaint of changes in bowel movements, associated with poor appetite, unintentional weight loss, and intermittent episodes of nausea and vomiting. She also reported an evolving erythematous skin rash on her thighs, buttocks, trunk, and axillae, with intense itching throughout her body for 11 months. The rash had erupted as multiple annular lesions with central darkness and erythematous margins that did not improve with prednisone and antihistamines. It evolved into numerous whorl-shaped plaques with distinguished erythematous margins and was accompanied by crippling pruritus. Her past medical history included hyperplastic polyps of the descending colon and rectum diagnosed through biopsies in 2012, together with uterine cancer and basal cell carcinoma of the left side of the nose. She had a 50 pack-year smoking history. Her family history was positive for breast cancer in her mother and basal cell carcinoma in her brother.

The patient underwent esophagogastroduodenoscopy and colonoscopy with biopsies, which revealed gastritis and a protruding ulcerated mass in the distal anus inside the dentate line. Digital rectal examination found a palpable mass spanning most of the anal canal, sparing a small portion anteriorly. The mass extended from the distal rectum into the mid- to distal anal canal. Anal biopsies and imaging studies confirmed the diagnosis of poorly differentiated infiltrating anal SCC (stage IIa, cT2cN0cM0).
She was referred to the dermatologist for an assessment of her unresolved skin rash [Figure 1 (left panel)]. Punch and shave biopsies from the skin rash on back and abdomen were consistent with hyperkeratosis and eosinophilic spongiosis, with eosinophilic-rich dermal infiltrate. The lesions were clinically diagnosed as EGR.

The rash was treated with topical glucocorticoids, and gabapentin was added to alleviate pruritus. Anal cancer was treated with concurrent chemotherapy (5-fluorouracil and mitomycin C) and pelvic radiation (50.4 Gy in 28 fractions). During the course of chemoradiation, the patient’s itching resolved, and her lesions faded to faint scattered hyperpigmented patches on her upper back in the distribution of the original rash [Figure 1 (right panel)]. She tolerated chemoradiation without any significant side effects and regained her appetite and weight. During her follow-up visit at 8 months, the cancer was in remission, and the rash did not recur.

DISCUSSION

Anal canal cancer is a rare entity that accounts for 0.5% of all new cancer cases and 4% of all lower gastrointestinal tract cancers. The SCC subtype of anal canal cancer comprises approximately 70% of all anal cancers morphologically. It is more common in women, but an upward trend of incidence in both men and women has been observed. Like cervical cancer, anal canal SCC is predominantly caused by the human papillomavirus. Other risk factors include smoking, anal intercourse, and an increased number of lifetime sexual partners.

The most common presenting symptoms of anal canal SCC are bleeding, followed by pain in the anal region and discomfort from the mass. Less common symptoms include anal pruritus, constipation, diarrhea, incontinence, fistula, or fissures. A cornerstone for the diagnosis of this condition is a detailed physical examination and visualization with anoscopy, proctoscope, or flexible sigmoidoscope.

Our patient had a history of smoking and presented with change in bowel habits, poor appetite, and weight loss. A nonspecific presentation, together with the rarity of this cancer, hinders timely diagnosis. Abdominoperineal resection, once the primary mode of treatment, has now been replaced by sphincter-saving surgery in combination with chemoradiation as first-line therapy. Abdominoperineal resection can be used as salvage treatment in patients experiencing recurrence. Our patient experienced diarrhea and blood in her stools only a few times during the course of treatment; otherwise, the patient’s response to the chemoradiation was excellent.

Paraneoplastic syndromes are unusual symptom complexes triggered by the altered immune response to the tumour and can be a telltale sign of underlying malignancies. These syndromes can affect various body systems: cardiovascular, neurologic, musculoskeletal, gastrointestinal, hematologic, renal, and skin. Cutaneous manifestations of paraneoplastic syndromes can include plaques, papules, ulcers, or nodules. Identification of such features and clinical suspicion for an underlying malignancy in appropriate patients is crucial for timely diagnosis.

Up to 8% of malignancies are associated with paraneoplastic syndrome manifestations, but paraneoplastic syndromes linked to anal SCC are rare. The only reported cases include motor axonal neuropathy and refractory hypercalcemia. Cutaneous manifestations of internal neoplasms are rare, but EGR is one. To the best of our knowledge, a cutaneous paraneoplastic manifestation in response to anal SCC has never been reported in the medical literature, with the exception of one image published by Megan and Deede.

The term “erythema gyratum repens” was first coined by Dr. John Gammel in 1952, when, in an elderly woman with poorly differentiated adenocarcinoma of the breast, he observed a cypress burn–like rash that resolved with tumour treatment. More than 30% of the patients who develop EGR have lung cancer, 8% have esophageal cancer, and 6% have breast cancer. The proximate cause and pathophysiology of the EGR rash is still unknown. It can be attributed to the underlying tumour, which induces an autoimmune response that cross-reacts with cutaneous molecules to generate an inflammatory response. On histopathology, the rash has nonspecific findings such as acanthosis, parakeratosis, spongiosis, and hyperkeratosis. As seen in our patient, diagnosis of the cancer usually occurs a few months after development of the rash, and therefore prompt identification of the paraneoplastic nature of the rash is essential, because it might provide a substantial clue to an underlying malignancy in its initial stage.

Treatment of EGR is achieved by treating the underlying malignancy. In our patient, chemoradiation not only cleared the rash, but also resulted in dramatic improvement of the patient’s debilitating pruritus, accompanied by regression of the anal tumour.

SUMMARY

Paraneoplastic syndromes are constellations of symptoms that arise because of an altered immune response to a tumour and often can be a telltale sign of underlying occult malignancy.

Paraneoplastic syndrome in association with anal canal SCC is rare. The characteristic EGR skin rash has been reported to be associated with lung, esophageal, and breast cancers, but it has never been reported in anal cancer. Skin rash as a paraneoplastic manifestation of underlying occult
malignancy typically precedes diagnosis of the malignancy. Definitive treatment of the cancer results in resolution of the rash and other cutaneous manifestations.

CONFLICT OF INTEREST DISCLOSURES
We have read and understood Current Oncology’s policy on disclosing conflicts of interest, and we declare that we have none.

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