# Primary serous papillary carcinoma arising from the omentum with metastasis to the parametrium and bilateral ovarian and fallopian tube serosal surface: A case report*

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## Abstract

***Introduction*** Primary peritoneal serous carcinoma is a rare, malignant, epithelial tumor arising from the peritoneum and associated tissues, that presents commonly with diffuse peritoneal involvement and ascites. Carcinomas that morphologically resemble papillary serous carcinoma of the ovary, with uninvolved or minimally involved ovaries, with the lesion of the peritoneum larger than other primary ovarian lesions, and with no other identifiable primary tumor, are categorized under such. The aim of this report is to contribute to the fund of knowledge pertinent to this rare lesion with a relatively poor prognosis.

***Case Summary*** This report describes a case of primary carcinoma of the omentum with papillary configuration in a 53-year-old woman who presented with abdominal distention. She had no prior surgical procedure other than bilateral tubal ligation. Immunohistochemistry studies support the diagnosis and Ki67 index and p53 expression complements the high-grade morphology. The immunohistochemistry of the tumor is compared with the immunohistochemistry of other reported cases.

***Conclusion*** This report contributes to the fund of knowledge of the clinical presentation, morphologic findings, and immunohistochemistry profile pertinent to this rare lesion for better understanding, leading to prompt diagnosis and improved quality of care.

***Key words***: Primary peritoneal serous carcinoma, omentum, serous carcinoma, malignant serous neoplasm

Primary serous carcinoma of the peritoneum is a rare malignancy with an incidence of 6.78 cases per 1,000,000 individuals, presenting commonly with diffuse peritoneal involvement and ascites.[1,2] First described by Swerdlow in 1959 as mesothelioma of the pelvic peritoneum, diagnosis of this entity is made for tumors that are histologically similar to serous carcinomas of the ovary, and requires that the presence of another primary tumor be excluded. Although this tumor's clinical behavior, histologic appearance, and treatment are similar to serous ovarian cancer stage III, evidence indicating a worse prognosis for the primary peritoneal lesion with a median survival rate of 12-25 months has been reported, making proper differentiation of the tumor with the ovarian counterpart is necessary.[3]

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## The Case

The patient is a 53-year-old woman who experienced increasing abdominal girth associated with a feeling of distention, easy fatigability, decrease in appetite, and weight loss of one month. Her only surgical procedure was a bilateral tubal ligation 28 years prior. Imaging studies showed a pelvo-abdominal mass with omental involvement that was interpreted as an ovarian carcinoma with omental metastases. The initial serum CA-125 was 487 u/mL preoperatively. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and omentectomy.

*Gross findings* (Figure 1)

The gross specimen was received in 10% phosphate buffered formaldehyde and consisted of the uterus, cervix, right and left ovaries, remnants of the right and left fallopian tubes, and the omentum. Dark brown to cream white, nodular to irregular, firm to hard masses replaced approximately 95% of the yellow fibrofatty tissues of the omentum. Several gray, thin-walled cysts measuring 0.5cm - 1cm in greatest dimension were also seen on the surface. Cut sections showed a cream white to tan-red, soft to firm surface with areas of necrosis. The masses were nodular infiltrates even within the yellow, fibrofatty tissues that appeared to be uninvolved on the external surface.

The entire uterus measured 4cm x 3.2cm x 2cm. The cervix was light-tan to cream, with no lesions or areas of hemorrhage. The anterior myometrium measured 1.5cm in thickness, and the posterior myometrium was 1.7cm thick. The outer surface of the uterus showed a tan to dark brown outer surface with several small, cream white to dark brown nodules noted to be adherent to the serosal surface.

