EJGO European Journal of Gynaecological Oncology

Pelvic squamous cell carcinoma of unknown primary: a case report and review of the literature

R. Abdallah[1], B. Morse[2], A. Hakam[3,4], M.M.K. Shahzad[1,5]

[1] *Department of Gynecologic Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*
[2] *Department of Radiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*
[3] *Department of Pathology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*
[4] *Department of Anatomic Pathology, School of Medicine, University of South Florida, Tampa, FL*
[5] *Department of Oncologic Sciences, Morsani School of Medicine, University of South Florida, Tampa, FL (USA)*

Summary

Retroperitoneal squamous cell carcinoma (SCC) of unknown primary is very rare with variable survival rates. Standard optimal therapeutic management is not yet established.

Key words: Squamous cell carcinoma; Carcinoma of unknown primary; Pelvic mass.

Introduction

Cancer of unknown primary represents a group of heterogeneous tumors with early apparent metastatic disease and no identifiable site of origin at the time of presentation, despite thorough medical history, physical examination, and other investigations [1]. It accounts for 3% to 5% of all invasive cancers, presenting a diagnostic and therapeutic dilemma despite current advances in imaging and immunohistochemistry [1, 2]. Adenocarcinoma is the most common histologic type (70% of cases), while squamous cell carcinoma (SCC) accounts for 5% to 20% of reported cases [1].

Patients with cancers of unknown primary have poor prognosis with a mean survival of five to ten months, with < 25% surviving up to one year. However, survival varies depending on the histology, site of involvement, tumor burden, gender, and performance status [1-3]. Here, the authors present a case of SCC of the pelvic retroperitoneum, with review of the current literature.

Case Report

A 64-year-old female presented to the emergency room with acute onset of lower abdominal pain. Her history was relevant for a supracervical hysterectomy 30 years ago for benign reasons and an appendectomy. Her last pap smear, two years ago, was negative for dysplasia or malignancy and a colonoscopy 18 months ago revealed benign polyps.

A CT of the abdomen and pelvis and MRI of the pelvis showed a 5 x 5-cm heterogeneous mass centered near the left greater sciatic foramen, involving the exiting sacral nerve roots, the left internal iliac vasculature, and a short segment of the rectum (Figures 1 and 2), with mildly enlarged left internal iliac and common iliac lymph nodes. The left ureter coursed anterior to the mass without any definite involvement.

A CT-guided percutaneous biopsy of the mass was consistent with metastatic SCC; however, origin could not be determined despite appropriate immunostains (Figure 3). A PET/CT scan showed the mass to be hypermetabolic with SUV maximum of 17.5. Colposcopy of the vulva, vagina, and cervix with biopsies were negative for dysplasia or malignancy. Pap smear was also negative for intraepithelial lesion or malignancy. On bimanual and rectovaginal exam, a fullness along the left pelvic sidewall extending posteriorly toward the sacrum was noted.

Extensive dermatologic, head and neck, and urologic evaluations failed to reveal any suspicious lesions, and examination under anesthesia with anoscopy, anal biopsies, and colonoscopy revealed high-grade anal intraepithelial neoplasia.

Given the involvement of the sciatic nerve roots and internal iliac vessels, she was not amenable to surgical resection, and a decision was made for treatment with primary chemotherapy and radiation, with a plan of three cycles of carboplatin and paclitaxel, followed by chemoradiation (external beam radiation therapy to the pelvic mass and regional lymph nodes and 5-fluorouracil-based regimen) and then further chemotherapy.

