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Paraneoplastic Erythroderma as the Initial Manifestation of Advanced Colorectal Carcinoma: A Case Report

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Case Report

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Abstract

Introduction and Importance:

Paraneoplastic syndromes are heterogeneous disorders caused by tumor-mediated immune and humoral mechanisms rather than direct tumor invasion. Cutaneous manifestations are an important subset and may provide early diagnostic clues to underlying malignancy. Paraneoplastic erythroderma is rare and has been infrequently associated with colorectal carcinoma.

Case Presentation:

A 35-year-old Kenyan man presented with a nine-month history of progressive generalized erythroderma beginning on the face and extending in a cephalocaudal distribution, associated with severe pruritus and functional decline. The cutaneous manifestations preceded constitutional and gastrointestinal symptoms. Laboratory evaluation revealed anemia, eosinophilia, hypoalbuminemia, and elevated inflammatory markers. Imaging demonstrated cecal wall thickening, lymphadenopathy, and hepatic lesions suggestive of metastases. Fine-needle aspiration confirmed metastatic adenocarcinoma. Colonoscopy revealed an obstructing ileocecal mass, and biopsy showed poorly differentiated carcinoma. The patient underwent right hemicolectomy, and histopathology confirmed a grade 4 undifferentiated cecal carcinoma with nodal metastases. Immunohistochemistry showed diffuse CK7 and CK5/6 positivity with loss of CK20, CDX2, and SATB2 expression. Skin biopsy demonstrated nonspecific perivascular inflammation without primary dermatosis. Following surgical resection, marked resolution of erythroderma occurred within one month without dermatologic therapy.

Clinical Discussion:

This case highlights paraneoplastic erythroderma as a rare initial manifestation of advanced colorectal carcinoma. Its occurrence prior to systemic symptoms contributed to diagnostic delay, while rapid resolution after tumor resection supports an immune-mediated paraneoplastic mechanism.

Conclusion

Paraneoplastic erythroderma may represent the initial manifestation of advanced colorectal carcinoma. Persistent or unexplained erythroderma should prompt evaluation for underlying malignancy to enable timely diagnosis and management.

Introduction

Paraneoplastic syndromes (PNS) are a diverse group of clinical disorders associated with underlying malignancies that are not attributable to direct tumor invasion, metastatic spread, or treatment-related

toxicity. They arise from tumor-derived humoral factors and immune-mediated mechanisms, including cross-reactivity between tumor antigens and normal host tissues [1, 2]. These syndromes may involve multiple organ systems, most commonly affecting endocrine, neurologic, hematologic, and dermatologic pathways [2].

Cutaneous paraneoplastic syndromes represent the second most frequently reported group of PNS after endocrine manifestations [3]. They are clinically significant because they may precede, accompany, or signal recurrence of an underlying malignancy, and in some cases serve as an early diagnostic clue to occult cancer [1, 3]. A wide range of paraneoplastic dermatoses has been described, including acanthosis nigricans, dermatomyositis, necrolytic migratory erythema, Leser–Trélat sign, figurate erythemas, and erythroderma, many of which are associated with internal malignancies of gastrointestinal, pulmonary, breast, gynecologic, and hematologic origin [2, 4].

Colorectal cancer is a major cause of cancer-related mortality worldwide and is associated with a wide spectrum of paraneoplastic manifestations [5]. Cutaneous involvement may occur before the diagnosis of the primary tumor, concurrently with disease presentation, or during recurrence or progression [1, 6]. Although several dermatologic paraneoplastic syndromes have been reported in colorectal cancer, erythroderma as an initial manifestation remains rare.

Here, we report a case of paraneoplastic erythroderma as the initial clinical manifestation of an underlying advanced colorectal carcinoma in a 35-year-old male, highlighting the diagnostic challenge of severe exfoliative dermatitis as a presenting feature of occult malignancy. This case report has been written in compliance with CARE guidelines [7].

Case presentation

A 35-year-old previously healthy male from Kenya presented with a nine-month history of progressively worsening generalized dermatologic manifestations. The illness initially began as erythematous lesions over the face associated with mild swelling and fine scaling. Over subsequent months, the lesions gradually extended in a cephalocaudal distribution involving the neck, trunk, upper extremities, and lower extremities, eventually progressing to generalized skin involvement.

