Colloid carcinoma of the cervix and endometrial adenocarcinoma: A case report of collision tumor*

By Ali Anjelica Uy-Abuan, MD and Maria Lora C. Tupas, MD, FPOGS, FSGOP
Department of Obstetrics and Gynecology, West Visayas State University Medical Center

ABSTRACT

Background: Collision tumors are defined by the co-existence of two or more tumors in the same or adjacent organs which are topographically and histologically distinct with minimal or no histological admixture. Collision tumors are rare but some have been reported in other organs, as well as the female genital tract.

Objectives: To define and explain the pathogenesis, histogenesis and management; as well as present previously reported collision tumors in different countries as well as in our local setting.

Clinical case: This is a rare case of a 68-year-old nulligravid who complained of postmenopausal bleeding. Imaging studies revealed a uterine mass. Differential diagnosis non-neoplastic conditions and benign and malignant neoplasms. Radical Modified hysterectomy with bilateral salpingo-oophorectomy with frozen section and complete staging was performed. Histopathology revealed a coexistence of a colloid carcinoma of the cervix and endometrial adenocarcinoma.

Conclusion: Collision Tumors are infrequent neoplasias, there are few reports about them in medical literature. Colloid carcinoma of the cervix is a rare subtype and few studies are reported in literature. Their prognosis is unknown since there are no previous similar cases. Colloid carcinomas present a histologic as well as clinical dilemma. Their histogenetic origin remains controversial and their rarity precludes determination of the best treatment options to improve survival outcomes.

Keywords: colloid carcinoma, endometrial adenocarcinoma, mucin, tumors

CASE PROTOCOL

This is the case of B.F, a 68-year-old , female, single, nulligravid from San Rafael, Iloilo who came in with a chief complaint of postmenopausal bleeding.

History of present illness

4 months PTC, the patient had episodes of vaginal discharge pinkish to purulent prompting consult with a private physician. Pelvic Ultrasound was requested but was not immediately complied. 1 month PTC, there was progression of vaginal discharge prompting the patient to have a transrectal ultrasound done. Which revealed the following findings.

Transrectal Ultrasound 4/3/18 – Atrophic anteverted uterine corpus; 3.3x2.9x3.2cm with a volume of 16.0ml. Homogenous myometrium. Smooth serosa. Thin endometrium. (0.2cm), isoechoic, with fluid in the endometrial cavity. The cervix is not recognizable, probably lost within the mass. There is a solid mass inferior to the uterus, 10.3x7.8x9.5cm with vascularities. Doppler studies: SD=1.66 RI= 0.40 PI= 0.54. Both ovaries not visualized but no adnexal mass noted.

Impression: Atrophic anteverted uterine corpus. Thin endometrium. The cervix is not recognizable. Both ovaries not seen. Hydrometra. Prolapsed Submucous Myoma vs New growth.

Patient was referred for comanagement with a gynecologic oncologist and was advised to undergo surgical operation in the form of Total abdominal Hysterectomy with Bilateral Salpingo-oophorectomy with frozen section biopsy of the uterine mass, thus this admission.

Past medical history

She had previous hospitalization for a cardiac problem (2015), She is a known hypertensive maintained on Losartan and Metoprolol and a diabetic maintained on Gliclazide.

*Third Place, Society of Gynecologic Oncologists of the Philippines Foundation, Inc. (SGOP) 17th Annual Interesting Case Contest, November 13, 2018, Meeting Room 6 (A. Mabini), Philippine International Convention Center (PICC)

Family history

Patient's mother was diabetic and father had hypertension. There is no known history of cancer in the family.

Personal and social

She is a retired teacher since 2010; Non-smoker and non-alcoholic beverage drinker.

Obstetric history

Patient is a G0. She had her menarche at 13 years of age, with regular intervals lasting for 2-3 days. She uses 4-5 pads per day, moderately soaked with no dysmenorrhea.

Patient had no sexual contact and had menopause at 50 years old.

Physical examination

General Survey

The patient was ambulatory, conscious, oriented, and conversant, not in cardiopulmonary distress.

VITAL SIGNS

BP: 110/70	Weight: 40.5 kg
CR: 92	Height: 144.5 cm
RR: 20	BMI: 19.39
T: 36.70 C	

SKIN

Patient had uniformly light brown skin. No cyanosis, jaundice or pallor. No active skin lesions.

HEAD, EYES, EARS, NOSE, AND THROAT

The patient has anicteric sclera and pinkish conjunctivae. There was no note of inflammation nor discharges from the eyes or ears. Buccal mucosa and lips was pinkish and moist. There was no note of cervical lymphadenopathy or neck vein engorgement.

CHEST AND LUNGS

The patient had normal respiratory rate with symmetrical chest expansion and clear breath sounds. The patient had an adynamic precordium, normal cardiac rate with regular cardiac rhythm and no appreciable heart murmur.

ABDOMEN

Patient had soft flabby, nontender abdomen, palpable mass movable approximately 14-week uterine size, normoactive bowel sounds.

