Parade of Roses at the EADV Poster Presentation

Squamous Cell Carcinoma of Unknown Primary Identified in an Inguinal Lymph Node

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Introduction

The following describes a case of squamous cell carcinoma (SCC) of unknown primary, outlining the extensive work-up ultimately leading to the diagnosis. Finally, the literature on such unusual cases is reviewed and discussed.

Case Synopsis

A 60 year-old Hispanic male with a history of hypertension, type two diabetes mellitus, and benign prostatic hyperplasia (BPH) presented with a painful left inguinal mass, persistently enlarging since his first hospital admission four months prior. At that time he was prescribed doxycycline for 21 days and referred for computed tomography (CT) scan of the abdomen and pelvis (CTAP), which revealed a prominent left inguinal lymph node measuring 4.59 cm by 3.64 cm with apparent central necrosis. The patient was referred to General Surgery, who prescribed a 10-day course of Keflex and referred him to Interventional Radiology (IR) for biopsy, but the patient was lost to follow-up.

Review of systems included weight loss and night chills for five months. Negative for history of tuberculosis, cough, dyspnea, or fever, smoking, alcohol abuse, multiple sexual partners, and family history of skin cancers or use of tanning beds. Exam included vital signs within normal limits. Labs were notable for a white blood cell count of 12 with 83% polymorphonuclear leukocytes (PMNs) and a calcium level of 11.4. Parathyroid hormone (PTH) was low (7.7), while there was a mild elevation in Parathyroid Related Protein (PTHrP).

CTAP revealed enlargement of the left inguinal region heterogeneous soft tissue mass measuring 11.2 by 7.4 cm, with adjacent smaller soft tissue masses extending slightly into the lower pelvis with multiple new enlarged lymph nodes or masses. The largest was located at the superior aspect of the main mass and measured 2.5 by 2 by 4.5 cm and extended into the pelvis adjacent to the left femoral-iliac vessels **[Figure 1]**. Given the presence of scrotal edema, a scrotal ultrasound was performed. Besides a small right epididymal head cyst and a mild left-sided hydrocele, the testicles and scrotum were unremarkable.

Dermatology consulted, performed a total-body skin exam, noting the large erythematous firm-to-hard inguinal lymph node and indurated nodule at left inguinal fold with overlying erosions, weeping serosanguinous fluid, and few satellite erythematous papules **[Figure 2]**. Exam unrevealing for primary cutaneous SCC; the left inguinal nodules appeared consistent with metastatic disease.

IR biopsy of the mass revealed metastatic squamous cell carcinoma (SCC); immunohistochemical analysis revealed no loss of nuclear expression of DNA Mismatch Repair (MMR) proteins with low probability of microsatellite instability. Subsequent CT scan of the chest was unremarkable for metastatic disease. Whole body positron emission tomography (PET)/CT demonstrated the metabolically active mass in the left groin with additional nodules/nodes along the left distal external iliac nodal station and the profunda vessels in the proximal thigh, along with avid cutaneous nodules in left proximal thigh. Esophagogastroduodenoscopy (EGD) and colonoscopy revealed four small polyps in the colon–two of which were tubular adenomas, the third was a colonic mucosa with lymphoid aggregate, otherwise unremarkable. Laryngoscopy was unremarkable. CTAP with contrast was remarkable for thickening of the posterior bladder wall; however cystoscopy demonstrated only bladder trabeculations which, per Urology, suggested the thickening observed was likely due to bladder outlet obstruction in the setting of BPH.

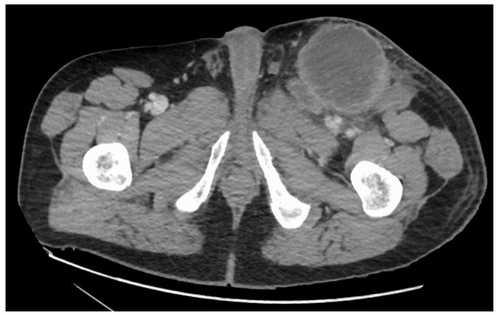

Figure 1: Repeat CT Abdomen and Pelvis revealing the left heterogeneous inguinal mass along with multiple enlarged lymph nodes/ masses.