As the disease progressed, the patient developed diffuse thick scaling involving the scalp, face, trunk, and extremities accompanied by progressive hyperpigmentation, widespread exfoliation, and severe generalized pruritus that significantly impaired sleep and daily functioning. He initially sought medical attention at a local health center, where symptomatic treatment including antihistamines, vitamin supplementation, proton pump inhibitors, and analgesics was prescribed without clinical improvement.

Approximately three months prior to hospital presentation, he developed additional constitutional and gastrointestinal symptoms including progressive loss of appetite, generalized weakness, easy fatigability, intermittent low-grade fever, unintentional weight loss, diffuse abdominal discomfort,

recurrent non-bloody loose stools, and recurrent non-bilious vomiting. Despite these systemic manifestations, the cutaneous disease remained the predominant complaint.

On presentation, the patient was wheelchair-bound due to progressive functional decline. Vital signs revealed low-grade fever (37.8°C), pulse rate of 103 beats per minute, blood pressure of 100/60 mmHg, respiratory rate of 21 breaths per minute, and oxygen saturation of 95% on room air. Physical examination demonstrated diffuse generalized scaly, exfoliative, and hyperpigmented skin lesions involving the scalp, face, trunk, and bilateral upper and lower extremities (Fig. 1). Cardiovascular, respiratory, abdominal, and neurologic examinations were otherwise unremarkable, with no palpable organomegaly, peripheral edema, or clinically appreciable lymphadenopathy.

Clinical images demonstrating diffuse erythematous, scaly, exfoliative, and hyperpigmented skin involvement affecting (A) the chest and abdomen, (B) the scalp and neck, and (C) the lower extremities.

Initial laboratory investigations demonstrated normocytic normochromic anemia (hemoglobin 9.9 g/dL), eosinophilia (approximately 20%), hypoalbuminemia (2.02 g/dL), elevated erythrocyte sedimentation rate (97 mm/hr), elevated C-reactive protein (18.6 mg/L), and vitamin D deficiency (19.7 ng/mL). Stool examination revealed trophozoites of *Entamoeba histolytica*.

Abdominopelvic ultrasonography showed circumferential bowel wall thickening involving the cecum, ascending colon, terminal ileum, and appendix, along with multiple enlarged periportal and mesenteric lymph nodes and multiple hepatic lesions suggestive of disseminated disease. Subsequent contrast-enhanced computed tomography (CT) of the abdomen and pelvis revealed marked circumferential edematous wall thickening involving the cecum and terminal ileum at the ileocecal junction (Fig. 2), associated with confluent abdominal and pelvic lymphadenopathy. Multiple non-enhancing hepatic nodular lesions were also identified, the largest measuring 1.7 × 1.6 cm.

(A) Axial and (B) coronal portal venous phase (PVP) CT images demonstrating marked circumferential edematous wall thickening involving the cecum and terminal ileum at the ileocecal junction (red arrows).

Further diagnostic evaluation included ultrasound-guided fine needle aspiration of hepatic lesions, which demonstrated malignant epithelial cells with marked pleomorphism and prominent nucleoli, consistent with metastatic adenocarcinoma. Colonoscopic evaluation subsequently revealed a mass at the ileocecal valve causing luminal stenosis with irregular surrounding mucosa. Histopathologic examination of endoscopic biopsy specimens demonstrated poorly differentiated carcinoma with infiltration of the mucosa and submucosa.

Following multidisciplinary evaluation, the patient underwent exploratory laparotomy. Intraoperative findings demonstrated a cecal mass with mesenteric lymphadenopathy and multiple metastatic liver lesions involving both hepatic lobes (Fig. 3). Right hemicolectomy with primary end-to-end anastomosis was performed, and simultaneous skin biopsy was obtained from representative exfoliative skin lesions.

Intraoperative photographs demonstrating (A) the gross appearance of the cecal mass and (B) the resected right hemicolectomy specimen following surgical resection.

Histopathologic examination of the resected specimen demonstrated grade 4 undifferentiated carcinoma of the cecum measuring 6 × 4.5 cm, with transmural invasion extending into adjacent terminal ileum, appendix, and pericecal adipose tissue (Fig. 4). Extensive lymphovascular and perineural invasion were also present. Of the 15 lymph nodes examined, 11 demonstrated metastatic involvement, establishing a final pathologic stage of pT4bN2b.