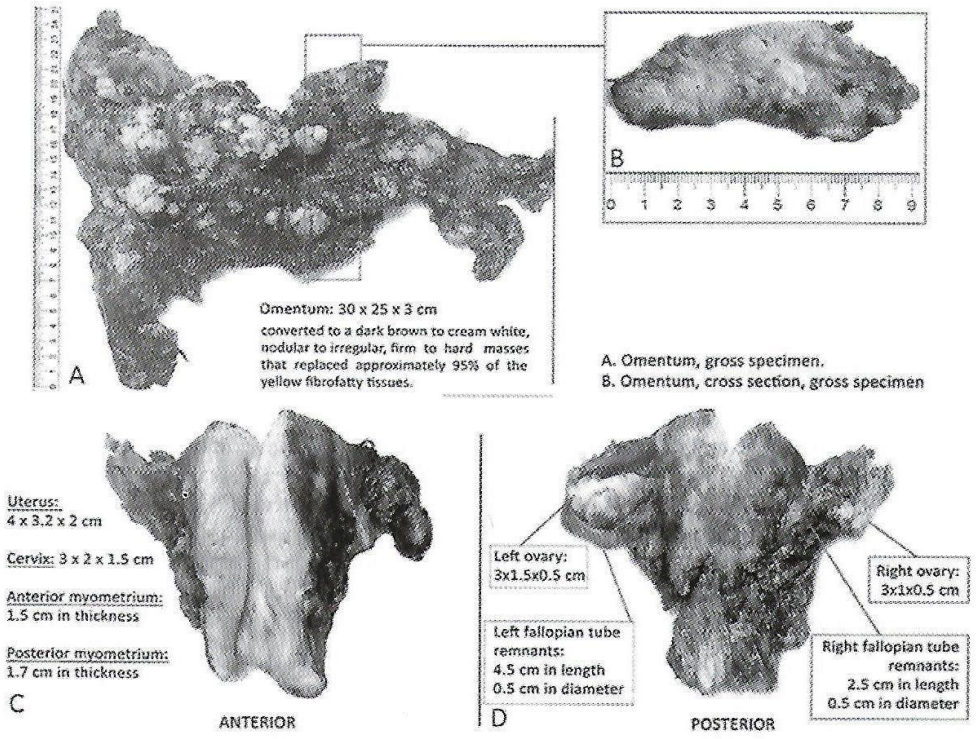


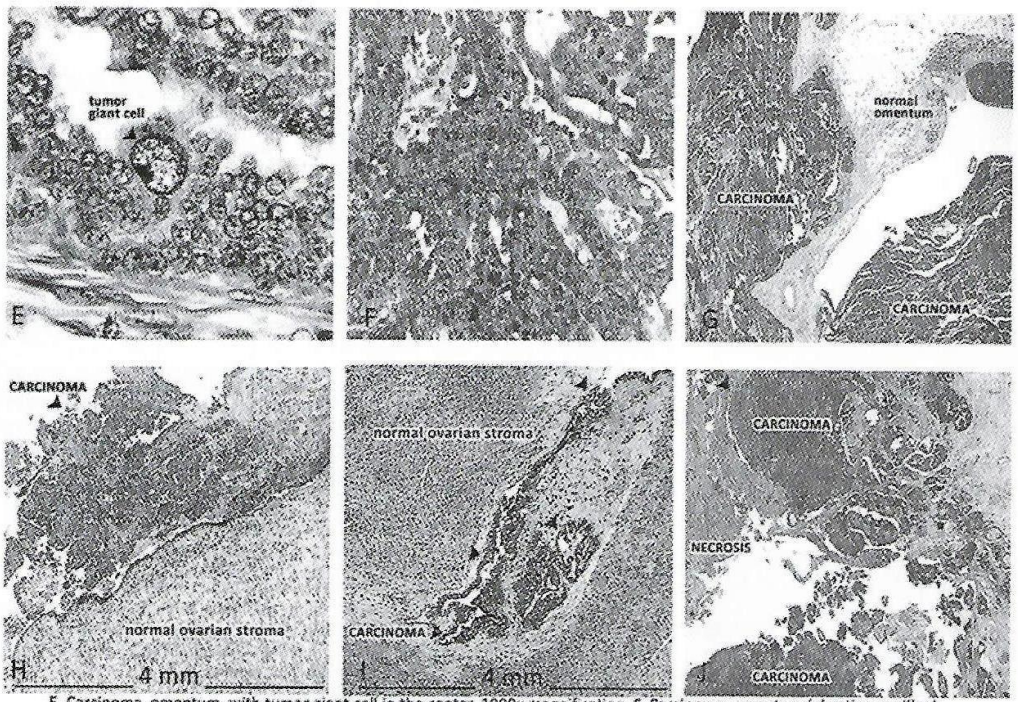

**Figure 1.** Gross specimen findings of the omentum (A & B), uterus, cervix, right and left fallopian tubes, and right and left ovaries (C & D).

