Int J Clin Exp Med 2016;9(8):16325-16331
www.ijcem.com /ISSN:1940-5901/IJCEM0021906

Original Article

Small cell neuroendocrine carcinoma of the uterine cervix: clinicopathological analysis and outcome of 26 cases

Li Chen[1], En Feng Zhao[1], Lei Song[1], Zhi Gang Song[2], Wei Ping Li[1], Yuan Qing Yao[1]

[1]*Department of Obstetrics and Gynecology, Chinese PLA General Hospital, Beijing, China;* [2]*Department of Pathology, Chinese PLA General Hospital, Beijing, China*

Received December 14, 2015; Accepted May 19, 2016; Epub August 15, 2016; Published August 30, 2016

Abstract: To reveal the clinicopathological data and prognostic outcome of 26 cases of small cell neuroendocrine carcinoma of the uterine cervix (SNCUC). In 2004-2014, the cases were retrospective reviewed and clinicopathological data were collected. Survivals were analyzed with Kaplan-Meier methods by SPSS 19.0. The median age of the patients was 42 years. Twenty-one cases (80.8%) were diagnosed as being early stage carcinoma (International Federation of Gynecology and Obstetrics stage I-IIa). Eight cases (30.8%) underwent neoadjuvant chemotherapy (NACT) before surgery. All patients received radical surgery that was followed by adjuvant therapy. The median overall survival period (OS) of all cases was 19.3 months and the median disease-free survival (DFS) time was 16.6 months. SNCUC is rare in female genital tract cancer. Lymph node metastasis and lymphovascular space invasion (LVSI) might occur in the early stage. Cases without parametrial involvement (PM) have better survivals periods than those with PM. Multimodality therapeutic methods could promote a patient outcome of suffering from SNCUC of the uterine cervix.

Keywords: Small cell neuroendocrine carcinoma, uterine cervix, treatment, prognosis, multimodality

Introduction

Cervical malignant tumor is one of the most common carcinomas in the female genital tract seriously endangers female health. Squamous cervical carcinoma (SCC) is the most frequent pathological type followed by adenocarcinoma of the cervix (ACC). SNCUC is very rare and it occurred less than 1% of all cervical cancers [1-3]. Characteristics of SNCUC such as early metastasis, lymph node involvement and lymph-vascular space invasion (LVSI) lead its survival rate less than SCC and ACC [4]. Because of the rarity and high mortality of the disease this study was undertaken to collect and analyze the clinicopathological character and summarize the experience in the management of SNCUC.

Materials and methods

Between January, 2004, and December, 2014, 26 cases of SNCUC were diagnosed and treated in our institution. We reviewed the general information and clinicopathological features of these cases. Every case was diagnosed by two experienced pathologists based of morphology and immunohistochemical (IHC) staining for at least one specific antibody such as synaptophysin, chromogranin A, Ki-67 and CD56. The International Federation of Gynecology and Obstetrics (FIGO) clinical staging criteria for cervical cancer were used in the assessment. Survival analysis of data was undertaken by the Kaplan-Meier method and the survival rate was compared by log-rank test. The Cox proportional hazards model was used to define negative prognostic indicators of clinical and pathological characteristics such as stage, lymph node metastasis, mass size, depth of stromal invasion, lymph vascular space invasion and treatment modalities with SPSS 19.0 (IBM, Armonk, NY, USA). A value of $P<0.05$ was considered to be a significant statistical difference.