PELVIC EXAMINATION

- Pelvic Exam
- I : Normal External Genitalia with intact hymen
- IE: Introitus admits one finger snugly. Smooth vaginal walls, atrophic cervix,
- BME: globular symmetrically enlarged corpus approximately 14 weeks uterine size, movable
- Rectal exam: parametria felt smooth and pliable, no intraluminal rectal mass, no cul de sac nodulation

EXTREMITIES

Full range of motion, no joint swelling or tenderness, no edema. Grade 2+ peripheral pulses on all extremities, pink nailbeds, capillary refill of <2 seconds.

Admitting diagnosis

G0 – Abnormal Uterine Bleeding – Malignancy (Uterine mass, probably malignant)

PLANS

The planned procedure for the patient was Exploratory laparotomy, peritoneal fluid collection, Total abdominal hysterectomy with bilateral salpingooophorectomy, frozen section biopsy of uterine mass, possible pelvic node sampling.

Labs were requested, and patient was cleared my Internal Medicine

On laparotomy, 400cc of peritoneal fluid washing was collected for cytology. On exploration, the liver, sub diaphragmatic surfaces, stomach, spleen, omentum, mesentery and bowels were smooth and grossly normal. The uterus was grossly enlarged to about 14 weeks size with smooth serosal surface, measuring 6x5x3cm with smooth serosal surface. The corpus was slightly enlarged; in comparison, the cervix was enlarged to about 12x12cm in length and width with smooth outer surface; soft to firm in consistency. Thus a Type 2 Hysterectomy (Modified Radical Hysterectomy) with Bilateral Salpingoophorectomy was done. The uterus measured 18x 12x6cms; of this the corpus was small, measuring 6x5x3cm. In contrast the cervix was enlarged, measuring 12x12x6cm, soft in consistency. On cut section of the uterus, a large polypoid mass (measuring 9.5x 7.0x 4.0 cm) was found to be attached via a 3cm wide stalk to the right posterior endometrial wall. This polypoid mass filled the uterine cavity and prolapsed into the endocervical canal. (Figure 1) The mass had tan-red, smooth to lobulated external surface and cut sections showed cream to pale yellow surface with abundant mucinous secretions and foul smelling purulent material. The endometrium is 0.15cm thick and both the anterior and posterior myometrium measures 1.5cm thick, respectively. The endocervical canal had an irregular surface, and the exocervix was tan-brown in color and fully effaced by a fungating cream-tan to dark brown mass with mucinous secretions. This cervical mass occupied 80% of the total surface of the endocervical canal and infiltrated more than 2/3 of the cervical stroma. The tumor extended

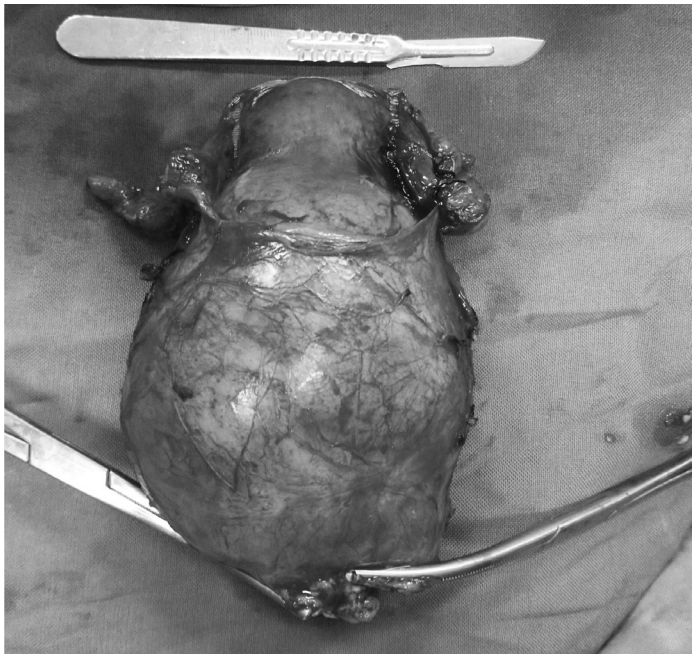

Figure 1. Gross picture of the actual specimen. The uterus is slightly enlarged. Cervix is enlarged with mucinous and foul-smelling fluid

cephalad to the isthmus of the uterus.

The specimen was sent for Frozen section and results showed Mucinous carcinoma of the endometrium with extension to the cervix. A Modified Radical Hysterectomy with bilateral salpingo-oophorectomy with peritoneal fluid collection and para-aortic lymph node sampling was done.

The rest of the patient's hospital stay was unremarkable. She was discharged on her 3rd post-operative day.

Figure 2. Cut section of the specimen revealed a large polypoid mass from the posterior endometrial wall prolapsing into the cervix with mucinous foul smelling purulent discharge. Cervix is enlarged with mucinous fungating mass.