The cut surface of the uterus and cervix showed no evidence of tumor involvement. The right and left ovaries were cream white, firm, and fibrous, and measured 3cm x 1 x 0.5cm and 3cm x 1.5cm x 0.5cm, respectively. Cut sections of both ovaries showed a homogenous, cream white, firm, fibrous surface, with no areas of gross hemorrhage. Several cream white nodules were noted in the outer surface with no gross extension observed within the ovarian stroma. The right and left fallopian tube remnants showed fibromuscular, elongated tissues adherent to the parametrium, and measured 2.5cm long, and 0.5cm in greatest diameter and 0.5cm long and 0.5cm in greatest diameter, respectively. The normal architecture of the right and left fallopian tube remnants could not be clearly delineated with several cream-white to tan brown, nodular to irregular, bosselated tissues adherent to the right and left paratubal tissues. Several nodules were also seen to be adherent to the parametrium.

*Microscopic Findings* (Figure 2)

Histologic sections of the omentum showed a tumor composed of malignant cells arranged in tubulo-papillary fronds with a fibrovascular core and solid nests with pseudolumen. The cells were ovoid to low cuboidal, with ovoid to pleomorphic large nuclei, coarse to open chromatin pattern, conspicuous to prominent nucleoli, and moderate to scanty basophilic cytoplasm. The lesion was a fungating and infiltrating mass replacing the fibrofatty omental tissues.

The tumor was adherent to the serosal surfaces of the right and left ovaries, remnants of the right and left fallopian tubes, and the parametrial tissues with confluence of the tumor in the lateral thickening of the serosal tissues. The surface of the right and left ovaries exhibited microscopic nodules 3-4 mm in diameter seen on the external surface of the right ovary and encroaching 4 mm into the stroma from




E. Carcinoma, omentum, with tumor giant cell in the center, 1000x magnification. F. Carcinoma, omentum (abortive papillae), 100x magnification. G. Carcinoma with remnants of normal omentum, 40x magnification. H, I. Metastasis to the ovarian serosal surface, right and left ovaries, 40x magnification. J. Metastasis to the paratubal soft tissues, right, 40x magnification.

**Figure 2.** E-J Microscopic specimen findings of the omentum, parametrium, right and left paratubal serosal surface, and right and left ovarian serosal surface.

the outer surface of the left ovary. Majority of the remaining stroma showed benign tissues with corpora albicantia. The remnants of the right and left fallopian tubes exhibited proliferation of the tumor cells on the paratubal soft tissues, and several islands of tumor cells in the associated lymphatic and vascular channels in the outer portion of the fibromuscular layer. The right and left parametrial tissues showed foci of conglomerations of malignant cells arranged as patchy clusters in the serosa and into the adherent outer muscular layer. Sections from the uterus and cervix did not show any tumor involvement.

*Immunohistochemistry Studies* (Figure 3)

Immunohistochemistry studies showed diffuse, strong, positive expression for WT1 (nuclear), CA125 (membrane), and EMA (membrane). There was focal expression of ER (nuclear), and CK 5/6 (cytoplasm). There was absent expression of calretinin in the malignant cells; positive expression was noted only in the remnants of the benign mesothelial lining. Ki67 and p53 showed nuclear expression in more than 90% and more than 80% of tumor cells, respectively.

*Follow-up and Outcomes*

The patient underwent chemotherapy that covered the lesions involving the ovaries, the parametrium, and the omentum. Subsequent serum CA-125 decreased to 5.80 u/mL six months post-operatively, but slowly increased to 5.80, 6.97 and 13.0 u/mL at 10, 11 and 14 months postoperatively, respectively. Since the submission of the surgical specimen for evaluation and definitive diagnosis, there has been no new specimen submitted for histopathologic evaluation that may correspond to a tumor recurrence or metastasis.