Discussion

SCC of unknown primary is rare, accounting for 5% to 20% of cancers of unknown primary and 0.25% to 1% of all invasive cancers [1, 2]. Recent data show that loco-regional treatments and platinum-based chemotherapy are effective modalities in SCC of unknown origin with a five-year relative survival ranging from 27% to 74% [1, 4-6]. SCC of the pelvic retroperitoneum is even more infrequent, with limited data regarding management and prognosis. The etiology and pathogenesis are unclear, but it might arise from squamous

Revised manuscript accepted for publication January 12, 2015

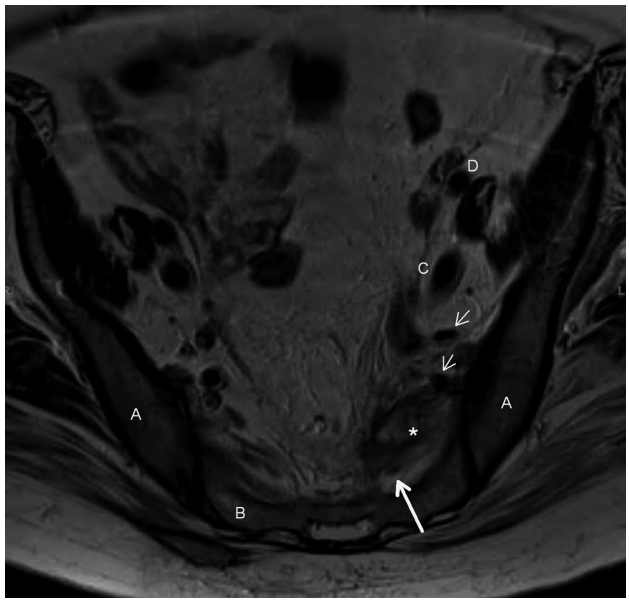

Figure 1. — Axial T2-weighted image of pelvic MRI shows an exiting sacral nerve root (large arrow) about to be encased by the mass. * = mass; A = iliac bone; B = sacrum; C = external iliac vein; D = external iliac artery; small arrows = branches of internal iliac artery; large arrow = exiting sacral nerve about to be encased by mass.

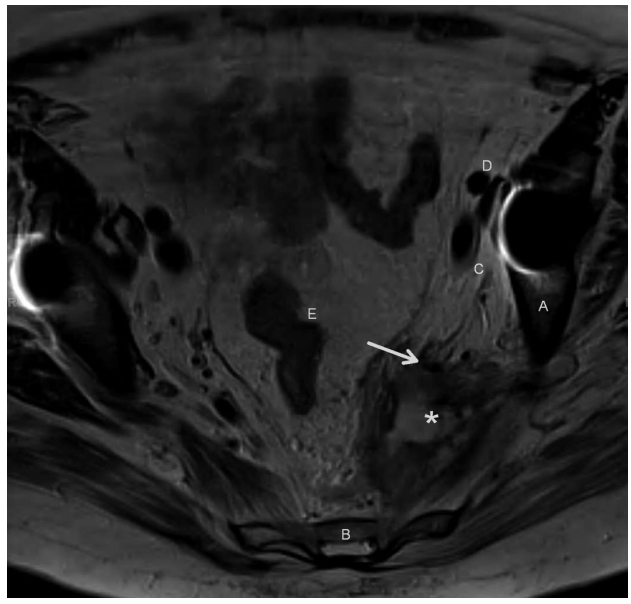

Figure 2. — Axial T2-weighted image of pelvic MRI shows involvement of the internal iliac artery (arrow). The vessels appear black secondary to flow void. * = mass; A = iliac bone (with surgical hardware); B = sacrum; C = external iliac vein; D = external iliac artery; E = colon; arrow = branch of internal iliac artery involved by mass.