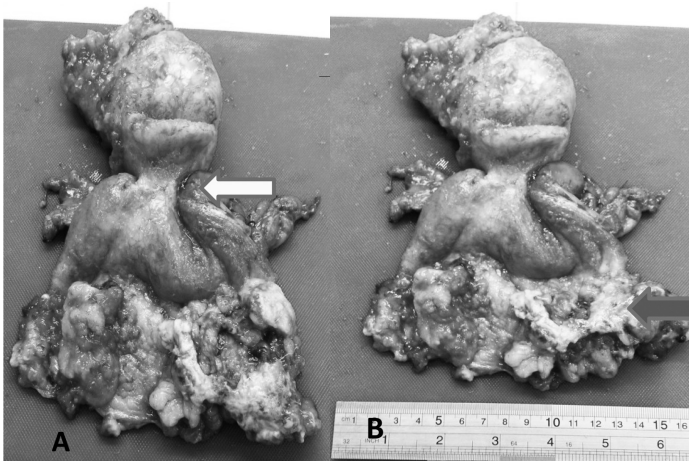

Figure 3. A. a large polypoid mass was found to be attached via a 3cm wide stalk to the right posterior endometrial wall (white arrow) **B.** Cervical mass (dark arrow)

Pathology

Microscopic examinations of the polypoid mass composed of markedly dilated glands filled with abundant pale eosinophilic mucinous secretions and partially lined by pseudostratified columnar epithelium showing cribriforming. The neoplastic cells have markedly pleomorphic, hyperchromatic nuclei with vesicular to coarse chromatin pattern, prominent nucleoli and ample eosinophilic to clear vacuolated cytoplasm. Brisk, occasionally atypical mitosis is noted. Many clusters of neoplastic cells are floating in mucin. The glands are separated by markedly attenuated fibrous tissue and mucin appears to insinuate into the surrounding tissue causing cells to detach and fall into mucin lakes. The rest of the endometrium has dysplastic endometrial glands and fused endometrial glands showing cribriforming with lining epithelium exhibiting pseudostratification and loss of polarity. There is invasion of the superficial portion of myometrium by neoplastic endometrial glands associated with strong lymphoplastic stromal response.

Sections from the cervix show a tumor composed of dysplastic to dilated glands with pale eosinophilic mucinous secretions and partially lined by pseudostratified columnar epithelium with cribriform pattern. Clusters of tumor cells and fibrous bands separating the glands appear to float in mucin lakes. The tumor cells have markedly pleomorphic, hyperchromatic nuclei with vesicular to coarse pattern, prominent nucleoli and ample eosinophilic cytoplasm. Brisk, occasionally atypical mitosis is seen. The tumor invades up to 2/3 of the cervical stroma. The sectionon from the lower uterine segment shows tumor extending to the superficial portion of the myometrium.

Final histopathologic diagnosis showed Collision Tumor: Colloid Carcinoma of the cervix with invasion

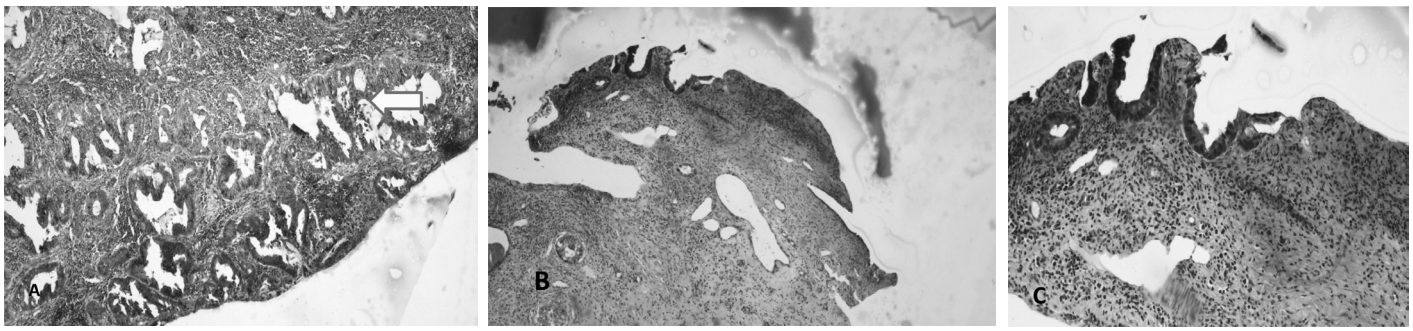

Figure 5. A. Dysplastic endometrial glands and fused endometrial glands showing cribriforming, indicated by the arrow. **B.** Dysplastic Lining of endometrium. **C.** H&E 40x closer view of dysplastic lining showing pseudostratification

