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Unusual Presentation of Metastatic Cervical Squamous Cell Carcinoma with Serum Positive Beta Human Chorionic Gonadotropin

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1. Abstract

We present a case of a 30-year-old female who presented with one month of worsening dyspnea. On admission she was having pleuritic chest pain with associated cough and worsening dyspnea. CTA showed a moderate sized pleural effusion with two hypodensities noted in the liver. Patient received several thoracenteses and had abdominal distension that required paracentesis, which showed transudative fluid initially. There was a noted supraclavicular lymph node, however the patient refused lymph node biopsy. Retroperitoneal lymph node, which was seen on CT abdomen, was eventually biopsied which showed metastatic carcinoma with squamoid differentiation with unknown primary. Beta subunit of human chorionic gonadotropin (b-HCG) was rechecked for the biopsy and was mildly elevated to 33. The patient refused gynecological evaluation, pelvic ultrasound revealed a distended endometrial cavity with heterogeneous contents and a complex left adnexal cyst. Pelvic MRI noted a large cervical mass (4.6 cm x 4.5 cm x 3.8 cm) with parametrial invasion. Subsequently her status declined and she was intubated for hypoxic respiratory failure. Patient unfortunately passed away. Autopsy confirmed metastatic cervical cancer with significant tumor burden as evidence of >80% of the liver with tumor. Although the patient's pap smear previously did not culture for HPV, the lymph node biopsy stained positive with Pap stain and shown that the carcinoid cells were most affected by HPV. Later is was found that 3.5 years prior the patient had a Pap smear positive for low-grade squamous intraepithelial lesion however was lost to follow up. Although there have been studies that have examined cervical cancer and the intracellular expression of b-hCG, serum b-hCG is not known to be elevated in squamous cell carcinoma of the cervix. For women presenting with wide spread disease, gynecological malignancies should be ruled out regardless of age.

2. Keywords: Metastatic cervical cancer; Pleural effusion; Virchow's lymph node; b-hCG

3. Introduction

We present a case of a 30-year-old female with history of low-grade squamous intraepithelial lesion on pap smear who had failed follow-up, presenting 3.5 years later with complaints of worsening dyspnea relates to advanced metastatic cervical cancer. Diagnosis was

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made only after incidental finding of elevated b-HCG. Cervical cancer is one of the most common gynecological malignancies in the world, with most of the cancers stemming from the HPV virus. Most early cervical cancers are asymptomatic and detected on routine pap smears, which are effectively eradicated surgically in early disease stages. Prevention lies in identifying and treating women with high grade dysplasia and with vaccination against HPV. Although some women are asymptomatic, most usually have signs of vaginal bleeding that typically worsens [1]. Presentation usually involves either vaginal bleeding or from local invasion of the primary tumor invading into the bladder or rectum leading to constipation, hematuria, fistula formation or ureteral obstruction [2]. Presentations with primary complaints related to problems arising from distant metastasis to extra pelvic lymph nodes, liver or lung are atypical and rare. Here we present a case of a young female with a history of low grade squamous intraepithelial lesion (LGSIL) who had failed to follow up presenting 3.5 years later with primary complaints related to advanced metastatic cervical cancer.

4. Case Presentation

The patient is a 30-year-old female with no known past medical history who presented to the emergency department with worsening dyspnea over one month that was associated with clear productive cough. The patient was seen in an urgent care facility several days prior to presentation and was prescribed Azithromycin at that time. On presentation the patient was having pleuritic chest pain with coughing and her dyspnea was progressing rapidly with even walking short distances. On presentation the patient was afebrile to 98.3F, tachycardic to 126 and regular, normotensive to 133/91, tachypneic to a respiratory rate of 24 and pulse ox showing 85% on room air, 91% on 5L oxygen via nasal cannula. On physical exam the patient was comfortable, well-nourished and of normal build. Exam was remarkable for conjunctival pallor, diminished breath sounds over the right lower lung fields and abdominal exam with tenderness to the right upper quadrant on palpation. Laboratory studies were remarkable for a normocytic anemia with hemoglobin 9.3 and a transaminitis with Alanine transaminase (ALT) 128, Aspartate transaminase (AST) 103 and Alkaline phosphatase (ALP) elevated to 248.

Table 1: Serum and Urine Laboratory Studies from Admission, Day 3, 7 and 14.