(A) Fine-needle aspiration of a hepatic lesion demonstrating cytologic features of metastatic carcinoma. (B–D) Hematoxylin and eosin (H&E)-stained sections. (B) Endoscopic biopsy of the cecal mass showing infiltrative sheets of markedly pleomorphic epithelial cells. (C) Low-power magnification and (D) high-power magnification of the resected cecal tumor demonstrating solid sheets of pleomorphic epithelial cells without glandular formation, consistent with poorly differentiated carcinoma.

Immunohistochemical analysis demonstrated a poorly differentiated colorectal carcinoma with an atypical immunophenotype, showing diffuse CK AE1/AE3, CK7, and CK5/6 positivity with loss of conventional intestinal differentiation markers, including CK20, CDX2, and SATB2. Despite CK5/6 expression, p63 was negative, arguing against squamous differentiation. Neuroendocrine markers (synaptophysin and chromogranin A) and other lineage-associated markers, including TTF-1, S100, and S100P, were negative. GATA3 and PAX8 showed weak nonspecific cytoplasmic staining. Mismatch repair protein testing revealed preserved nuclear expression of MSH2 and MSH6, with equivocal PMS2 staining despite adequate internal controls. MLH1 immunostaining was unavailable. Overall, the findings were consistent with a mismatch repair–proficient (pMMR), microsatellite-stable (MSS) poorly differentiated colorectal carcinoma without evidence of microsatellite instability-high (MSI-H) disease.

Histopathologic examination of the skin biopsy demonstrated epidermis of normal thickness without evidence of spongiosis, interface dermatitis, or lichenoid inflammatory changes. The dermis showed a prominent perivascular and periappendageal inflammatory infiltrate composed predominantly of plasma cells and lymphocytes, with scattered eosinophils. Subepidermal melanin incontinence was noted. No granulomatous inflammation, atypical lymphoid infiltrates, psoriasiform changes, or histopathologic features suggestive of drug eruption were identified (Fig. 5).

Hematoxylin and eosin (H&E)-stained sections. (A) Skin biopsy demonstrating an epidermis of normal thickness without evidence of spongiosis, interface dermatitis, or lichenoid inflammatory changes. (B) Periappendageal and (C) perivascular inflammatory infiltrates composed predominantly of plasma cells and lymphocytes with scattered eosinophils.

The postoperative course was complicated by transient surgical site infection requiring wound care and broad-spectrum antimicrobial therapy. Subsequently, progressive clinical improvement was observed during follow-up. Within one month following surgical resection, the previously persistent dermatologic

manifestations demonstrated marked regression, with substantial improvement in generalized pruritus, diffuse scaling, exfoliation, and hyperpigmentation without additional targeted dermatologic therapy.

Discussion

Paraneoplastic erythroderma represents a rare dermatologic manifestation of internal malignancy that develops without direct cutaneous invasion by tumor cells. It accounts for approximately 1% of erythroderma cases and may occasionally serve as the initial or only clinical indicator of an occult cancer [8]. Clinically, it presents as a generalized erythematous and desquamative eruption with extensive scaling affecting more than 90% of the body surface area, frequently accompanied by significant pruritus [2, 3, 8, 9], as observed in the present case.

In this report, we describe a 35-year-old previously healthy male who developed progressive generalized erythroderma over nine months, beginning with facial erythematous lesions and evolving into diffuse exfoliative dermatitis. Notably, the cutaneous disease preceded the development of constitutional and gastrointestinal symptoms, including weight loss, anorexia, and abdominal discomfort, thereby representing the initial clinical manifestation of an advanced underlying malignancy. This atypical presentation contributed to diagnostic delay, as the severity of dermatologic disease initially masked the presence of systemic pathology.

Subsequent evaluation revealed advanced colorectal cancer involving the cecum with regional lymph node metastases and hepatic dissemination. Histopathological analysis confirmed a poorly differentiated carcinoma with aggressive features, including lymphovascular and perineural invasion. Immunohistochemistry demonstrated an unusual phenotype characterized by diffuse CK7 and CK5/6 positivity with loss of typical colorectal differentiation markers (CK20, CDX2, SATB2), further reflecting tumor dedifferentiation.