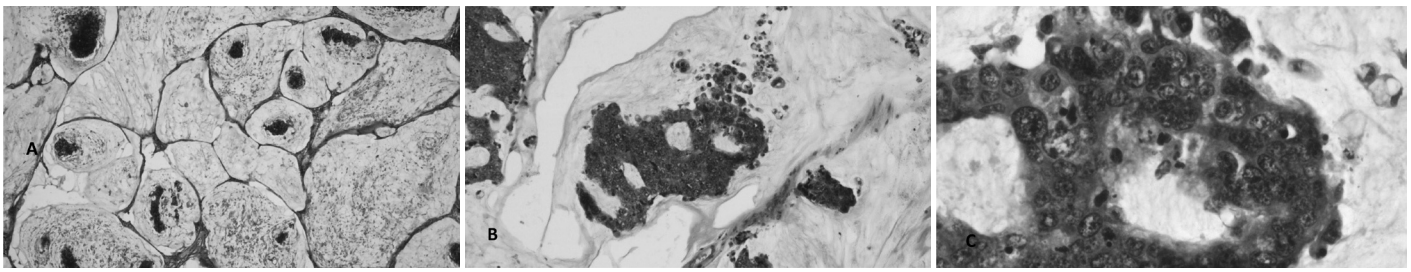

Figure 6. Sections from the cervical mass **A** Clusters of tumor cells and fibrous bands separating the glands appear to float in mucin lakes. **B** Closer view of tumor cells floating in mucin (H&E 40x) **C.** pleomorphic, hyperchromatic nuclei with vesicular to coarse pattern.

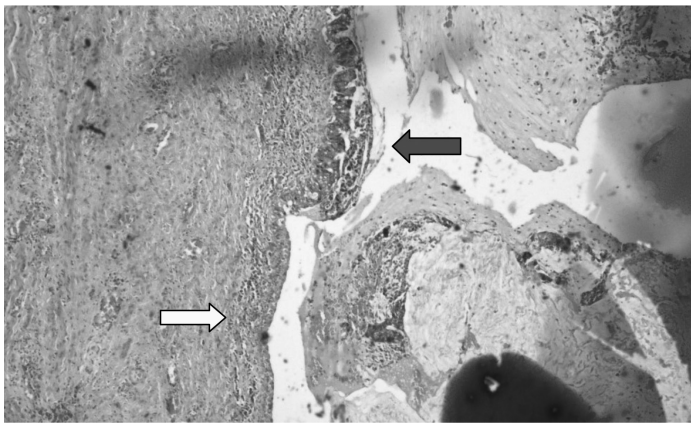

Figure 7. Scanner view of a section from the cervix displaying squamous metaplasia (dark arrow) and adenocarcinoma in situ (white arrow)

of more than 2/3 of cervical stroma and extension to the endometrium, and endometrial adenocarcinoma, endometrioid type, FIGO grade 1, with superficial myometrial wall invasion. Negative for lymphovascular space invasion. Negative for tumor in bilateral parametria, right and left pelvic lymph nodes and peritoneal fluid. Paratubal cysts bilateral

Final Diagnosis for this case is GO, Collision Tumor; Colloid carcinoma of the cervix Stage IB2 and Endometrial Adenocarcinoma endometrioid type FIGO GRADE 1 Stage IA.

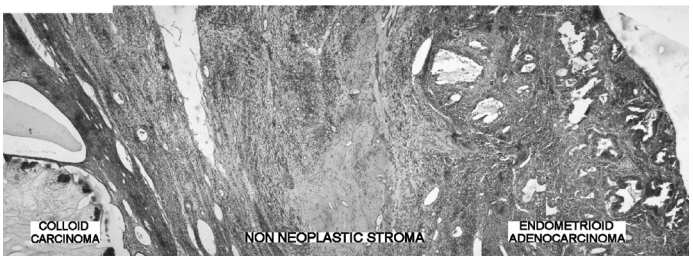

Figure 8. Collision of two tumors histologically distinct with minimal or no histological admixture; each mass has a distinct boundary and is separated by non-neoplastic stroma.

DISCUSSION

Collision tumors are defined as the co-existence of two or more topographically and histologically distinct tumors in the same or in adjacent organs with minimal or no histological admixture. In each mass has a distinct boundary and is separated by non-neoplastic stroma. The different components are considered to be separate primary tumors. Collision tumors have been described in case reports of various organs notably the thyroid, brain, adrenal gland and stomach. Collision tumors involving the female genital tract specifically the uterus is rare with only a few reported cases.[1,2]

Pathogenesis

There are several hypotheses put forward by various authors to explain the rare phenomenon of collision

tumors: (1) The first and simplest, though not necessarily the most likely explanation is the coincidental occurrence of two primary neoplasms within a common location.[3] (2) For other authors collision tumors may represent the simultaneous proliferation of two different cell lines, with a common origin from a pluripotent precursor cell that would differentiate into two components.[3-5] For instance, Kersmaekers, A et al compared the generic alterations in two epithelial collision tumors of the cervix. They concluded that the squamous cell carcinoma and adenocarcinoma components in both tumors most likely had one cell of origin because many genetic alterations were the same in each component.[4] (3) The third theory is the interaction of a carcinogenic agent with different tissues inducing different tumors, (4) Fourth, an oncogenic growth factor produced in a metastatic tumor may induce the growth of a different primary cancer at the site of metastasis or may cause the differentiation of the metastatic lesion to mimic the histology of a primary tumor from the organ of metastasis. For example a colonic primary tumor metastasizing to the cervix produced an adenocarcinoma mimicking a primary cervical adenocarcinoma. (5) Lastly an alteration in the microenvironment by the primary tumor, like inflammation and angiogenesis could promote the growth of metastasis from a second primary tumor from another organ.[2]

Cases of collision tumors

Numerous case reports of collision tumors involving the uterus have been published. The following table summarizes the clinicopathologic features of the reported cases. Majority of the cases stated here were reported as a series by Jang et al in 2012.[2]

A total of 14 patients had separate tumors in the uterine corpus, which included epithelial, mesenchymal, mixed epithelial and mesenchymal, lymphoid and myeloid, as well as trophoblastic tumors. The average age of diagnosis was 61 years. FIGO stage ranged from Ia to IIIc. With majority, 7 out of the 14 patients had stage III disease while 5 had stage I disease.