	On Admission	Day 3	Day 7	Day 14
WBC	9.9 x10e^3/mm^3	11.6	10.7	11.7
Hgb	9.3 g/dL	8.4	8.6	9
Platelets	403 x10e^3/mm^3	294	282	289
ESR	49 mm/hr	-	-	-
Retic Count	4.10%	-	-	-
PT	15.7 sec	-	15.4	24.4
INR	1.37	-	1.35	2.12
PTT	27.6 sec	-	32.1	32.6
Sodium	136 mmol/L	133	135	133
Potassium	3.5 mmol/L	3.8	3.3	4.1
Chloride	101 mmol/L	99	100	96
Bicarbonate	22 mmol/L	21	23	23
Calcium	8.7 mmol/L	8.4	8.1	8.1
BUN	6 mg/dL	7	4	15
Creatinine	0.52 mg/dL	0.5	0.41	0.42
Total Protein	7.1 g/dL	6.4	5.8	5.8
Albumin	3.6 g/dL	3.2	2.8	2.6
Alk Phos	248 IU/L (30-99)	264	274	435
ALT	103 IU/L (4-35)	98	79	93
AST	128 IU/L (5-35)	140	154	347
Direct Bilirubin	-	0.7	1.95	-
Total Bilirubin	1.08 mg/dL (0.2-1.2)	1.54	2.42	5.64
LDH	381 IU/L (95-255)	-	-	-

Magnesium	2.1 mg/dL (1.7-2.4)	2	-	2.7
Phosphorus	3.6 mg/dL (2.5-4.5)	3.5	-	2.8
Iron	12 mcg/dL (50-170)	-	-	-
TIBC	378 mg/dL (259-446)	-	-	-
Transferrin	264 mg/dL (205-360)	-	-	-
Ferritin	59 ng/mL (11-306.8)	-	-	-
CRP	-	-	83 (1-4.9)	-
TSH	3.173 uIU/mL	-	-	-
HIV	Neg	-	-	-
ACE	-	36 (14-82)	-	-
b-hCG	-	-	33	31
Ca 19-9	-	-	-	191 (0-35)
AFP	-	-	-	1 (0-8)
CA 125	-	-	-	>600
CEA	-	-	-	4.2 (0.1-5)
Urine Analysis	-	-	-	-
Spec Gravity	1.016	-	-	-
pH	6	-	-	-
Protein	neg	-	-	-
Leuk Est	neg	-	-	-
Nitrites	neg	-	-	-
Blood	<5	-	-	-
WBC	<5	-	-	-
Bacteria	None	-	-	-
Casts	None	-	-	-
b-hCG	Neg	-	-	-
Ur Drug Screen	Neg	-	-	-

Chest X-ray showed a small right sided pleural effusion however the CTA chest was remarkable for a moderate sized pleural effusion with two hypodensities noted in the liver.

The following day the patient received a thoracentesis with a bloody tap.

Table 2: Thoracentesis and Paracentesis Results.

Thoracentesis	**Day 2**	**Day 8**	**Day 15**	**Paracentesis**	**Day 15**
Appearance	bloody	Cloudy	Cloudy	Appearance	Cloudy
Colour	Red	Orange	Yellow	Colour	Yellow
RBC	79320 cells/mcl	22728	11000	RBC	3150
Nucleated Cells	2178 cells/mcl	1846	1890	Nucleated Cells	803
Diff Cells#BF	100	-	-	Diff Cells#BF	-
Neutrophil	4	9	7	Neutrophil	3
Eosinophil	1	1	-	Lymphocyte	33
Lymphocyte	50	39	34	Macrophage	57
Macrophage	41	48	63	Albumin	<0.7
Mesothelial	4	3	3	LDH	146
Albumin	1.7	1.4	0.9	Protein	2
LDH	168	161	151	pH	7.49
Protein	3	2.5	1.4	Glucose	91
ADA	-	2	-	-	-
Amylase	-	31	-	-	-
Chol	-	45	-	-	-

Lipase	-	25	-	-	-

Echocardiogram was unremarkable as was the right upper quadrant ultrasound. The patient had a prolonged hospitalization, during which time she had continued elevation of her transaminitis over three weeks to a peak of ALT 151, AST 555, ALP 374, Gamma glutamyl transferase (GGT) elevated to 275 and a total bilirubin, which was initially 1, trended up to 5.89 and direct bilirubin of 4.02 (Table 1). In addition, the patient had multiple laboratory studies to work up atypical immunological diseases which could be causing the illness; however, the studies were remarkably negative.

Table 3: Immunological Serum Studies.

