Case report

Blastic variant of plasma cell myeloma mimicking squamous cell carcinoma of the uterine cervix in a super-morbidly obese female

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1. Introduction

Gynecologic malignancies complicated by paraneoplastic secretion of parathyroid hormone related protein (PTHrp) resulting in humoral hypercalcemia of malignancy are rare, and when involving the cervix are typically squamous cell carcinomas. We present the case of a 35 year-old super morbidly obese female with hypercalcemia, anemia, renal dysfunction and a cervical mass. Although initially presumed to have a squamous cell cervical cancer, after an extensive workup, her final pathology revealed plasmablastic lymphoma (PBL) versus blastic variant of plasma cell myeloma.

2. Case description

A 35 year-old nulligravida presented with one week of worsening abdominopelvic pain, urinary frequency, anorexia and nausea. She denied vaginal discharge, fevers, chills, night sweats, cough and unintentional weight loss. Her past medical history was significant for super morbid obesity (weight 516 lbs., BMI 81 kg/m^2) and prior optic glioma for which she underwent tumor resection with a ventriculoperitoneal shunt placement at age 14. Because of her super morbid obesity, she had not left her home or sought medical care in 3 years. On physical examination, the patient was tachycardic but normotensive and afebrile. Pelvic examination was very limited due to the patient's body habitus but no masses were palpated and she exhibited mild left adnexal tenderness. Her abdominal exam was significant for bilateral lower quadrant pain without rebound or guarding. Her laboratory values were significant for leukocytosis (WBC 13.4), elevated serum calcium level (> 15 mg/dL), low parathyroid hormone (10.9 pg/mL), elevated PTHrp (62 pg/mL), normal 1, 25 dihydroxyvitamin D (50 pg/mL), elevated lactic acid (7.3), and elevated creatinine (1.15 mg/dL). Pelvic sonogram demonstrated an enlarged left ovary to 10.7 cm.

The patient received intravenous fluid hydration and pamidronate to treat her hypercalcemia. In consultation with endocrinology, it was

thought that based on a low PTH, normal 1, 25 dihydroxyvitamin D, and a high PTHrp she likely had paraneoplastic secretion of PTHrp due to malignancy. Serum protein electrophoresis (SPEP) and urine protein electrophoresis (UPEP) were performed demonstrating no monoclonal gammopathy. Tumor markers were also performed and demonstrated a normal CA-125 (28 U/mL), CEA (1 ng/mL), Ca 19-9 (15 U/mL), and inhibin B (< 10 pg/mL) but an elevated LDH (356 U/L). Computed tomography (CT) scan of the abdomen and pelvis (without intravenous contrast) demonstrated approximately 4.5 cm bilateral nonspecific inguinal lymph nodes, emphysematous cystitis, and an ovoid mass-like structure deep in the pelvis, inseparable from her cervix, either representing a bulky cervix or the reported enlarged left ovary (Fig. 1). Due to her body habitus, she was unable to fit in the MRI machine for better characterization of this lesion.

A gynecologic oncology consultation was obtained and bimanual examination revealed a barrel-shaped cervix dilated to approximately 1 cm with a mass extruding the endocervical canal, which was markedly different than her previous exam 16 days ago. She underwent an examination under anesthesia, human papilloma virus testing, cervical biopsies, endometrial biopsy, cystoscopy and rigid proctoscopy. Intraoperatively, she was found to have a 4 cm necrotic cervical mass encompassing the entire cervix, parametrium, pelvic sidewalls, upper and lower 1/3 of the vagina. There was no involvement of the rectovaginal septum or rectum on proctoscopy but cystoscopy revealed tumor invasion with multiple nodular masses inside the bladder. Her exam was clinically consistent with stage IVA cervical cancer. Preliminary consultation with pathology revealed likely a poorly differentiated squamous cell carcinoma.