It is interesting to note that endometrial adenocarcinoma was the most frequent histologic type encountered (9/14, 64.3%), followed by endometrial stromal sarcoma (5/14, 35.7%). It is also noteworthy that 12 out of the 14 uterine collision tumors were composed of an endometrial (endometrioid or serous adenocarcinoma) and a mesenchymal tumor (leiomyosarcoma or endometrial stromal sarcoma). These collision tumors may be examples of the epithelial-mesenchymal transition theory, in which epithelial cells lose their cell polarity and cell-cell adhesion, and acquire migratory and invasive properties to become mesenchymal stem cells. These stem cells are multipotent stromal cells that can differentiate into different cell types.[6]

All patients underwent hysterectomy with lymph node dissection performed in 5 cases. Adjuvant treatment in the form of chemotherapy, radiotherapy of both was administered in 7 of the 14 patients. One patient with an endometrial stromal sarcoma component was given megesterol acetate. Follow up information was obtained from 10 cases. Four patients, all of whom had stage III disease, died 4 to 18 months after diagnosis. In contrast patients who had lower FIGO stage (Ia-Ib) were alive as of their last follow up at 1-8 years after diagnosis. Regardless of tumor type, the outcome depended on the tumor stage, with those of a relatively lower FIGO stage having better prognosis.

There are 3 Local cases of collision tumors of the uterus reported in literature. Sazon in 1996 reported a case of a triple collision tumor of squamous cell carcinoma large cell non-keratinizing and an adenocarcinoma, endocervical type stage IB, and adenocarcinoma endometrial type stage IA, in a 49-year-old G6P6 patient. Sotto in 1997 reported another case of collision tumor in a 43-year-old G7P5 patient who underwent Radical hysterectomy with bilateral salpingooophorectomy with lymph node dissection, final diagnosis was a collision tumor of a squamous cell carcinoma, large cell non-keratinizing and endometrioid adenocarcinoma.[6] Huevos in 2004 reported another case of a collision tumor of endometrial adenocarcinoma and low grade stromal sarcoma. The patient, a 49-year-old multipara underwent total hysterectomy with bilateral salpingoophorectomy, peritoneal fluid cytology and pelvic and para aortic lymph node dissection with a FIGO stage of IC, She eventually underwent adjuvant complete radiotherapy and with no evidence of disease on last follow up.[7]

We are presented with a case of a 68 year old nulligravid who came in with a chief complaint of postmenopausal bleeding. Patient underwent modified radical hysterectomy with bilateral salpingoophorectomy, with pelvic lymph node dissection. Cut section of the uterus revealed two separate masses in the corpus and cervix. Histopathologic diagnosis was a collision tumor of Endometrial Adenocarcinoma, endometrioid type and a Colloid carcinoma of the cervix. What distinguishes this case of a collision tumor of the uterus from the 3 previously cited reports is the presence of very rare cervical component namely, colloid carcinoma. To date, there are only 3 cases of colloid carcinoma of the cervix in medical literature. This is probably the first ever reported case of a collision tumor between a Colloid carcinoma of the cervix and endometrial adenocarcinoma both locally and internationally.

Endometrioid adenocarcinoma is the most common type of endometrial cancer accounting for approximately

Table 1. Summary of reported uterine collision tumors

Case	Age	Diagnosis	Therapy	Stage	Outcome	Ref
1	55	Adenocarcinoma Leiomyosarcoma	NA	NA	NA	2
2	69	Adenocarcinoma, well differentiated High Grade stromal sarcoma	TAH with BSO	Ib	N	2
3	67	Endometrioid adenocarcinoma Homologous sarcoma	TAH	IIIb	6 mo, died	2
4	72	Serous carcinoma Heterologous sarcoma	TAH, prior CTx	IIIc	18 mo, died	2
5	49	Endometrioid adenocarcinoma Malignant rhabdoid tumor	TAH with BSO, Rtx	IIIb	4 mo, died	2
6	85	Endometrioid adenocarcinoma Endometrial stromal sarcoma, high grade	TAH with BSO	IIIa	1.5 yr, alive	2
7	47	Endometrial adenocarcinoma Endometrial stromal sarcoma, high grade	TAH with BSO	Ib	6.5 yr, alive	2
8	68	Hepatoid carcinoma Carcinosarcoma	TAH with BSO	IIIa	NA	2
9	79	Papillary serous carcinoma Small cell carcinoma	TAH with BSO LN dissection, Rtx	IIIc	5 mo, died	2
10	70	Papillary serous carcinoma Endometrioid adenocarcinoma Malignant Mixed mullerian tumor	TAH with BSO, Pelvic paraaortic LN dissection, CTx, Rtx	IIIc	8 yrs, alive	2
11	36	Endometrioid adenocarcinoma Endometrial stromal sarcoma	Laparoscopic assisted vaginal hysterectomy, megesterol acetate	Ia	3.5 yrs, alive	6
12	55	Endometrial adenocarcinoma Endometrial stromal sarcoma	TAH with BSO, Pelvic paraaortic LN dissection, CTx, Rtx	IIb	4 yrs, alive	6
13	59	Endometrial adenocarcinoma Endometrial stromal sarcoma	TAH with BSO, Pelvic paraaortic LN dissection	Ib Ia	Lost to ff up	6
14	52	Endometrioid adenocarcinoma, undifferentiated carcinoma, choriocarcinoma	RHBSO and pelvic LND, CTx	stage Ib2	1 yr, alive	7