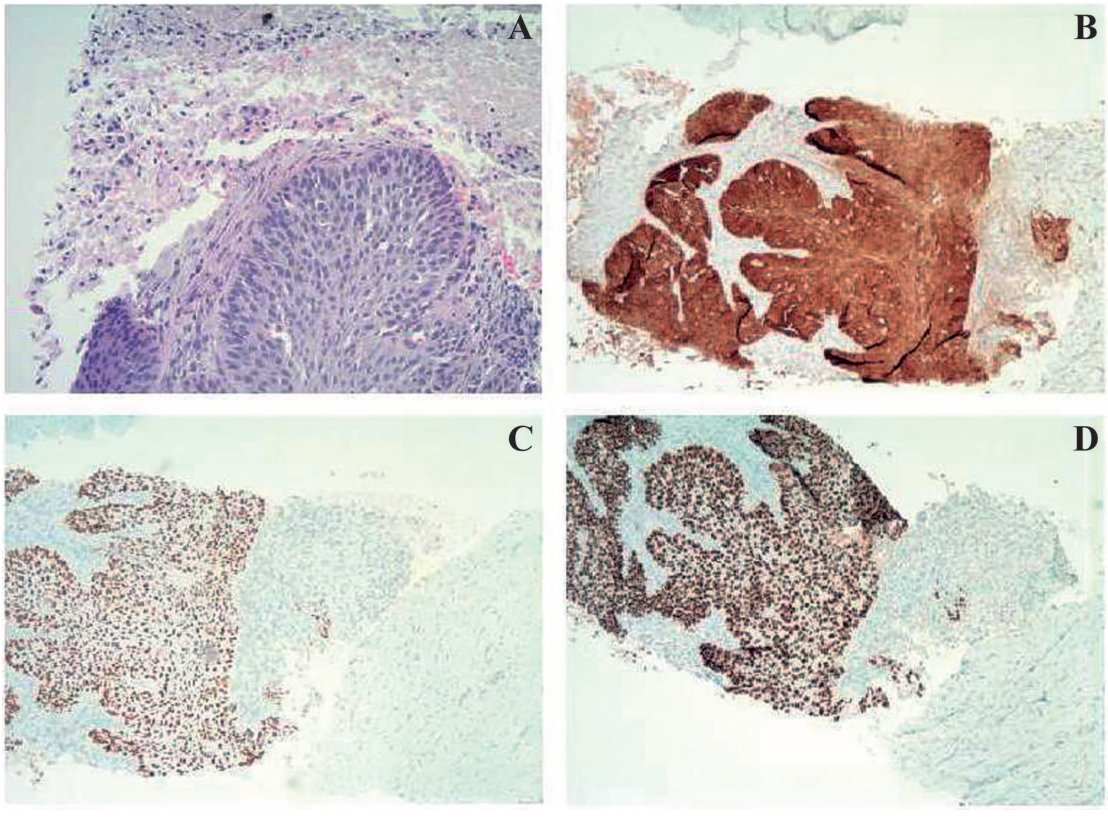

Figure 3. — Biopsy of the pelvic mass. A: Squamous cell carcinoma (hematoxylin and eosin stain at x100). B: Tumor cells strongly positive to p16. C: Tumor cells strongly positive to p40. D: Tumor cells strongly positive to p63.

Table 1. — *Summary of available case reports.*

Case	Location	Initial Treatment	Outcome
Khalil *et al.*, 2005 [11]	Right retroperitoneal pelvic mass involving the ureter	Surgery followed by chemotherapy (PF)	Unresectable pelvic recurrence after 2 cycles; DOD at 6 months*
Lee *et al.*, 2008 [12]	Retroperitoneal pelvic mass adherent to the iliac vessels	Multiple lines of chemotherapy (PF, EAP, IP)	Pelvic recurrence at 61 months;* AWD at 88 months*
Chen *et al.*, 2011 [13]	Left retroperitoneal parametrial mass involving the ureter	Chemo-radiation (pelvic IMRT and weekly cisplatin)	NED at 50 months*
Ruy *et al.*, 2012 [14]	Right retroperitoneal pelvic mass involving the iliac vessels	Radiation therapy and chemotherapy (TC followed by PF)	PR after 2 lines of chemotherapy AWD at 4 years†
Present case	Left retroperitoneal pelvic mass involving the internal iliac vessels and the sacral nerve roots	Chemotherapy (TC) and radiation therapy	-

