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Poorly Differentiated Adenocarcinoma of Anal canal Presenting as a Vulval Lump

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Abstract

Primary adenocarcinoma of the anal canal is a rare malignancy, accounting for fewer than 10% of anal cancers. It often presents with non-specific perianal symptoms and can be clinically mistaken for benign conditions such as a perianal abscess or Bartholin's cyst, leading to diagnostic delay. A 69-year-old postmenopausal multipara woman presented with a three-month history of a painless, hard mass extending from the left labia majora to the left gluteal fold. She initially underwent incision and drainage for a presumed perianal abscess. Histopathological report of the excised tissue revealed poorly differentiated adenocarcinoma. Subsequent workup, including serum carcinoembryonic antigen (CEA) (2.02 ng/mL), chest x-ray, abdominal ultrasound, and CT-guided FNAC of a right lung mass, confirmed metastatic adenocarcinoma. Imaging revealed multiple pulmonary nodules in both lungs with right-sided pleural effusion, cholelithiasis, and mild endometrial collection. On immunohistochemistry (IHC), the perianal tissue sections demonstrated poorly differentiated adenocarcinoma. Our final diagnosis was carcinoma of the anal canal (Grade II, poorly differentiated adenocarcinoma) with pulmonary metastases. This case highlights that a hard, painless labio-gluteal lump in an older woman should raise suspicion for anal canal adenocarcinoma rather than benign inflammatory lesions. Early diagnosis and metastatic evaluation are essential to guide appropriate oncological management.

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Introduction

Adenocarcinoma of the anal canal is a rare malignancy, accounting for less than 10% of all anal cancers and approximately 1-2% of all gastrointestinal tract malignancies.[1] Unlike squamous cell carcinoma of the anal canal, which is strongly associated with human papillomavirus infection and has well-established treatment protocols combining chemoradiotherapy, primary anal canal adenocarcinoma remains poorly characterized in terms of pathogenesis and optimal management strategies.[2] The rarity of this entity often leads to diagnostic delays, as its clinical presentation can mimic several benign anorectal conditions. The clinical manifestations of anal canal adenocarcinoma are notoriously non-specific. Patients commonly present with perianal pain, bleeding, pruritus, or a sensation of a mass.[3] More indolent presentations, such as a painless progressive lump extending into the perineal or labial region, are exceptionally rare and frequently misinterpreted as inflammatory conditions, including perianal abscess, Bartholin's cyst, or hidradenitis suppurativa.[4] This diagnostic

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challenge is compounded by the fact that many clinicians initially treat presumed benign lesions with incision and drainage and obtain tissue for histopathological examination, followed by immunohistochemistry. Lung metastases from anal canal adenocarcinoma are uncommon, occurring in approximately 10-15% of patients with metastatic disease.[5] The haematogenous spread typically involves the liver as the most frequent site, followed by the lungs, bones, and brain.[5] However, isolated pulmonary metastases without concurrent liver involvement are relatively unusual and may present with subtle respiratory symptoms or remain asymptomatic until advanced stages.[6] The prognostic significance of poorly differentiated histology in anal canal adenocarcinoma is substantial. Poorly differentiated tumors demonstrate aggressive biological behavior with higher rates of lymphovascular invasion, lymph node metastasis, and distant dissemination compared to well or moderately differentiated counterparts.[7] Evidence highlighted that patients with poorly differentiated anal adenocarcinoma have significantly reduced overall survival, emphasizing the need for prompt diagnosis and comprehensive metastatic workup at presentation.[7,8] This case report describes a 69-year-old woman with poorly differentiated adenocarcinoma of the anal canal who presented with a painless hard lump extending from the left labia majora to the left gluteal fold, initially mistaken for a perianal abscess. This case highlights the diagnostic challenges posed by this rare tumor and emphasizes the need for tissue diagnosis – rather than assuming benign disease – when evaluating atypical perineal lumps.