TAH – Total Abdominal Hysterectomy
RHBSO – Radical Hysterectomy with Bilateral Salpingo-oophorectomy
BSO – Bilateral Salpingo-oophorectomy
LND – Lymph node dissection
CTx – Chemotherapy
RTX - Radiotherapy

60% of cases. The term endometrioid derives from the tumor's predominant glandular pattern, which resembles proliferative phase endometrium. Most tumors develop slowly in the setting of hyperestrogenism against a background of atypical endometrial hyperplasia, although some arise in atrophic endometrium. Endometrioid carcinoma carcinoma is predominantly a disease of the sixth and seventh decades and 75% of cases occur after menopause. They are low-grade, associated with a good prognosis and often develop after a long history of anovulatory cycles or estrogen therapy. Women most often present with abnormal vaginal bleeding, which means in the majority of cases postmenopausal bleeding. There are two types of endometrial cancers, type 1

and type 2. Molecular analyses show that these two tumor types have distinctively different gene expression profiles. Type 1 tumors are estrogen dependent and may demonstrate microsatellite instability, inactivated PTEN tumor suppressor gene, KRAS mutations. In contrast Type 2 tumors are estrogen independent tumors and show loss of heterozygosity at different loci, altered p53 and abnormalities in the mitotic checkpoints. Synergies between independent genetic events that produce endometrioid carcinoma centers on these mentioned pathways.[10]

Colloid carcinoma of the cervix is a rare variant of mucus – producing adenocarcinoma of the uterine cervix. They are characterized by the presence of a large amount of extracellular mucin resulting in the formation of mucous lakes with a relative paucity of neoplastic cells within them. It is an extreme variant of mucus-producing adenocarcinoma which are most frequently seen in the stomach, large intestine and less commonly in the breast, biliary tract, pancreas, prostate and lung. A comprehensive review of endocervical adenocarcinoma and its variants were performed by Young and Clement. They classified Mucinous adenocarcinoma as; gastric type (minimal deviation adenocarcinoma) and intestinal type which includes signet-ring cell and colloid adenocarcinoma. According to the World Health Organization classification, Mucinous adenocarcinoma is classified into gastric, intestinal, signet ring cell, villoglandular and not otherwise specified types.[10] While Colloid carcinoma it is treated as a variant of the endocervical type, it's histopathologic classification remain unclear.

Recent breakthroughs in immunohistochemistry has allowed characterization of the various kinds of mucin produced by cervical adenocarcinomas and by the different gastrointestinal mucosa and the adenocarcinomas derived from them. Only 3 studies about colloid carcinoma of the cervix have been reported in literature, and they described morphological and immunohistochemical characteristics of the tumor. One study is by Shintaku et al in 2010, where they reported a case of a colloid carcinoma of the cervix, focusing on its mucin immunohistochemistry. MUC genes are tissue specific. MUC2 is an intestinal type mucin and not expressed by endocervical cells, but undergoes aberrant expression in malignant transformation, i.e. Endocervical adenocarcinomas. MUC5AC is a gastric epithelial type of mucin while MUC6 favors pyloric gland type. CDX2 is a transcription factor expressed by the entire intestinal type of cervical adenocarcinomas and some conventional cervical adenocarcinomas. Immunohistochemical studies showed positivity for MUC2 and CDX2, but negative for MUC5AC and MUC6. It was concluded that the tumor cells which produced mucin was intestinal phenotype.[10]

Ishida et al in 2014 reported a second study of colloid carcinoma and its immunohistochemistry in a 47-year-old Japanese female with a bulky mass in the cervix. Biopsy from the cervix revealed adenocarcinoma; subsequently, total hysterectomy was performed. Histopathologic study revealed colloid carcinoma endocervical type with adenocarcinoma in situ (AIS). Immunohistochemistry demonstrate MUC5AC and MUC6 positivity but MUC2 and CDX2 negative confirming the adenocarcinoma was of the endocervical type. In addition, human papillomavirus 16 was detected in both the colloid carcinoma and AIS components.[12]