Hematologic oncology consultation was obtained for the patient's chronic microcytic anemia and a peripheral smear that demonstrated marked rouleaux with features suggestive of myeloma. A free light chain (FLC) ratio was found to be elevated concerning for multiple myeloma (MM) or another lymphoproliferative disorder. Bone marrow biopsy was deferred at the patient's request. With treatment the

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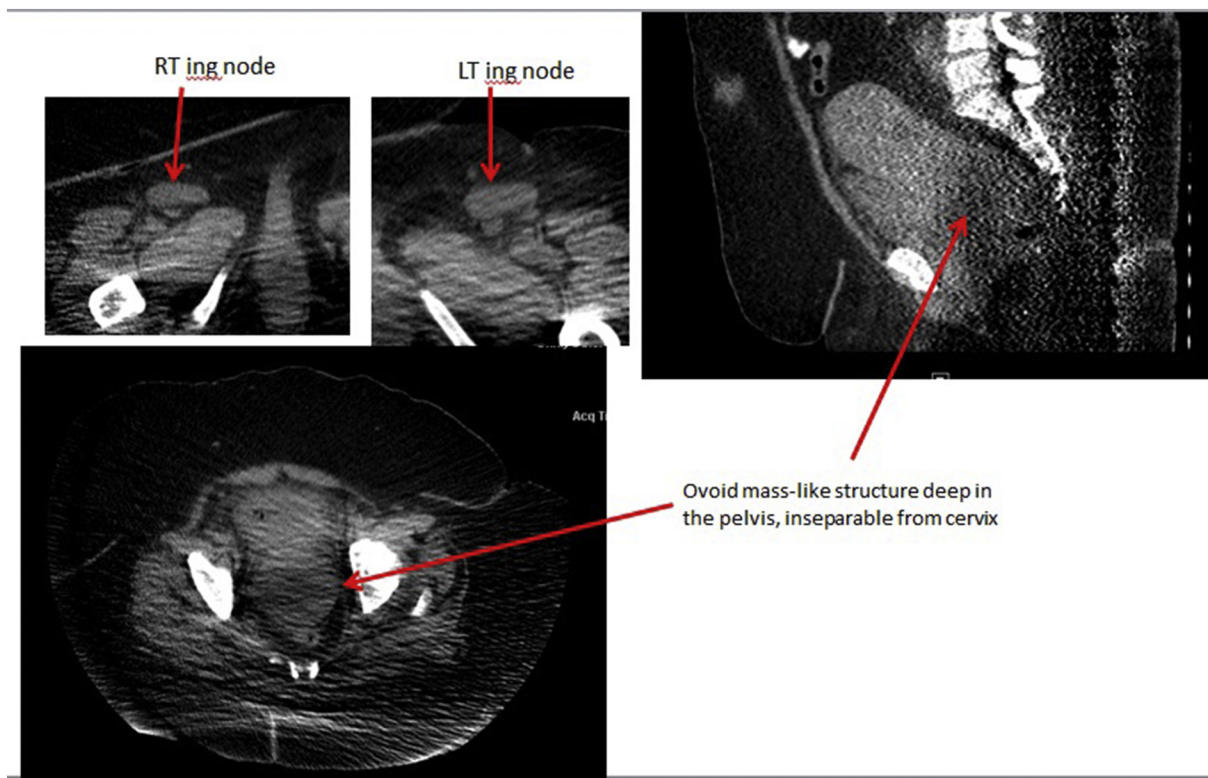
Fig. 1. FIG. 1–4. Patient's computed tomography (CT) scan of the abdomen and pelvis (without intravenous contrast). FIG. 1–1. Sagittal CT image of the enlarged cervix (red arrows) degraded by beam hardening artifact. FIG. 1–2. Axial CT image of enlarged cervix degraded by beam hardening artifact. FIG. 1–3. Axial CT image of 2.2 × 4.2 cm right inguinal lymph node. FIG. 1–4. Axial CT image of 1.7 × 4.6 cm left inguinal lymph node. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

patient's calcium stabilized but her creatinine continued to worsen (peak > 12 mg/dL). Given suspicion of obstructive uropathy from tumor burden in the bladder interventional radiology was consulted to place a percutaneous nephrostomy tube. This was unable to be accomplished due to the patient's body habitus.

On postoperative day two, the patient became febrile and hypotensive with worsening leukocytosis (WBC 31). Workup revealed *Bacteriodes fragilis* bacteremia and IV broad spectrum antibiotics were initiated. On postoperative day four, the patient was found to have a left labial pain. Physical examination demonstrated, a 15 cm tender indurated mass without fluctuance encompassing the left vulva. Given concern for necrotizing fasciitis, she underwent an examination under anesthesia with plans for excision and debridement. In the operating room, a vulvectomy was not performed as her examination was consistent with rapid tumor infiltration of the entire left vulva, tracking to the mons superiorly, and down to the left gluteus. This was significant progression of disease from her last examination eight days prior. Intraoperative frozen section demonstrated small blue cell morphology concerning for lymphoma.