PF: Cisplatin and 5-fluorouracil; EAP: etoposide, adriamycin, and cisplatin; IMRT: intensity-modulated radiation therapy; IP: ifosfamide and cisplatin; TC: paclitaxel and carboplatin; DOD: dead of disease, AWD: alive with disease; NED: no evidence of disease; PR: partial response.
*From completion of primary treatment. †From initial diagnosis.

metaplasia of pre-existing embryonic rests, which is thought to be the consequence of chronic peritoneal irritation [7]. It may also originate from an extragenital mixed mesodermal (Müllerian) tumor as reported by Solis *et al.* [8].

Complete surgical resection is the most important prognostic factor for retroperitoneal neoplasms. However, this is not always feasible due to the risk of vascular and neurological sequelae. Therefore, rates of complete resection are variable (44% in some studies), with some requiring vascular reconstruction [9, 10]. The present patient was diagnosed with SCC in an isolated pelvic mass without any identifiable origin. This mass involved the iliac vasculature and sciatic nerve roots and thus was not considered surgically resectable.

In 2005, Khalil *et al.* first reported on a 57-year-old female with 6 x 6-cm right pelvic mass with involvement of the distal ureter and hydronephrosis. She underwent en-bloc resection of the tumor with the distal ureter, hysterectomy, bilateral salpingo-oophorectomy (BSO), upper vaginectomy, and ureteroneocystotomy. Pathology revealed poorly differentiated SCC involving only the mass. She received two cycles of cisplatin and 5-fluorouracil, but then had a pelvic recurrence with a vesicovaginal fistula and died of uremia six months later [11].

In 2008, Lee *et al.* reported a case of recurrent pelvic SCC discovered incidentally in a 47-year-old female with endometrial hyperplasia. Laparotomy with hysterectomy and BSO were performed. The 3 x 4-cm pelvic mass could not be removed due to its adherence to pelvic sidewall and iliac vessels. None of the reproductive organs were involved. She was treated with radiation therapy and chemotherapy and achieved complete response after the third cycle. She remained in remission for five years, when she developed a pelvic recurrence and received an additional line of chemotherapy without response. Subsequently, she was managed conservatively and was still alive more than two years after recurrence [12].

Chen *et al.* reported the case of a 44-year-old woman with left retroperitoneal mass measuring 5 x 4 cm, requiring a radical hysterectomy, BSO, bilateral pelvic lymphadenectomy, and left distal ureterectomy with ureteroneocystostomy. Pathology showed SCC of the mass without involvement of the remaining specimen. She received concurrent chemoradiation with weekly cisplatin and pelvic intensity-modulated radiation therapy with boost to the high-risk area over 5.5 weeks. She experienced 50 months of progression-free survival up to the time of the report [13].

Ryu *et al.* reported on a 66-year-old female with an unresectable 7 x 5-cm retroperitoneal pelvic mass that was fixed to the right pelvic sidewall and attached to the iliac vessels at the time of an exploratory laparotomy, without apparent involvement of other pelvic structures. Frozen biopsy was consistent with SCC. Postoperative PET/CT revealed no uptake elsewhere. She received concurrent chemoradiation with a partial response and decrease in size of the mass on CT from 7.2 to 6.6 cm. This was followed by additional chemotherapy, with stable findings. She refused additional treatment and continued to have stable disease for at least four years from initial surgery [14].

The management of retroperitoneal SCC is quite variable in the literature with inconsistent outcomes (Table 1). Surgery remains the cornerstone of treatment; however, most of these tumors present at an unresectable stage with involvement of regional neurovascular bundles and are either not amenable to primary surgery or would require extensive radical operation with increased morbidity with vascular and neurological sequelae and thus would best be managed primarily with radiation and/or chemotherapy. The optimal regimen is yet to be determined. Given the rarity of these tumors, it is difficult to establish a standard therapeutic modality and to draw conclusions concerning their prognosis.