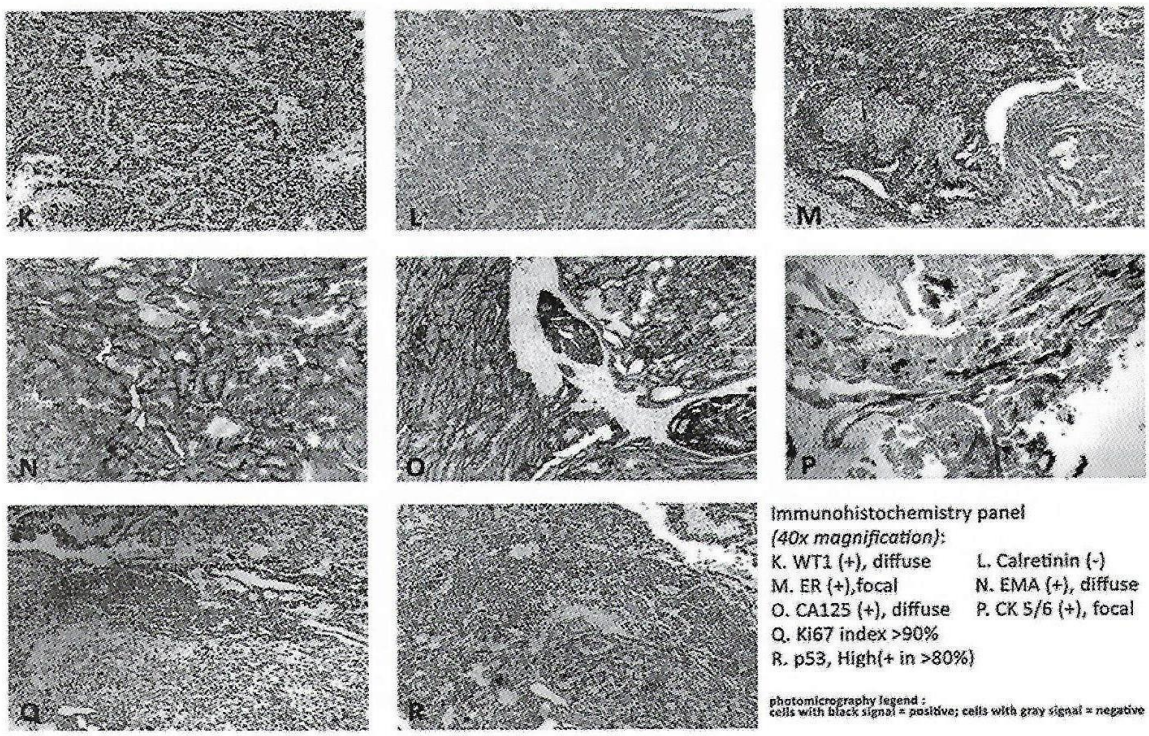



**Figure 3.** Immunohistochemistry panel findings (K to P)

## Discussion

The diagnosis of primary serous papillary carcinoma in this case was established through the step-wise approach of gross and microscopic evaluation with respect to the adaptation of the Gynecologic Oncology Group Guidelines of the College of American Pathology in 2015 for Peritoneal Tumors, and strengthened by the immunohistochemistry profile (Table 1).

In this patient, all the criteria for a primary serous lesion of the peritoneum were fulfilled, with the omentum identified as the site of tumor origin.[3] The immunohistochemistry findings established the difference between the lesion in this case, and malignant mesothelioma, which must be ruled out when evaluating a primary peritoneal lesion. The diagnosis of a serous carcinoma of ovarian primary is also not supported by the immunohistochemistry profile of a focal ER expression in this case, since serous carcinomas from the ovary would more likely have a strong, diffuse positive expression of ER and not a focal expression. The high p53 expression in tumor cells has been used as a surrogate marker for TP53 mutation in high-grade serous carcinoma, as in this case with the p53 expression seen in more than 80% of tumor cells.

Comparison of this case with the twelve published reports discussing the immunohistochemistry profile used after initial morphologic diagnosis and fulfilling the criteria for a primary peritoneal lesion showed that the most commonly utilized stains to characterize the tumor are ER and WT, which are both expressed in this case. Calretinin is consistently negative in serous carcinoma. Although CK 5/6 is commonly negative, focal positive expression of CK 5/6 has been documented in serous carcinoma, as seen in this case, and is differentiated from the diffuse positive expression of CK 5/6 which is seen in malignant mesothelioma (Table 2).[4,5,6-18]

Since the pathogenesis of ovarian serous carcinoma has been greatly studied and the diagnosis of peritoneal serous carcinoma stipulates that it should be similar or identical to those of ovarian serous carcinoma of any grade, it may be postulated that the high-grade serous carcinomas of the peritoneum originate from seeding of tubal epithelium that underwent transformation into a carcinoma, with similar if not identical mutations to those that occur in the ovary, particularly for TP53. Although this should require sequencing of the TP53 of the tumor cells, immunostaining of the p53 has been used as a surrogate marker for TP53 in high-