Case Summary

A 69-year-old postmenopausal multipara woman from Netrokona district of Bangladesh, presented to the outpatient department in August of 2024, with a chief complaint of a hard lump extending from her left labia majora to the left gluteal fold, present for three months. She reported being reasonably well until three months prior, when she suddenly noticed a painless, non-tender, hard lump in the left labiogluteal region. The lump gradually increased in size over the following months. Her bowel and bladder habits remained normal, and she denied any history of perianal bleeding, pruritus, or alteration in stool caliber. No significant past medical or surgical history was found including absence of hypertension, diabetes mellitus, or other chronic illnesses. She has been menopaual for the last 20 years. She had 10 parity – all had normal vaginal delivery (last childbirth 30 years ago). General examination revealed pallor without jaundice. Blood pressure was 130/80 mmHg, pulse 70 beats per minute. Systemic examination showed a soft, non-tender abdomen. Perineal examination revealed a hard, non-tender lump measuring approximately 10 cm × 5 cm extending from the left labia majora to the left gluteal fold, with no local temperature elevation.

The patient underwent incision and drainage of the perianal swelling under the clinical impression of a perianal abscess. However, histopathology revealed poorly differentiated adenocarcinoma. Immunohistochemistry (IHC) showed perianal tissue having poorly differentiated adenocarcinoma. Her laboratory investigations revealed 8.10g/dL of haemoglobin and 2.02 ng/mL of serum carcinoembryonic antigen (CEA). Liver and renal function tests were normal. Ultrasonogram of the whole abdomen was of normal findings except an 8-mm echogenic focus at neck with shadowing (suggesting cholelithiasis). Chest x-ray revealed bilateral round pulmonary opacities and obliterated right CP angle suggesting multiple pulmonary

metastases as well as small right pleural effusion. CT-guided FNAC (right lung lump) report revealed malignant cells with a gland-like pattern (i.e., metastatic adenocarcinoma) (Fig. 1). Our final diagnosis was carcinoma of the anal canal (poorly differentiated adenocarcinoma, Grade II) with pulmonary metastases. Then, the patient was referred to the National Institute of Cancer Research and Hospital (NICRH), Dhaka, for palliative chemotherapy. She remained stable with no procedural complications.

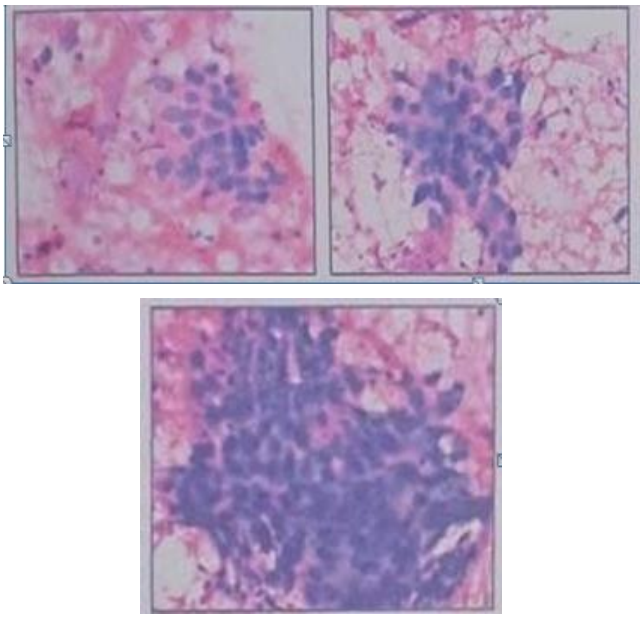

Fig. 1: Cytopathology (FNAC of lung) showing malignant cells with a gland-like pattern (metastatic adenocarcinoma).