References

[1] Briasoulis E., Pavlidis N.: "Cancer of unknown primary origin". *Oncologist*, 1997, *2*, 142.

[2] Pavlidis N., Briasoulis E., Hainsworth J., Greco F.A.: "Diagnostic and therapeutic management of cancer of an unknown primary". *Eur. J. Cancer*, 2003, *39*, 1990.

[3] Abbruzzese J.L., Abbruzzese M.C., Hess K.R., Raber M.N., Lenzi R., Frost P.: "Unknown primary carcinoma: natural history and prognostic factors in 657 consecutive patients". *J. Clin. Oncol.*, 1994, *12*, 1272.

[4] Guarischi A., Keane T.J., Elhakim T.: "Metastatic inguinal nodes from an unknown primary neoplasm. A review of 56 cases". *Cancer*, 1987, *59*, 572.

[5] Colletier P.J., Garden A.S., Morrison W.H., Goepfert H., Geara F., Ang K.K.: "Postoperative radiation for squamous cell carcinoma metastatic to cervical lymph nodes from an unknown primary site: outcomes and patterns of failure". *Head Neck*, 1998, *20*, 674.

[6] Pragya S., Deepak G., Shyam S.B., Pant M.C., Bhatt M.L., Srivastava K., Negi M.P.: "Metastatic squamous cell carcinoma neck with occult primary: A retrospective analysis". *Indian J. Med. Paediatr. Oncol.*, 2009, *30*, 124.

[7] Schatz J.E., Colgan T.J.: "Squamous metaplasia of the peritoneum". *Arch. Pathol. Lab. Med.*, 1991, *115*, 397.

[8] Solis O.G., Bui H.X., Malfetano J.H., Ross J.S.: "Extragenital primary mixed malignant mesodermal tumor". *Gynecol. Oncol.*, 1991, *43*, 182.

[9] Boneschi M., Erba M., Cusmai F., Eusebio D., Miani S., Bortolani E.M.: "Primary retroperitoneal tumors. Treatment modality and prognostic factors". *Minerva Chir.*, 1999, *54*, 763.

[10] Chen F., Yang Y., Shi Z., Fu W., Jiang J.: "Resection of pelvic retroperitoneal neoplasm and reconstruction of iliac blood vessels: report of 22 cases". *Zhonghua Wai Ke Za Zhi*, 2000, *38*, 858.

[11] Khalil A.M., Shabb N.S., Hourani M.H., Shamseddine A.I., El-Hajj M.I., Seoud A.F.: "Primary squamous cell carcinoma of the pelvic retroperitoneum presenting as an adnexal mass: a case report". *J. Obstet. Gynaecol.*, 2005, *25*, 92.

[12] Lee H.J., Yun H.J., Jo D.Y., Suh K.S., Kim S.: "Metastatic squamous cell carcinoma of unknown primary site occurring in pelvic cavity". *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 2008, *138,* 239.

[13] Chen C.H., Yeh S.D., Chiou J.F., Lin Y.H., Chang C.W.: "Optimum Treatment for Primary Squamous Cell Carcinoma of the Pelvic Retroperitoneum". *J. Exp. Clin. Med.*, 2011, *3*, 304.

[14] Ryu M.J., Chung Y.W., Bae H.S., Lee J.K., Lee N.W., Song J.Y.: "Primary squamous cell carcinoma arising from the pelvic retroperitoneum". *Korean J. Obstet. Gynecol.*, 2012, *55*, 782.

Address reprint requests to:
M.M.K. SHAHZAD, M.D., Ph.D.,
Assistant member of Women's Oncology
H. Lee Moffitt Cancer Center and University of
South Florida Morsani School of Medicine,
12902 Magnolia Dr., MCC GYN
Tampa, FL 33612 (USA)
e-mail: Mian.Shahzad@moffitt.org