Her case was discussed at tumor board where her final pathology revealed a plasmablastic lymphoma versus a blastic variant of plasma cell myeloma (Fig. 2). The treatment plan was to initiate dexamethasone, perform a bone marrow biopsy and once clinically stable, administer dialysis-dosed chemotherapy. Unfortunately, before treatment her condition rapidly deteriorated and she expired on hospital day twenty-three from multi-system organ failure.

3. Discussion

Female genital tract involvement by non-Hodgkin's lymphoma is a rare clinical phenomenon. The disease can arise from lymph nodes and secondarily involve the female genital organs in up to 40% of disseminated lymphomas (Dursun et al., 2005). Primary lymphoma of the female genital tract is extremely rare, with diffuse large B-cell lymphoma (DLBCL) being the most common histologic subtype (Nasioudis et al., 2017). Plasmablastic lymphoma (PBL) is a distinct subtype of DLBCL but rarely involves the female genital tract (Stein et al., 2008). In contrast, MM is characterized by the neoplastic proliferation of plasma cells typically exhibiting bone marrow involvement but extramedullary disease can be present in up to 7–18% of newly diagnosed patients with MM (Bladé et al., 2012). Extramedullary plasmacytomas in the female genital tract are also rare and can present as a solitary plasmacytomas or as part of disseminated MM (Cordorniz et al., 2017).

This case provides a unique example of the clinical challenges in diagnosing plasma cell myeloma with predominant involvement of the female genital tract. The patient's hypercalcemia was initially presumed to be from end-stage cervical carcinoma as the pattern of invasion mimicked that of a locally-advanced squamous cell carcinoma of the cervix. Gynecologic malignancies complicated by paraneoplastic secretion of PTHrp resulting in humoral hypercalcemia of malignancy are rare but have been reported for organs such as the uterus, cervix, ovary, vulva and vagina. A systematic review identified 34 cases occurring over 22 years demonstrated only 34 cases with two of them being cervical malignancies both of which were squamous cell carcinoma (Savvari et al., 2009). However, hypercalcemia is often most common in those with myeloma who have the greatest tumor volume and elevated serum PTHrP is not a consistent finding in myeloma patients (Oyajobi, 2007).

The diagnosis of MM requires the presence of clone bone marrow plasma cells ≥ 10% or biopsy-proven boney or soft tissue plasmacytoma with presence end organ impairment such as anemia, hypercalcemia, renal insufficiency, and bone lesions. The presence of a biomarker associated with near inevitable progression to end-organ damage such as
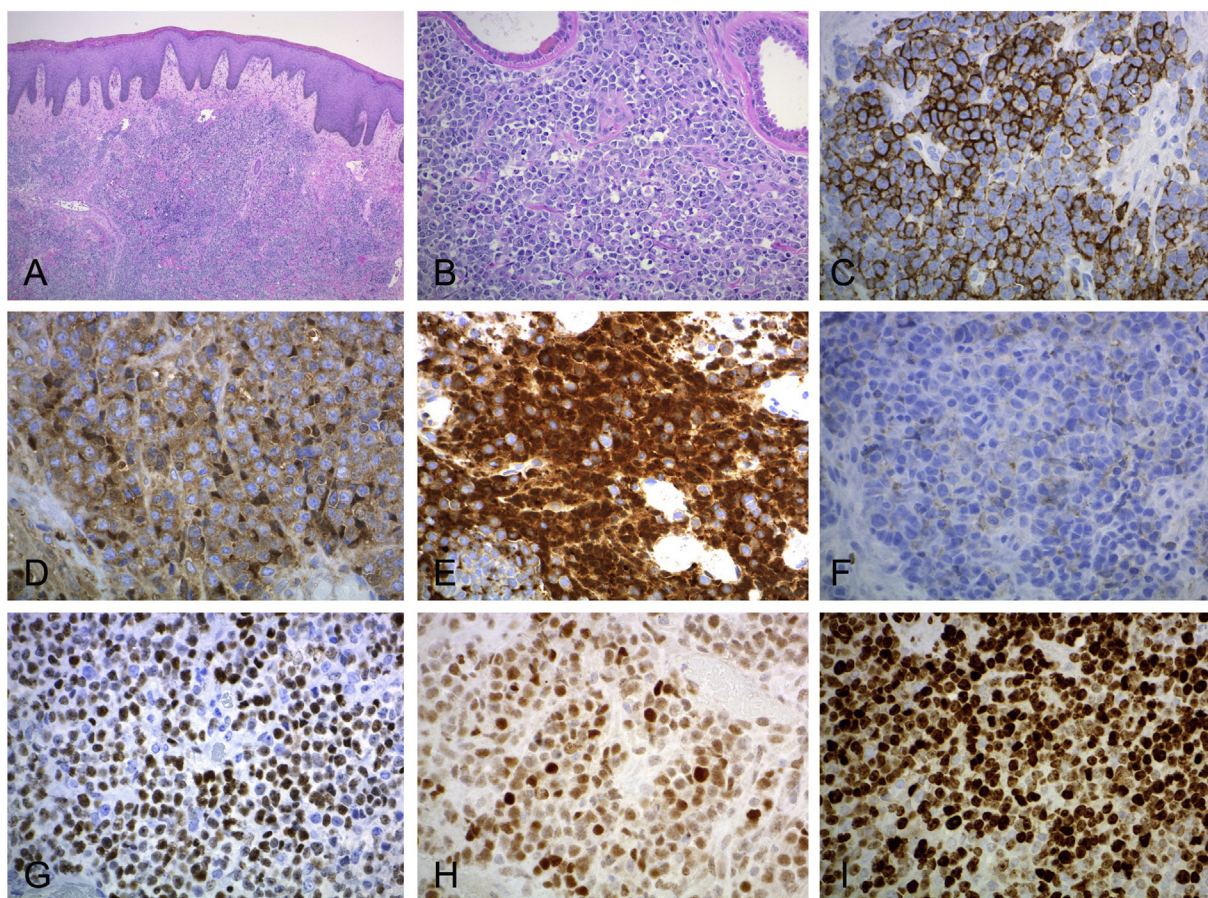
Fig. 2. There is diffuse infiltrate of medium to large-size atypical lymphoid cells in the cervix (A), original magnification ×40; (B), original magnification ×200. They are positive for CD138 (C), IgA (D), lambda (E), but negative for kappa (F). They are also positive for CMYC (G) and P53 (H). Ki67 is > 90% (I).