Immunological studies			
C_3 Complement	122 mg/dL (72-180)	Rheumatoid Factor	<10.0
C_4 Complement	32 mg/dL (11-59)	Sclrdrm Ab CL70.	<0.2
Completment Total	26 units/mL (42-60)	Smooth Musc Ab.	8 (0-19)
a1-antitrypsin	232 mg/dL (90-200)	TTG IgA.	<2
AdenoDNA PCR	<500 copies/mL	Total IgA	332 mg/dL (87-352)
Antribosml P Ab	<0.2	Total IgG	1121 mg/dL (700-1600)
Atypical pANCA	<1:20	Total IgM	391 mg/dL (26-217)
CCP IgG/IgA Ab	3 units (0-19)	IgG subclass 4	62 mg/dL (2-96)
Ceruloplasmin	47.3 mg/dL (19-39)	CMV IgG	0.27 (0-0.9)
Chromogranin A	<1	EBV DNA PCR	Neg
CMV IgM	<30	Hep A IgM	Non-reactive
CMV PCR Ql	Neg	Hep Bs Ag	Non-reactive
Crbhdrt Ag 19-9	191 units/mL (0-35)	Hep B Core IgM	Non-reactive
Cyoplsmc C-ANCA	<1:20	Hep C Ab	Non-reactive
DNA NS Ab	0	HSV-1 DNA	Neg
EBV Ab VCA IgM	<36	HSV-2 DNA	Neg
EBV DNA PCR RT	Neg	ANA Screen	Positive
Endomysial IgA	Neg	ANA Titer	1:160.
Histone Abs	0.6 (0-0.9)	ANA Titer Pattern	Homogenous
Lepspra IgM.	Non-reactive	Sjogren's Anti-SS-A	<0.2
Lvr-Kid Mcrs Ab	0.5 (0-20)	Sjogren's Anti-SS-B	<0.2
Mitochondral Ab	2.8 (0-20)	Smith Antibody.	<0.2
Perinucl P-ANCA	<1:30	-	-

The patient had a re-accumulation of her right pleural effusion and a new left sided pleural effusion. She had two more thoracentesis done on bilateral sides that showed transudative effusions with initial negative cytologies (Table 2). The patient also went for a

hepatic CT triple phase that was remarkable for mesenteric and retroperitoneal lymphadenopathy, hepatomegaly and markedly heterogeneous 3 phase hepatic enhancement, possibly reflecting hepatitis. Angular and irregular sub capsular perfusion defects pronounced in segment 7 that represented infarcts and moderate abdominal ascites. The patient prior to this exam was having progressively worsening abdominal distension and required a paracentesis, which showed transudative fluid (Table 2). On exam the patient was noted to have a 1cm supraclavicular lymph node which was not present on initial exam, however after the patient refused a supraclavicular lymph node biopsy.

On day 14 of hospitalization, interventional radiology was consulted for a biopsy of the retroperitoneal lymph node for which the final report was metastatic carcinoma with squamoid differentiation;

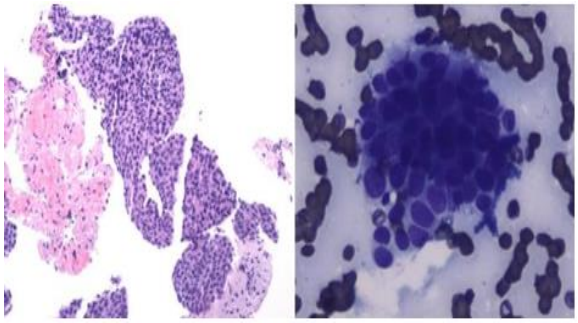

Figure 1: Pathology and cytology of lymph node biopsy showing metastatic carcinoma with squamoid differentiation.

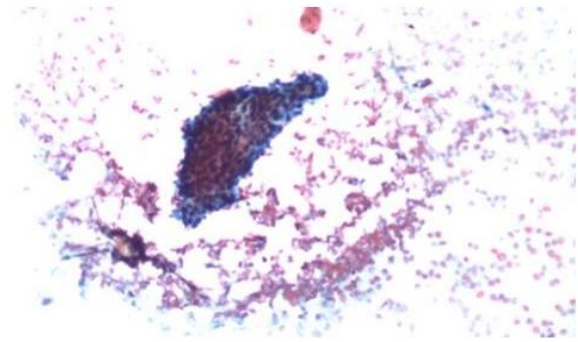

Figure 2: Lymph node biopsy with pap stain showing malignant cells.

however, they were unable to identify a primary tumor. Initial pregnancy test on admission was negative, b-HCG was rechecked and on hospital day 14 was mildly elevated to 33. The patient was refusing gynecological evaluation or a transvaginal ultrasound; however pelvic ultrasound revealed a distended endometrial cavity with heterogeneous contents and a complex left adnexal cyst. The patient went for an MRI pelvis that was remarkable for a large cervical mass (4.6x4.5x3.8 cm) extending superiorly to the lower uterine segment and inferiorly to the upper half of the vagina, which was highly suspicious for malignancy; findings suggestive of parametrial invasion. MRI of the liver showed multiple areas of hepatic infarctions. After thorough counseling the patient was agreeable to a vaginal exam that showed a Cervix with an 8cm firm, irregular tumor involving the right parametrium, left pelvic sidewall and upper 1cm of vagina. Following the latter two thoracenteses described above, final cytology was noted positive for malignant cells. At this point we were finally able to obtain prior outpatient records which showed those 4 years prior to presentation the patient had a Pap smear which showed LGSIL, however the patient had failed to follow up following the findings.