The third case of colloid carcinoma was presented by Koc, et al in a 51-year-old who had postmenopausal bleeding from a 5 cm cervical tumor. She underwent surgery with complete staging. Colloid carcinoma was found in the cervical tumor together with Adenocarcinoma in situ of intestinal and usual types detected in superficial areas. Immunohistochemical staining revealed that the colloid carcinoma cells were positive for MUC5AC and MUC2, focal positive for CDX2, and negative for MUC6. (Table 2)[9]

Table 2. Summary of Immunohistochemical studies by different authors

	MUC2 (intestinal)	CDX2 (intestinal)	MUC5AC (endo-cervical)	MUC6 (endo-cervical)
Shintaku et al (2010)	+	+	-	-
Ishida et al (2014)	-	-	+	+
Koc et al (2018)	+	Focal +	+	-

It can be concluded based on previous studies that the mucin producing neoplastic cells of colloid carcinomas may be heterogeneous group of tumors exhibiting endocervical as well as intestinal phenotypes. Also, the presence of human papilloma virus in the tumor cells may point to some colloid carcinomas being HPV-related but further studies need to be done to confirm this.

A possible differential diagnosis for a primary colloid carcinoma of the cervix can include metastatic colloid adenocarcinoma arising from gastrointestinal sites. However, Immunohistochemical staining alone is insufficient to differentiate one from the other since immunophenotyping of metastatic colloid adenocarcinoma from the gastrointestinal tract may be the same as that of a primary colloid carcinoma of

the cervix. In their case report Koc et al ruled out a metastatic tumor from the gastrointestinal tract based purely on the absence of gastrointestinal tumors on clinical examination of the patient.[9]

It would be interesting to study the histogenesis of the colloid carcinoma of our patient in order to determine whether it is of gastrointestinal of primarily cervical in origin. However, based on the 3 reports cited above, Immunohistochemical staining may not be helpful in the differential diagnosis. Most primary malignancies of the cervix evolve from a sequence of epithelial dysplasias, e.g. from CIN 3 to carcinoma in situ to invasive squamous cell carcinoma. Our patient exhibited areas of Adenocarcinoma-in-situ, the supposed precursor lesion of primary cervical Adenocarcinoma; this confirms that the cervical tumor is NOT metastatic in nature. The cervical tumor is also most likely NOT HPV-related since the patient's clinical history and physical examination confirm the absence of any sexual activity that may have led to acquisition of a HPV infection.

Diagnosing collision tumors based on physical exam and imaging may be difficult. Based on the previous reports of collision tumors, the physical examination as well as the findings in imaging studies do not provide clinicians any clue as to their existence. Most collision tumors are diagnosed postoperatively through histologic examination of the specimen, therefore it is crucial to carefully sample areas to diagnose collision tumors.

The management of collision tumors can be challenging, particularly if the components of the collision tumor are of diverse histologic types. Surgical management with appropriate adjunct therapy, guided by histology, patient state, and preference is recommended. It is unclear whether aggressive surgery and multimodal adjuvant treatment can increase survival rates in these patients. Rosas Guera et al. recommend using a combination of therapies, treating each tumor component as if it were the only one.[4] On the other hand, Ahmed et al suggests that post surgical management be determined by the most aggressive component of the collision tumor and the stage which will ultimately determine prognosis.[16]

In planning post-operative management, the presence of colloid carcinoma and endometrial adenocarcinoma in our patient were considered separately. As far as the endometrial carcinoma is concerned, no further management is required since her tumor is Stage IA, FIGO Grade I which carries a very good prognosis. The colloid carcinoma of the cervix was staged as StageIB2. The Clinical practice Guidelines of SGOP recommend adjuvant chemoradiation due to the large size of the tumor, the deep stromal invasion and the potentially aggressive nature of her colloid carcinoma. Though colloid carcinoma is histologically distinct and rare form of cervical adenocarcinoma, it is treated in a similar manner with chemotherapy and or radiotherapy depending on the stage of the disease. Since very few cases of colloid carcinoma of the cervix have been reported in the literature, information regarding the prognosis is scarce. The patient is currently undergoing pelvic radiotherapy with concurrent chemotherapy.

In summary, this is a rare case of a collision tumor of endometrial adenocarcinoma endometrioid type and colloid carcinoma. Collision tumors are infrequent neoplasias whose prognosis is unknown. The physical examination as well as the findings in imaging do not confirm the existence of these tumors. They are diagnosed postoperatively by histopathologic examination of the specimen. The management of collision tumors is dictated by the histology of its individual components. Thorough pathological examination of the specimen as well as awareness of the existence of collision tumors is important to accurately diagnose these rare entities. Accurate diagnosis, in turn, is essential in order to guide in planning the appropriate treatment in the hope of improving prognosis. Colloid carcinomas present a histologic as well as clinical dilemma. Their histogenetic origin remains controversial and their rarity precludes determination of the best treatment options to improve survival outcomes. ■

REFERENCES

1. Murthaiah P, Truskinovsy A, Shah S and Dudek A. Collision Tumor versus Multiphenotypic Differentiation: A Case of Carcinoma with Features of Colonic and Lung Primary Tumors. *Anticancer Res May*. 2009; 29(5)1495-1497.