an elevated FLC can serve as a substitute to organ impairment. Most but not all patients have an M-protein in serum and/or urine but in approximately 3% of patients M-protein will note be detectable in the serum or urine (Rajkumar et al., 2014). It is challenging to differentiate plasmablastic plasma cell myeloma from PBL based on a histopathologic and immunophenotypic features and thus clinical correlation is essential to establish the diagnosis (Harmon and Smith, 2016).

Our patient's case, most closely meets the clinical picture of a blastic variant of plasma cell myeloma with extramedullary involvement of the genital tract as she meets the diagnostic criteria for MM with her clinical manifestations of hypercalcemia, anemia, renal dysfunction and confirmatory tissue diagnosis from her cervical biopsy. It could have been plausible that the patient truly had primary PBL with extranodal involvement of the genital tract or from disease arising within lymph nodes with lymphomatous dissemination secondarily involving the female genital tract. However, her diagnosis favors that of plasma cell myeloma given her clinical manifestations more closely resemble that of a multiple myeloma disease process. Unfortunately, the patient succumbed to her disease process before a bone marrow biopsy could be performed which would have further supported the diagnosis of her disease process as well as possibly a treatment plan tailored to that of plasma cell myeloma.

The diagnosis of plasma cell myeloma with extramedullary involvement of the genital tract is extremely rare with insight into the diagnosis, treatment and disease course limited to sparse case reports as only twenty-four cases of gynecologic plasmacytomas that have been report with 7 cases of solitary plasmacytomas and 17 cases as either part of disseminated MM with involvement of a gynecologic organ or lacking complete work-up to rule out MM (Cordorniz et al., 2017; Feldman et al., 2017). Given this is a rare clinical condition that can

portend a poor clinical prognosis, expeditious diagnosis and treatment with systemic chemotherapy before clinical deterioration may help improve clinical outcome.

Author contributions

Dr. Tymon-Rosario and Dr. Gressel conceived of the presented ideas. Dr. Tymon-Rosario abstracted the data from the medical records and wrote the manuscript in consultation with Dr. Gressel, Dr. Shi and Dr. DiVito. Drs. DiVito and Shi provided images and figure legends for radiology and histology respectively. Input from all of the authors was used for the final editions to the manuscript.

Consent statement

Written informed consent was not able to be obtained from the patient for publication of this case report and accompanying images as she was deceased at the time of manuscript preparation. The patient had no next-of kin or family members to provide consent.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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