**Table 1.** Application of the Gynecologic Oncology Group guidelines

Application of the GOG Criteria for Primary Serous Carcinoma to the Gross and Histologic Findings

| Gynecologic Oncology Group (GOG)) Criteria for the Diagnosis of Primary Serous Carcinoma of the Peritoneum Adapted by the Protocol for the Examination of Specimen From Patients with Tumors of the Peritoneum, College of American Pathologists 2015 : | CASE |
|---|---|
| Both ovaries are either normal in size or enlarged by a benign process | + |
| The bulk of the tumor involves the peritoneum, or the extent of tumor involvement at 1 or more extraovarian sites is greater than that on the surface of or within either ovary | + |
| Microscopic examination of the ovaries reveals any of the following: | |
| (a) no tumor | |
| (b) tumor confined to the surface epithelium, with no evidence of cortical invasion | |
| (c) tumor involving the ovarian surface and the underlying cortical stroma, but less than 5 x 5 mm in diameter | + |
| (d) tumor less than 5 x 5 mm within the ovarian substance, with or without surface involvement | |
| The histologic and cytologic characteristics of the tumor are predominantly serous and similar or identical to those of ovarian serous papillary carcinoma of any grade. | + |
| If an oophorectomy has been performed in the past, a confident diagnosis of primary peritoneal serous carcinoma requires 1 of the following:<br>(a) a pathology report to document the absence of carcinoma in the ovarian specimen, with review of all the slides if the oophorectomy has been performed within 5 years of the current procedure<br>(b) if the oophorectomy has been performed more than 5 years before the current procedure, the pathology report of the specimen should be obtained, and the slides should be reviewed if still available. The peritoneal tumor should be interpreted in light of the ovarian findings. | NO HISTORY OF PRIOR OOPHORECTOMY |

**Table 2.** Comparison of the Immunohistochemistry Panel findings.

Comparison of IHC Characteristics of Ovarian and Peritoneal Serous Carcinomas with the Case

| IHC | Immunoreactivity Patterns of Serous Carcinoma ( Adapted from S Nofech-Mozes et al. 2008 [14]) | | IHC PATTERN OF THE CASE |
|---|---|---|---|
| | Ovary | Peritoneum | |
| WT1 | Strong, diffuse | **Strong, diffuse** to weak, focal | **Strong, diffuse** |
| P53 | More commonly Strong, diffuse | **Strong, diffuse** | **Strong, diffuse** |
| ER | More commonly strong, diffuse | More commonly weak, focal to **moderate, focal;** may be absent | **Moderate, focal** |
| CK 5/6 | More commonly absent | More commonly absent | Moderate, focal |

Comparison of IHC Characteristics of Malignant Mesothelioma and Serous Carcinomas with the Case

| IHC | Immunoreactivity Patterns of Malignant Mesothelioma Vs High Grade Serous Carcinoma (Ordoñez 2006) | | IHC PATTERN OF THE CASE |
|---|---|---|---|
| | Malignant Mesothelioma | High Grade Serous Carcinoma | |
| Calretinin | Strong, diffuse | **Absent** | **Absent** |
| CK 5/6 | Strong, diffuse | **Moderate, focal** | **Moderate, focal** |
| CA-125 | Strong, diffuse | Strong, diffuse | Strong, diffuse |
| EMA | Strong, diffuse | Strong, diffuse | Strong, diffuse |

grade serous ovarian carcinoma and may be applied to the peritoneal counterpart as well.[14,19]

The diagnosis of primary serous papillary carcinoma was established through the stepwise approach of gross and microscopic evaluation with respect to the adoption of the Gynecologic Oncology Group Guidelines of the College of American Pathology in 2015 for Peritoneal Tumors, and strengthened by the immunohistochemistry profile. This report contributes to the fund of knowledge of the clinical presentation, morphologic findings, and immunohistochemistry profile pertinent to this rare lesion for better understanding, leading to prompt diagnosis and improved quality of care.

## Informed Consent

The authors did not perform any procedure on the patient. This case report included only the specimen submitted by the attending physician to the Section of Anatomic Pathology for surgical histopathology evaluation with full, informed consent for specimen evaluation and academic discussion.