Table 1. Clinicopathological character of the study (n=26)

Median age	42 years (range 15-76)
FIGO stage	
IB1	14 (53.8%)
IB2	3 (11.5%)
IIA	4 (15.4%)
IIB	4 (15.4%)
IIIB	1 (3.8%)
IHC marker	Positive/review numbers
Ki-67 (index ≥75%)	16/23 (61.5%)
chromogranin A	9/16 (56.2%)
CD56	15/20 (75%)
synaptophysin	20/24 (83.3%)
Therapeutic method	
NACT	8 (30.8%)
Adjuvant chemotherapy	24 (92.3%)
Adjuvant radiotherapy	15 (57.7%)
Recurrence	8 (30.8%)
Early stage	5 (19.2%)
Advanced stage	3 (11.5%)
Death of disease	9 (34.6%)
Early stage	5 (19.2%)
Advanced stage	4 (15.4%)

Results

The median age of the 26 patients was 42 years (range 15-76 years) (**Table 1**). 5 (19.2%) of the patients were menopausal. Prior to diagnosis, 24 (92%) patients had symptoms. These included 22 cases (84.6%) of abnormal vaginal bleeding and 2 cases (7.7%) of abnormal leucorrhea. Another 2 patients (7.7%) had no symptoms and were detected during the health examination. 14 cases (53.8%) were diagnosed as International Federation of Gynecology and Obstetrics (FIGO) stage IB1, 3 cases (11.5%) were IB2, 4 cases (15.4%) were IIA, 4 cases (15.4%) were IIB (one case was actually stage IV because metastasis was found at omentum majus during the operation), 1 case (3.8%) was IIIB. SCC antigen, which was the most important cervical tumor marker, was detected in 14 cases. The median value was 0.65 μg/L (range 0.2-1.3 μg/L).

All cases had biopsy before diagnosis. 8 (30.8%) patients underwent NACT before surgery. The principles in using NACT were large tumor size and advanced stage (IIB-IV). The regimes included paclitaxel plus carboplatin (37.5%, TC), paclitaxel plus cisplatin (25%, PT), cisplatin plus mitomycin and vincristine (25%, PMV) and cisplatin plus tegaur (12.5%). The median cycle of NACT was 1 (range 1-4). Finally all patients received surgery. Of whom eight (30.8%) were performed with radical hysterectomy (RH) and bilateral salpingo- oophorotomy (BSO) plus pelvic lymphadenectomy (PLE). Twelve (46.2%) had RH plus PLE. Three (11.5%) had RH plus PLE + para-aortic lymphadenectomy (PALE). One (3.8%) had RH and BSO plus PLE + PALE. The other two (7.7%) (IIB and IIIB) were undertaken RH and BSO plus PLE + focal lesion clearance. After surgery the specimens were stained by HE and IHC, then diagnosed by a pathologist and reviewed by another experienced pathologist. Nine (34.6%) cases were purely SNCUC, six (23.1%) had an adenocarcinoma component and eleven (42.3%) had a squamous carcinoma component. IHC showed a positive rate of chromogranin A (9/16), synaptophysin (20/24), Ki-67 (index ≥75%, 16/23) and CD56 (15/20). In the post-operative histopathologic examination 12 (46.2%) cases had positive pelvic lymph nodes. In which 7 (58.3%) were early stage and 5 (41.7%) were late stage. LVSI was seen in 14 cases (53.8%) in which 11 (78.6%) early stage patients occurred. Except one case that had accepted LEEP before surgery, 18 (72%) cases had a depth of cervical stromal invasion of more than 50%. Two (7.7%) cases had parametrial involvement. In one of which, metastases in part of the omentum majus, ovarian and rectum were detected. Part of ileum and sigmoid flexure was involved in another. A large size tumor (≥ 4 cm) was seen in 10 (38.5%) cases. All of the cases had a negative resection margin of the vagina.

After operation, 24 (92.3%) cases accepted adjuvant chemotherapy (CT) and 15 (57.7%) accepted adjuvant concurrent chemoradiotherapy (CCRT). The CT protocol included PT in 8 (30.8%) cases, TC in 9 (34.6%) cases, PMV in 3 (11.5%) cases, cisplatin plus cyclophosphamide (PC) in 1 (4%) case and PMV followed by TC in 3 (11.5%) cases. The median cycles of adjuvant CT were 2 (range 0-6).