The exact pathophysiology of erythroderma remains incompletely understood. However, it is thought to involve dysregulation of immune and inflammatory pathways, particularly those mediated by adhesion molecules that regulate leukocyte–endothelial interactions and facilitate migration of inflammatory cells into the skin. Increased expression of adhesion molecules such as VCAM-1, ICAM-1, E-selectin, and P-selectin has been implicated in exfoliative dermatitis, contributing to dermal inflammation and subsequent epidermal hyperproliferation through cytokine-driven mechanisms. Elevated levels of inflammatory mediators, including interleukins (IL-1, IL-2, IL-8) and tumor necrosis factor (TNF), further enhance keratinocyte turnover, shortening epidermal transit time and resulting in excessive loss of skin cells from the surface [8].

Skin biopsy findings in erythroderma are often nonspecific, showing only subtle inflammatory changes without definitive features of a primary dermatosis, and primarily serve to exclude alternative diagnosis such as psoriasis, cutaneous T-cell lymphoma, and drug-induced eruptions [2, 8]. In the present case, the absence of diagnostic features of psoriasis, cutaneous lymphoma, interface dermatitis, or drug-related

eruptions, together with the exclusion of other identifiable causes, supported a secondary process in keeping with a systemic etiology.

Definitive management of erythroderma is primarily directed toward identification and treatment of the underlying etiology, as cutaneous manifestations typically reflect an underlying systemic process rather than a primary dermatologic disease. Severe cases are considered dermatologic emergencies and often require hospital admission for close monitoring and supportive management, including fluid resuscitation to maintain euvolemia, correction of electrolyte disturbances, and general skin care measures such as lukewarm compresses and regular emollient application. Low-potency topical corticosteroids, such as 1% hydrocortisone, may provide symptomatic relief, while sedating antihistamines can help reduce pruritus [8, 9]. Narrow-band UVB phototherapy has also been used as an adjunct for symptom control [2]. In the present case, definitive treatment with right hemicolectomy resulted in marked improvement of the extensive cutaneous manifestations within one month, despite the absence of targeted dermatologic therapy. This dramatic clinical response strongly supports a paraneoplastic mechanism underlying the erythroderma and highlights the critical role of treating the primary malignancy.

To the best of our knowledge, although various forms of paraneoplastic dermatoses [4, 10–12] and aberrant immunophenotypic expression patterns involving CK7, CK20, and CDX2 in colorectal carcinoma [13] have been individually reported, no previous report has described paraneoplastic erythroderma as the initial manifestation of a poorly differentiated cecal carcinoma with an aberrant CK7-positive/CK20-negative/CDX2-negative/SATB2-negative immunophenotype.

In conclusion, this case highlights erythroderma as a rare initial presenting feature of advanced colorectal carcinoma. The temporal relationship between the onset of cutaneous disease and subsequent detection of malignancy, together with the marked resolution of dermatologic symptoms following surgical resection, underscores the importance of considering internal malignancy in patients presenting with unexplained generalized exfoliative dermatitis. This case further emphasizes the diagnostic value of early recognition of paraneoplastic dermatoses and the need for thorough systemic evaluation, particularly in atypical or treatment-refractory cases.

Conclusion

This case highlights paraneoplastic erythroderma as a rare and diagnostically challenging initial manifestation of advanced colorectal carcinoma. The absence of early systemic symptoms and the predominance of severe exfoliative dermatitis contributed to delayed recognition of the underlying malignancy, further compounded by presentation in a relatively young patient. The close temporal relationship between onset of cutaneous disease, subsequent identification of metastatic colorectal cancer with supportive histopathological findings, and rapid resolution of erythroderma following oncologic resection strongly supports a paraneoplastic mechanism. This report underscores that erythroderma, particularly when unexplained or refractory to conventional therapy, should prompt

thorough evaluation for internal malignancy irrespective of age. Early recognition of paraneoplastic dermatoses remains essential, as it may facilitate timely diagnosis and management of otherwise occult advanced malignancies.

Abbreviations

PNS
Paraneoplastic syndromes
CT
Computed tomography
H&E
Hematoxylin and eosin
TNF
Tumor necrosis factor

Declarations

Ethics approval: Ethical approval by the ethics committee is not required for case report publication deemed not to constitute research as per the policies of the institution. This case report was prepared in accordance with the ethical principles outlined in the Declaration of Helsinki.