### References


1. Goodman MT, Shvetsov YB. Incidence of ovarian, peritoneal and fallopian tube carcinomas in the United States, 1995-2004. Cancer Epidemiol Biomarkers Prev 2009; 18: 132-9.
2. Bhuyan P, Mahapatra S, Mahapatra S, Sethy S, Parida P, Satpathy S. Extraovarian primary peritoneal papillary serous carcinoma. Arch Gynecol Obstet 2010; 281: 561-4.
3. Gwin K, Branton P, Nucci M, Oliva E, Cooper K. Protocol for the examination of specimens from patients with tumors of the peritoneum. Available from: http://www.cap.org/ShowProperty?nodePath=/UCMCon/Contribution%20Folders/WebContent/pdf/peritoneum-15protocol-3201.pdf. [Accessed Oct 29, 2016].
4. Alvarez JV, Gomez MM, Prats MDG, Agorreta JMRC, López JIL, Goyanes JPR. Extraovarian primary peritoneal carcinoma: A case report. Rev Esp Patol 2007; 40(1): 47-52.
5. Bhanvadia VM, Parmar JK, Madan YG, Sheikh SS. Primary peritoneal serous carcinoma: a rare case and palliative approach. Indian J Palliative Care 2014. Available from: http://www.jpalliativecare.com. [Accessed Oct 29, 2016].
6. Heda K, Indushekar V, Pachori G, Sharma A. Primary peritoneal serous carcinoma: A diagnostic dilemma of pelvic epithelial neoplasms. Clin Cancer Investig J 2015; 4: 551-4.
7. Hou T, Liang D, He J, Chen X, Zhang Y. Primary peritoneal serous carcinoma: A clinicopathological and immunohistochemical study of six cases. Int J Clin Exp Pathol 2012; 5(8): 762-9.
8. Hutton RL, Dalton SR. Primary peritoneal serous borderline tumors. Arch Pathol Lab Med 2007; 131(1): 138-44.
9. Kim JW, Lee HS, Shin KS, Gam YH, Baik KD. Primary peritoneal serous papillary carcinoma presenting as a large mesenteric mass mistaken for ovarian cancer: A case of primary peritoneal carcinoma. Obstet Gynecol Sci 2015; 58(3): 246-50.
10. Sun JY, Gebre W, Dong YM, Shaun X, Robbins R, Podrumar A. Primary peritoneal carcinoma metastasizing to breast: a single case report and literature review from clinic to biology. Cancer Biol Med 2016; 13(3): 389-95.

11. Liu Q, Lin JX, Shi QL, Wu B, Ma HH, Sun GQ. Primary peritoneal serous papillary carcinoma: A clinical and pathological study. Pathol Oncol Res 2011; 17(3): 713-9.
12. Lockyer MG, Deavers MT, Zarrin-Khameh N. Concurrent primary peritoneal low-grade serous carcinoma and endometrial high-grade serous carcinoma. Int J Gynecol Pathol 2015; 34(3): 288-92.
13. Nofech-Mozes S, Khalifa MA, Ismiil N, Saad RS, Hanna WM, Covens A, Ghorab Z. Immunophenotyping of serous carcinoma of the female genital tract. Mod Pathol 2008; 21(9): 1147-55. DOI: 10.1038/modpathol.2008.108.
14. Pollock C, Maddula M, McAleer B. Peritoneal mesothelioma - a case report. Respir Med CME 2009; 2: 80-3.
15. Sehgal S, Agarwal R, Goyal P, Singh S, Kumar V, Gupta R. Primary serous carcinoma of peritoneum: A case report. Int J Case Reports Images 2012; 3(10): 16-20.
16. Von Riedenauer WB, Janjua SA, Kwon DS, Zhang Z, Velanovich V. Immunohistochemical identification of primary peritoneal serous cystadenocarcinoma mimicking advanced colorectal carcinoma: A case report. J Med Case Rep 2007; 1: 150.
17. Yun WS, Bae JM. Primary peritoneal serous carcinoma, an extremely rare malignancy: A case report and review of the literature. Oncol Lett 2016; 11(6): 4063-5.
18. Tai YJ, Lin MC, Wu CJ, Chen CA, Cheng WF. Solitary primary peritoneal carcinoma arising from the omentum. Taiwan J Obstet Gynecol 2014; 53(2): 256-9.
19. Cole AJ, Dwight T, Gill AJ, et al. Assessing mutant p53 in primary high-grade serous ovarian cancer using immunohistochemistry and massively parallel sequencing. DOI: 10.1038/srep26191 www.nature.com/scientificreports/. [Accessed Oct 30, 2016].