The patient's status rapidly declined at day 19. She was upgraded to the progressive care unit and subsequently to the medical ICU requiring intubation for hypoxic respiratory failure. On hospital day 23, as the patient’s disease continued to progress, the patient’s family decided that withdrawing care would be in the patient’s best interest and unfortunately the patient passed soon after. Autopsy confirmed the diagnosis of metastatic cervical cancer with signs of significant tumor burden as evidence of >80% of the liver with tumor.

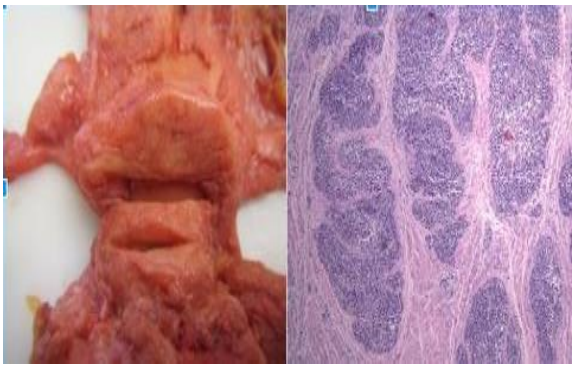

Figure 3: Autopsy of cervical mass and pathology showing

invasive squamous cell carcinoma of the cervix.

Figure 4: Autopsy of liver showing a liver which has been diffusely replaced with yellow-tan lesions of metastatic carcinoma.

Although the patient's Pap smear previously did not culture for HPV, the lymph node biopsy stained positive with Pap stain and provided information that the carcinoid cells were most likely affected by HPV

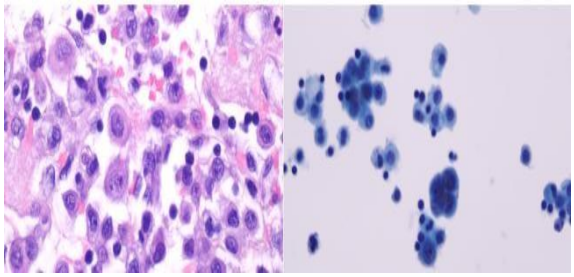

Figure 5: Cervical mass cell block and thin prep showing positivity for malignant cells.

5. Discussion

Cervical cancer was at one time a leading cause of cancer deaths in American women. However, due to significant advancements in screening, testing and noting high-risk human papillomavirus (HPV) as a causative agent, cervical cancer incidence and mortality over the last half century have profoundly decreased. Cervical Cancer is the fourth most common cancer in women worldwide, third most common cause of female cancer mortality [3]; it is estimated that in 2018, 13,240 new cases of invasive cervical cancer will be diagnosed, with 4170 deaths occurring in the United States alone [4]. Amongst cervical cancers, squamous cell carcinoma is also the most frequent type followed by a small percentage of adenocarcinoma.

HPV is central to the development of cervical neoplasia and can be detected in 99.7 percent of cervical cancers [5]. Most signs and symptoms suggestive of cervical cancer are non-specific and usually associated with other diseases. One of the most common symptoms is postcoital bleeding; however, reports show a wide range of 0.7% to 39% of Patients [6,7]. Typically viewed as a warning sign, about 6% to 10% of patients present with this primary symptom [8]. Increased blood-streaked vaginal discharge, intermenstrual pelvic pain and postmenopausal bleeding are also typical symptoms. Other symptoms on presentation can also include lymphedema in lower extremities (from lymphatic compression of locally invaded pelvic lymph nodes), pelvic pain if lymph nodes are involved and also backaches [9]. Most often, cervical cancer is asymptomatic until it becomes advanced. In our patient, the difficulties in making the diagnosis were seen from the point of the initial presentation. The history, physical exam and studies, although remarkable and indicating a systemic process, were nonspecific and made the diagnosis difficult. Our patient's presenting symptoms were more medically related and thus a gynecologic process was not initially considered. Conditions concerning pulmonary and cardiac disease were eliminated with a full medical work-up first due to her primary complaint of respiratory decline. The difficulties in diagnosis also arose with the process of waiting for laboratory analysis and pathological studies. Although the pleural effusion from the original thoracentesis did eventually show pathological atypical carcinoma cells, the second thoracentesis done because of reaccumulation was performed before the pathology had come back. Following as the second thoracentesis was evident of a chylothorax; our suspicions lied towards a lymphoma at that time. It was not until the pathology of the retroperitoneal biopsy and the elevated serum b-hCG did we search out a source in the gynecological system as the patient was young and had no complaints of gynecological importance initially.