Consent to participate declaration: Not applicable

Consent for publication: Written informed consent has been obtained from the patient for publication of the case report and any accompanying images. A copy of the written consent is available for review upon request by the editor In chief of this journal.

Availability of data and materials: The data on this case report is available and will be provided to the editor in chief of the journal upon request.

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Authors' contributions:

Y.M.H.: Writing – original draft, writing – review and editing, conceptualization, data curation, and supervision. B.M.H.: Writing – original draft, writing – review and editing, conceptualization, data curation, and supervision. Y.M.Y.: Investigation, Data curation and writing – review and editing. A.S.K.: Investigation, Resources and writing – review and editing. P.S.A.: Visualization, Data curation and writing – review and editing. M.J.A.: Resources and writing – review and editing. A.H.Y.: Resources and writing – review and editing. S.A.Y.: Writing – review and editing and supervision.

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Figures

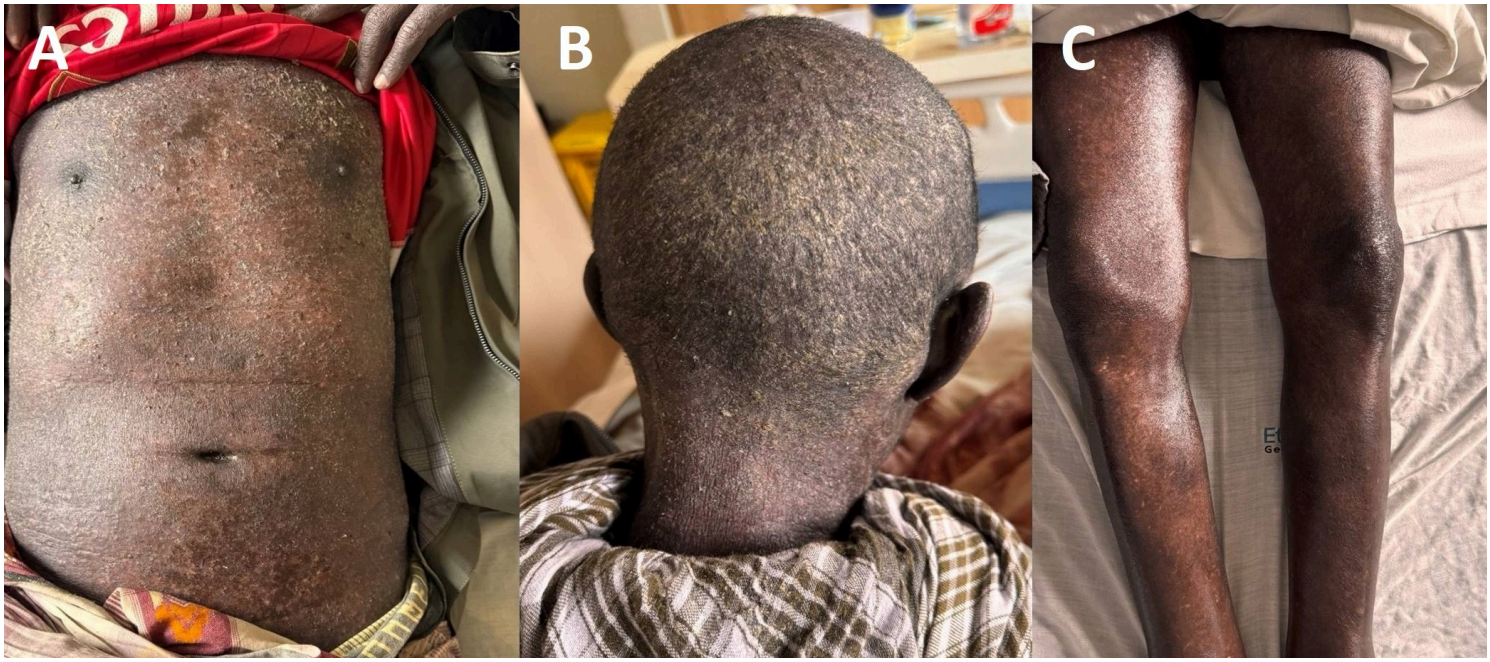


Figure 1

Extensive generalized erythroderma involving the scalp, trunk, and extremities.