2. Jang K S, Lee W M, Kim Y J, & Cho S H (2012). Collision of Three Histologically Distinct Endometrial Cancers of the Uterus. Journal of Korean Medical Science, 27(1), 89-92. http://doi.org/10.3346/jkms.2012.27.1.89.

3. Oscar Zenón Rosas-Guerra, Jorge Alfonso Pérez-Castro y Vázquez, Gumaro Hugolino Andrade-López, Fernando Vera-Rodríguez, Heriberto Garza-de la Llave. Metastatic Collision Tumor: A case Report. Cirugia y Cirujanos (English Edition) vol 83, ISSUE 3, May-June 2015, Pg 238-242.

4. Kersemaekers A, van de Vijver M, Fleuren GJ. Comparison of the genetic alterations in two epithelial collision tumors of the uterine cervix. A report of two cases. *International Journal of Gynecological Pathology*. July 2000. Volume 19-Issue 9 Pg 225-230.

5. Kim-Huyen, Pham-Amin, Ramzan-Esther, Elishaev-Paulette, Mhawech-Fauceglia. Endometrioid adenocarcinoma associated with endometrial stromal sarcoma: A rare, oftern unrecognized collision tumor.

6. Rivera-Enghong L, Rivera L S, Espino-Strebel E. Triple Collision Tumor of the Ovary. *Philippine Journal of Obstetrics and Gynecology*. March, 2011. Volume 35. (No.1)

7. Huevos, A. Endometrial adenocarcinoma and low grade stromal sarcoma: A case report of collision tumor. *Philippine Journal of Obstetrics and Gynecology*. September 2004; Vol. 28, 113-118.

8. Kurman R J, Carcangiu M L, Herrington C S, Young RH. WHO Classification of Tumours of Female Reproductive Organs.

9. Koc, Nermin, Sevcan Arzu Arinkan, Nurver Ozel Ozbay, Selcuk Selcuk. Colloid Carcinoma of the Uterine Cervix and Its Immunohistochemical Analysis: A Case Report. *Journal of Pathology and Translational Medicine*. *JPTM*. 2018; 52(1):56-60. Published online 2018 January. DOI: https://doi.org/10.4132/jptm.2017.04.08 .

10. Shintaku M, Kurusshima R, Abiko K. Colloid carcinoma of the intestinal type on the uterine cervix: mucin immunohistochemistry. *Pathol Int*. 2010; 60:119-24.

11. Mardi K. (2013). Colloid carcinoma of the intestinal type in the uterine cervix. *South Asian Journal of Cancer*, 2(4), 295. http://doi.org/10.4103/2278-330X.119918

12. Ishida M, Iwai M, Kagotani A, Yoshida K, Okabe H. Colloid carcinoma of the uterine cervix: a case report with respect to immunohistochemical analyses. *Int J Gynecol Pathol.* 2014; 33: 248-52.

13. Bostanci MS, Yildirim OK, Yildirim G, Bakacak M, Ekinci ID, et al. (2015) Collision Tumor: Dermoid Cysts and Mucinous Cystadenoma in the Same Ovary and a Review of the Literature. *Obstet Gynecol Cases Rev,* 2:031. 10.23937/2377-9004/1410031.

14. Calvin Sung-Anup Shetty-Christine Menias-Roozbeh Houshyar-Shreya Chatterjee-Thomas Lee-Paul Tung-Mohammed Helmy-Chandana Lall. Collision and composite tumors; radiologic and pathologic correlation - Abdominal Radiology - 2017

15. Choo Y, & Naylor B. (1984). Coexistent squamous cell carcinoma and adenocarcinoma of the uterine cervix. Gynecologic Oncology,17(2), 168-174. doi:10.1016/0090-8258(84)90073-8.

16. Eliyaz Ahmed-Shatrughan Sah-Anilkumar Adikesavalu-Krishnaswamy Madhavan-Khalil Razvi Unusual Collision Tumor of Ovary: Endometrioid Adenocarcinoma and Teratoma - Clinical Ovarian and Other Gynecologic Cancer - 2012.

17. Xiu X X, Wang H L, Yun-Yi L, Fan-Dou K, & Jin-Ping H. (2017). Endometrial stromal sarcoma in combination with mixed type endometrial carcinomas: A case report and literature review. Medicine, 96(49), e8928. http://doi.org/10.1097/MD.0000000000008928.

18. Masuyama H, Haraga J, Nishida T, Ogawa C, Kusumoto T, Nakamura K, Hiramatsu Y. (2016). Three histologically distinct cancers of the uterine corpus: A case report and review of the literature. *Molecular and Clinical Oncology*, 4(4), 563-566. http://doi.org/10.3892/mco.2016.770.

19. Tanveer N, Gupta B, Pathre A, Rajaram S, & Goyal N. (2017). A Rare Collision Tumour of Uterus - Squamous Cell Carcinoma and Endometrial Stromal Sarcoma. *Journal of Clinical and Diagnostic Research*: JCDR, 11(2), ED20-ED22. http://doi.org/10.7860/JCDR/2017/23532.9405.