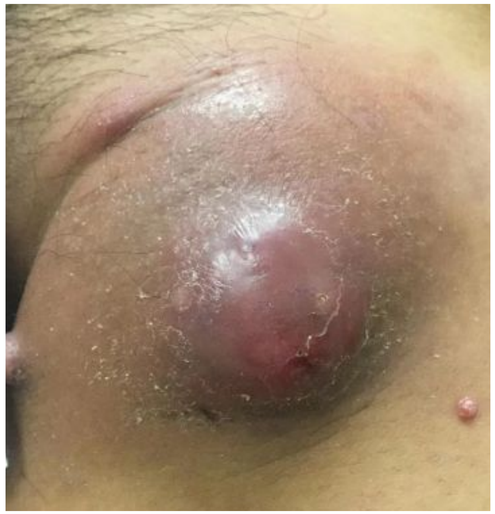

Figure 2: Large erythematous firm-to-hard inguinal lymph node and an indurated nodule on left inguinal fold with overlying erosions, and few satellite erythematous papules

Diagnosis and Management

The patient was presented as a case of SCC of unknown primary at Tumor Board, where it was determined that he would start on chemotherapy (Taxol/Carboplatin weekly) and radiation therapy (RT) for three weeks with later re-evaluation for possible surgical intervention. His hypercalcemia was managed primarily with intravenous (IV) normal saline and zoledronic acid. At follow-up, the primary remained unknown. Per General and Plastic Surgery, no surgical intervention was feasible given the extent of the disease. It was decided that the patient would continue to receive chemo and RT until completion, at which point further chemotherapy regimens would be considered. Chemotherapy and weekly Taxol/Carboplatin was completed. The patient followed-up with the clinic. Although physical examination was limited due to the necessity of utilizing televisits during the COVID-19 pandemic, the option to pursue chemotherapy with Gemcitabine/Cisplatin was presented and discussed, and the patient accepted.

Discussion

Cancer of unknown primary (CUP) refers to a classification of metastatic disease of various histologic subtypes that cannot be traced to an identifiable primary tumor despite extensive work-up.[1] CUPs comprise approximately 3-5% of invasive cancers and 2-3% of all epithelial malignancies, the vast majority of which are adenocarcinomas and undifferentiated carcinomas;[1-3] SCC, neuroendocrine carcinomas, and other uncommon histologies account for only approximately 10% of this 2-3%.[3]

The diagnostic work-up in CUP is highly dependent on immunohistological (IHC) analysis for tumor characterization along with the aid of molecular techniques, although efforts to determine the molecular biology of CUP and to use gene expression profiling have reportedly been generally unsuccessful.[2] CUP is associated with poor survival, and is identified as the fourth most common cause of cancer deaths.[2] Among the many possible histologic subtypes, poorly differentiated carcinomas have been observed to demonstrate the most favorable outcomes.[2]

As a histologic subtype, SCC is rare–accounting for only ~5% of CUPs–but considered favorable, and is noted to occur most frequently in the head and neck.[1,4] Finally, patients with either isolated inguinal lymph-nodal metastatic SCC or with one metastatic lesion are classified as having restricted disease. After undergoing typical management with local dissection with or without local radiation treatment, they usually enjoy long, disease-free survival.[1]

When traditional methods are unsuccessful, work-up of CUP has been advanced by new imaging and endoscopic technologies–including PET/CT, magnifying endoscopy in combination with narrow band imaging, and transoral robotic surgery–which may identify the primary site in between 44-71% of cases.[5] Fluorodeoxyglucose (FDG)-PET/CT has been identified as an effective method of conducting one-time whole-body imaging in SCC-UP in particular, although it demonstrates generally low specificity.[4] Not only can variations in physiologic uptake and inflammatory-related uptake in common potential locations of a primary affect false positive rates, but image indication bias (radiologists' or nuclear medicine physicians' tendency to call more abnormal findings for SCC-UP than for other indications) may contribute to high false positive rates as well.[4]

Conclusions

SCC of unknown primary is unusual and documented infrequently in the literature, as is the physical skin manifestation of such an extensive malignancy. While very few epithelial malignancies are without a known primary, an exceedingly small subset of these are SCCs, diagnosed based on immunohistological analysis and molecular techniques. Because of its rarity, the affected population is poorly characterized, particularly in regard to management and outcomes.

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References

1. Pavlidis N, Pentheroudakis G. Cancer of unknown primary site. *Lancet*. 2012;379:1428–35. [PMID: 22414598].
2. El Rassy E, Kattan J, Pavlidis N. A new entity of abdominal squamous cell carcinoma of unknown primary. *Eur J Clin Invest*. 2019;49:e13111. [PMID: 30908618].
3. Bochtler T, Löffler H, Krämer A. Diagnosis and management of metastatic neoplasms with unknown primary. *Semin Diagn Pathol*. 2018;35:199–206. [PMID: 29203116].
4. Liu Y. FDG PET/CT for metastatic squamous cell carcinoma of unknown primary of the head and neck. *Oral Oncol*. 2019;92:46–51. [PMID: 31010622].
5. Kang H, He H, Ma J, et al. Carcinoma of unknown primary detected by whole-body diffusion-weighted imaging: A case report and review of the literature. *Radiol Case Rep*. 2020;15:983–7. [PMID: 32426081].