Clinical images demonstrating diffuse erythematous, scaly, exfoliative, and hyperpigmented skin involvement affecting (A) the chest and abdomen, (B) the scalp and neck, and (C) the lower extremities.

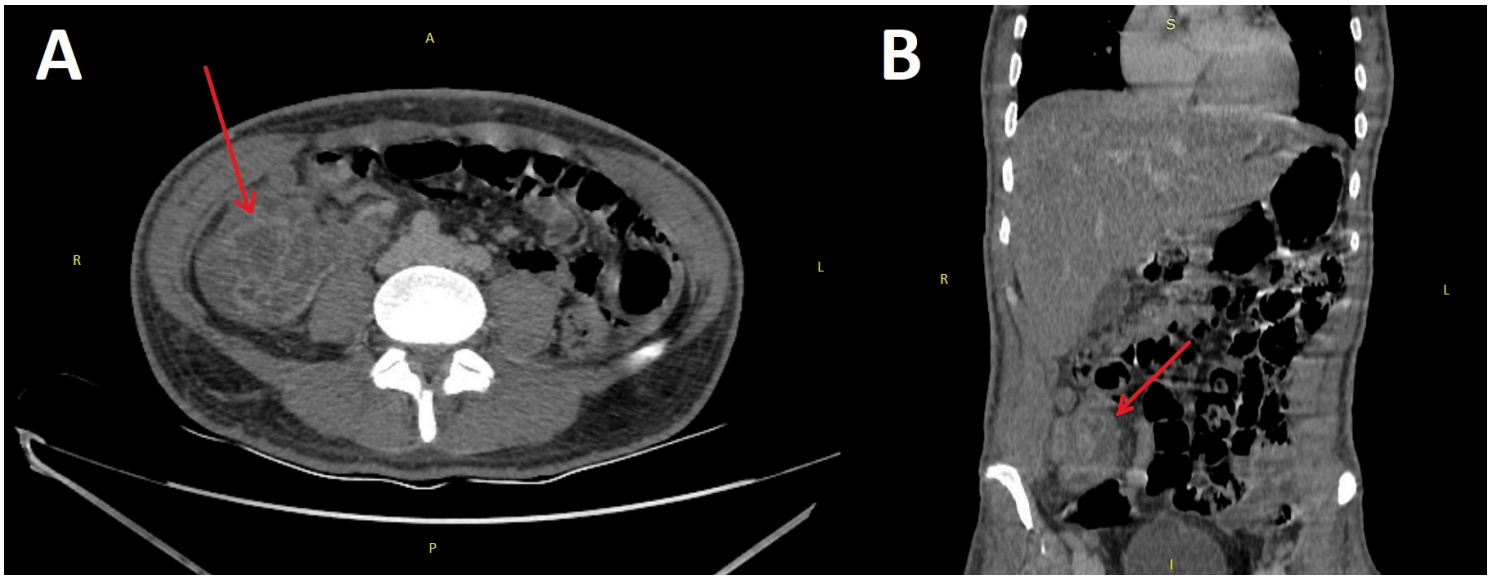


Figure 2

Multiplanar contrast-enhanced computed tomography of the abdomen.

(A) Axial and (B) coronal portal venous phase (PVP) CT images demonstrating marked circumferential edematous wall thickening involving the cecum and terminal ileum at the ileocecal junction (red arrows).