Discussion

The present case describes a 69-year-old postmenopausal multipara woman with poorly differentiated adenocarcinoma of the anal canal who initially presented with a painless labio-gluteal lump and was subsequently found to have right sided pulmonary metastases. This case highlights several important clinical lessons regarding, atypical presentations, and the aggressive nature of poorly differentiated histopathology. The most significant finding in this case is the initial diagnosis of the perianal lump as an abscess leading to incision and drainage procedure. This diagnostic pitfall has been documented in previous reports, where benign conditions such as perianal abscess, Bartholin's cyst, or hidradenitis suppurativa mimic malignancy.[4,9] Approximately 15% of anal canal adenocarcinomas were initially treated as benign anorectal conditions, with a mean diagnostic delay of 4-6 months.[9] The painless nature of the lump in this patient should have raised suspicion for malignancy, as inflammatory lesions typically present with tenderness, warmth, and fluctuance. Clinicians should maintain a high index of suspicion for anal canal malignancy when encountering a hard, non-tender, progressive lump in the perineal region, particularly in older adults.[4] The histopathological finding of poorly differentiated adenocarcinoma in this case carries important prognostic implications. Poorly differentiated tumors demonstrate loss of glandular architecture, high nuclear-to-cytoplasmic ratios, and frequent mitotic figures, all of which were observed in this patient's biopsy.[6,7] Evidence showed that poorly differentiated anal adenocarcinoma is associated with recurrence[10] as well as significantly worse survival compared to moderately or well- differentiated tumours, with a reported 5-year survival rate of approximately 20-30% versus 50-60% for better- differentiated counterparts.[7,11] The aggressive biological behavior of poorly differentiated tumours includes higher rates of lymphovascular invasion, regional lymph node metastasis, and early haematogenous dissemination.[11] This patient’s presentation with synchronous pulmonary metastases, without prior treatment, is consistent with this aggressive phenotype. The pattern of metastatic spread observed in this case is noteworthy. Unlike squamous

cell carcinoma of the anal canal, which tends to spread locally and to inguinal lymph nodes, adenocarcinoma of the anal canal more frequently metastasizes haematogenously.[12] The liver is the most common site of distant metastasis, occurring in approximately 50-60% of metastatic cases, followed by the lungs (20-30%), bones, and brain.[5,12] Isolated pulmonary metastases without liver involvement, as seen in this patient, are less common but have been reported in up to 15% of metastatic anal adenocarcinoma cases.5 The presence of bilateral pulmonary nodules with pleural effusion in this patient indicates advanced metastatic disease. Her serum CEA level was 2.02 ng/mL, i.e., within the conventional normal range (<5.00 ng/mL), which indicates limited sensitivity in anal adenocarcinoma. Up to 40% of patients with metastatic anal adenocarcinoma have normal CEA levels, making imaging essential for accurate staging.[12] The diagnostic workup in this case appropriately included histopathology from the primary site, followed by CT-guided FNAC of a pulmonary lesion to confirm metastasis. The finding of malignant cells with a gland-like pattern on FNAC was consistent with metastatic adenocarcinoma. Immunohistochemistry (IHC) has a valuable role in confirming the anal canal origin of metastatic lesions, with cytokeratin 7 (CK7) positivity and cytokeratin 20 (CK20) negativity being characteristic of anal canal adenocarcinoma, distinguishing it from colorectal adenocarcinoma (CK7-/CK20+) and other primary sites.[13] Management of metastatic anal canal adenocarcinoma presents significant challenges. Unlike squamous cell carcinoma of the anal canal, which is highly radiosensitive and often curable with chemoradiotherapy, adenocarcinoma is relatively radioresistant and has a poorer response to standard chemoradiation protocols.[2,7,12] For patients with metastatic disease, palliative systemic chemotherapy remains the mainstay of treatment. Fluorouracil-based regimens, often combined with oxaliplatin or irinotecan, have demonstrated modest activity, with response rates of 20-40% and median overall survival of 12-18 months.[7,8,12] More recently, targeted therapies and immune checkpoint inhibitors are being investigated, but no standard targeted agent has been established for anal adenocarcinoma.[12] The patient in this case was referred for palliative chemotherapy, which is appropriate given her good performance status (ECOG 2) and absence of contraindications.

Conclusion

This case underscores the importance of considering poorly differentiated anal canal adenocarcinoma in older adults who present with a hard, painless perineal lump. Poorly differentiated histopathology portends an aggressive clinical course with early metastatic spread. Timely tissue diagnosis, comprehensive metastatic workup, and referral to specialized oncology centers are essential to optimize outcomes in this rare and challenging malignancy.

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