An important finding in our patient that led us to a

gynecological disease process was the patient's elevated b-hCG. B-hCG is normally produced by the placenta and elevated b-hCG levels are most commonly associated with pregnancy. False-positive elevations occur in hypogonadal states, noted marijuana use and with multiple carcinomas, including endometrial cancer, choriocarcinoma, mixed cell tumors and dysgerminomas [9]. Although the elevation in b-hCG helped give the direction of the patients' case to a gynecological malignancy, the finding of cervical cancer was unexpected. There have been several studies which evaluated various tumor markers such as squamous cell carcinoma antigen (SCC), Ca 125 and Ca 15.3, however the evaluation of elevations of b-hCG are not well studied [9]. Hameed et al published a study which looked at the frequency of expression of b-hCG in squamous cell carcinoma of the cervix. Of 63 patients with poorly differentiated invasive squamous cell carcinoma of the cervix, 52% showed localization of b-hCG within the tumor cells [10]. In the patients with primary disease, the intracellular expression of b-hCG can also be a negative prognostic indicator as the 4-year survival was 14% in those with positive b-hCG immunostaining and 79% in those without [10]. Although there have been studies that have examined cervical cancer and the intracellular expression of b-hCG, literature reviews have not shown studies which have examined the serum levels of h-hCG in squamous cell carcinoma of the cervix.

6. Conclusion

Cervical Cancer is a common cause of a gynecological malignancy in women. As we could see in this case, screening is irreplaceable and invasive disease can be missed and be devastating in young women. As presentations of cervical cancer are well documented and studied, highly aggressive and wide spread disease may not be as straightforward. For women with presentations concerning for malignancy, gynecological disease should be ruled out as it may present atypically. Testing for cancer emitting hormones, such as b-hCG, may be helpful in uncovering underlying pathologic disease processes that are masked by their sequelae of disease as seen in our patient.

Although b-hCG is usually released by gestational trophoblastic diseases and germ cell tumors, advanced, undifferentiated, carcinomas may also produce the tumor marker and low levels may point to cancers of less common sources.

7. Author's Contribution

Sonia Randhawa: Made substantial contributions to conception, significant in literature search, formation of discussion and conclusion of this case report.

Erika Correa: Involved primarily in-patient care and made contributions to the formation of this case report.

Ekamjeet Randhawa: Made substantial contributions to acquisition, analysis and interpretation of data, primarily formed patient case presentation and was primary physician involved in patients care. Author is also accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Written Permission and consent were obtained from the patient for this case report.

References

1. Hoffman, Barbara. Cervical Cancer. Williams Gynecology, 3rd ed. 2016; New York, NY: McGraw Hill. 657-678.
2. Cecelia H Boardman. Cervical Cancer Clinical Presentation. Medscape. Obstetrics & Gynecology. 2018.
3. Barbera L, Thomas G. Management of early and locally advanced cervical cancer. Semin Oncol. 2009; 36: 155-169.
4. American Cancer Society. Key Statistics for Cervical Cancer. 2018.
5. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, et al. Human

papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol. 1999; 189: 12.

6. Petignat P, Roy M. Diagnosis and management of cervical cancer. BMJ. 2007; 335: 765-768.

7. Clare L Newton, Timothy A Mould. Invasive Cervical Cancer. Obstetrics, Gynaecology and Reproductive Medicine. 2017; 27: 7-13.

8. Fazal Hussain. Gynecologic Tumor Markers Tumor Marker Overview. Medscape. 2018.

9. G Scambia, P Benedetti-Panici, E Foti, G Ferrandina, F Leone, M Marciano, et al. Multiple tumour marker assays in advanced cervical cancer: Relationship to chemotherapy response and clinical outcome. Eur J Cancer. 1996; 32: 259-263.

10. Crawford R, Iles R, Carter P, Caldwell C, Shepherd J, Chard T. The prognostic significance of â human chorionic gonadotrophin and its metabolites in women with cervical carcinoma. J Clin Pathol 1998; 51: 685-688.

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