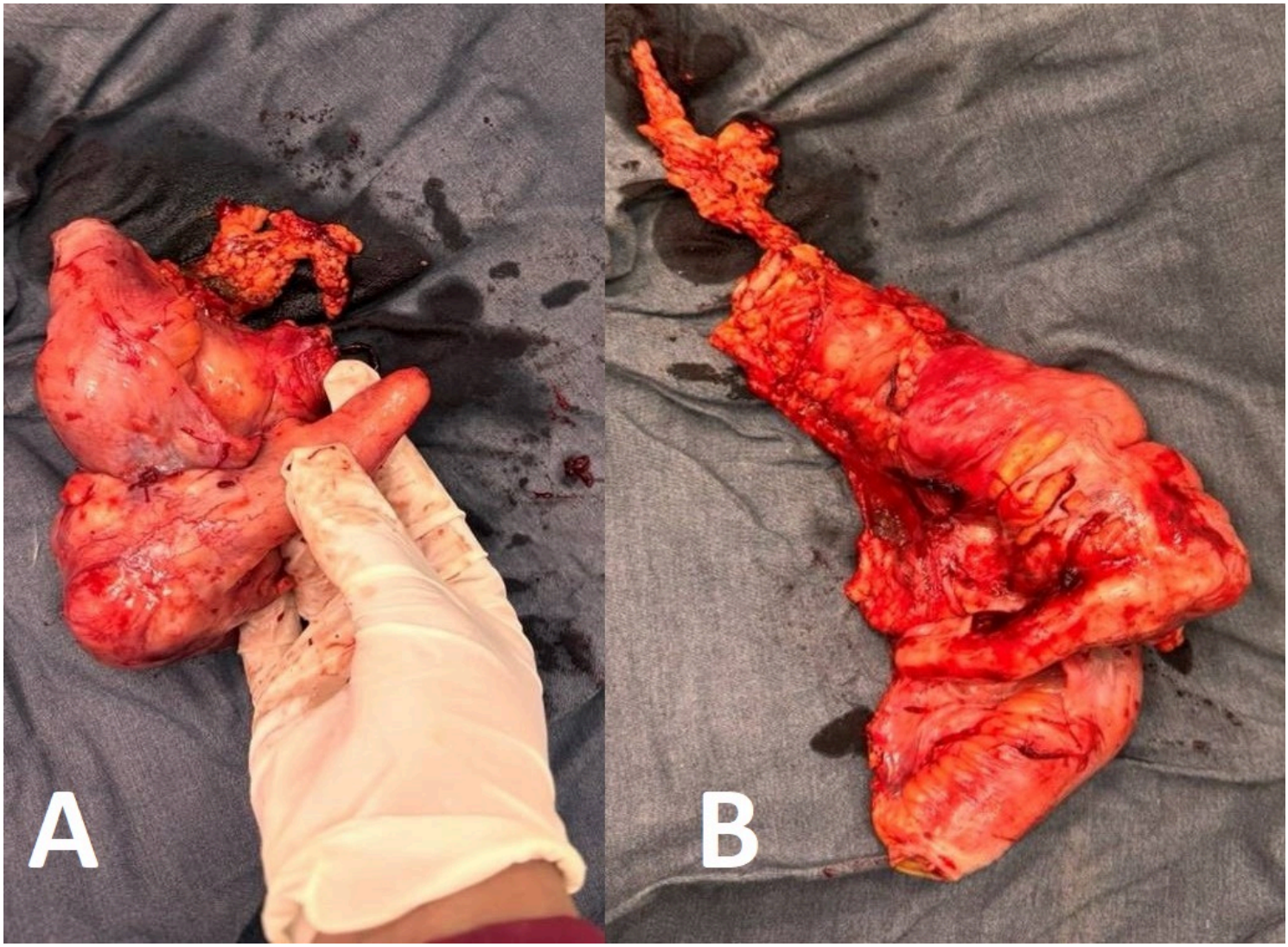


Figure 3

Intraoperative findings during exploratory laparotomy.

Intraoperative photographs demonstrating (A) the gross appearance of the cecal mass and (B) the resected right hemicolectomy specimen following surgical resection.

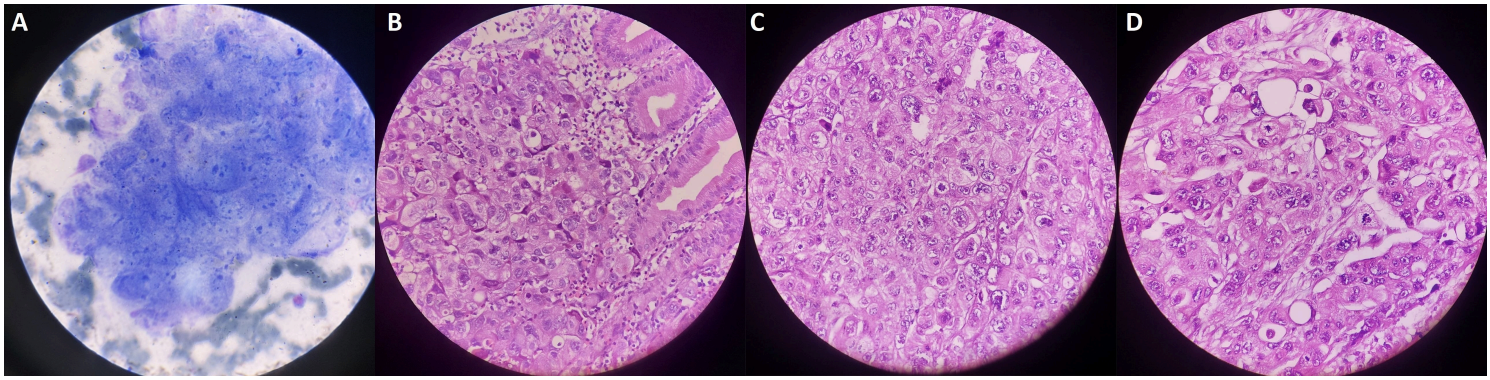


Figure 4

Pathologic findings from the hepatic lesion and cecal tumor.

(A) Fine-needle aspiration of a hepatic lesion demonstrating cytologic features of metastatic carcinoma. (B–D) Hematoxylin and eosin (H&E)-stained sections. (B) Endoscopic biopsy of the cecal mass showing infiltrative sheets of markedly pleomorphic epithelial cells. (C) Low-power magnification and (D) high-power magnification of the resected cecal tumor demonstrating solid sheets of pleomorphic epithelial cells without glandular formation, consistent with poorly differentiated carcinoma.

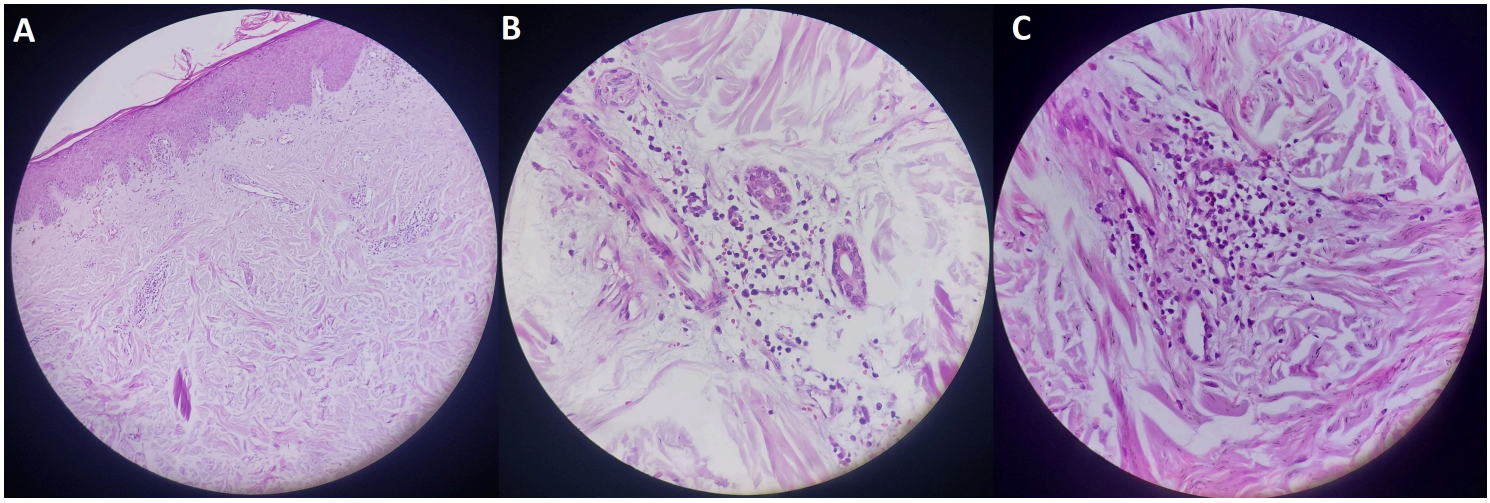


Figure 5

Histopathologic findings of the skin biopsy.

Hematoxylin and eosin (H&E)-stained sections. (A) Skin biopsy demonstrating an epidermis of normal thickness without evidence of spongiosis, interface dermatitis, or lichenoid inflammatory changes. (B) Periappendageal and (C) perivascular inflammatory infiltrates composed predominantly of plasma cells and lymphocytes with scattered eosinophils.