The median follow-up time was 19.6 months (range 6.2-120.6 months) until July 31, 2015. After treatment 24 (92.3%) cases experienced complete remission (CR) of the disease and 2

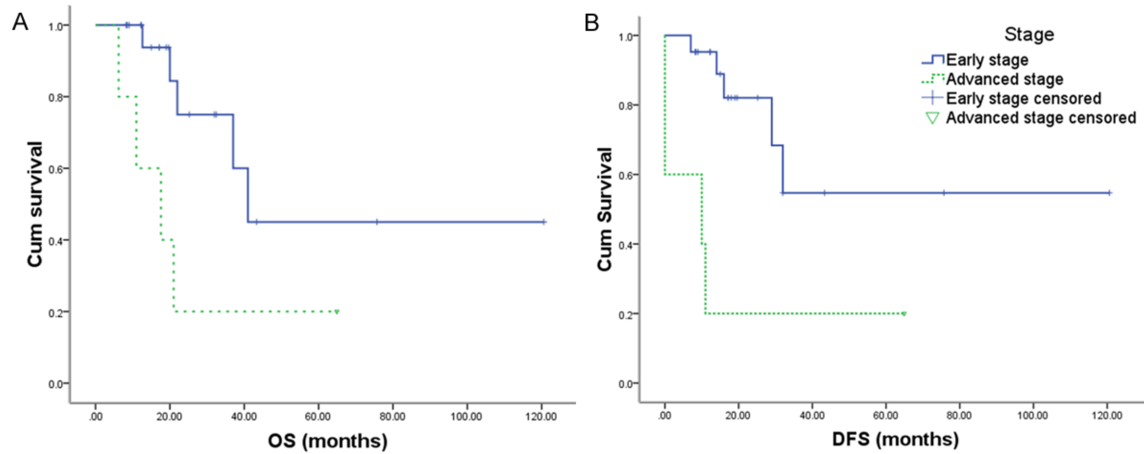

Figure 1. OS (A) and DFS (B) outcomes according to disease stage. The OS was different (41 vs. 17.6 months, P = 0.030) and the DFS was also different (not reached vs. 10.0 months, P = 0.006) between early-stage and advanced-stage SNCUC patients, respectively.

Table 2. Univariate and multivariate analysis of OS based on clinicopathological factors

	Univariate analysis	Multivariate analysis		
	P	P	HR	95% CI
Stage (IIb-IV)	0.030[a]	0.407		
Age	0.568	0.203		
PM	0.001[a]	0.003[a]	14.555	2.414-87.769
HP	0.111	0.373		
LN	0.108	0.223		
LVSI	0.051	0.061		
Size	0.269	0.328		
DOI	0.669	0.461		
RT	0.151	0.058		

PM = Parametrial involvement, HP = histopathologic type, LN = lymph node metastasis, DOI = depth of invasion, LVSI = lymph vascular space invasion, RT=radiotherapy. [a]Statistically significant difference.

(7.7%) cases experienced progression disease (PD). Eight (33.3%) had a recurrence of the disease. Three patients relapsed in first and second years respectively after surgery. Another 2 had recurrence within third years. Nine (34.6%) patients died of disease before the end of the follow-up period. Of whom 5 (19.2%) were early stage (I-IIA) patients. Among these five cases one suffered recurrence in the pelvic and bone and died at 12.6 months post-operation. Two cases relapsed in the liver and died at 20 and 22 months respectively after surgery. One case died at 15 months after initial treatment with recurrence in the lungs. One case had relapse in the pelvic and abdominal soft tissue and died at 37 months after initial treatment. Four advanced-stage cases died of disease at 6, 11, 17 and 20 months respectively after surgery. The median OS of all patients was 19.3 months (range 6.2-120.6 months)–. The median DFS was 16.6 months (range 0-120.6 months).

When all cases were divided into two groups based on FIGO stage as early stage (I-IIa) and later stage (IIb-IV), the median OS of the early stage group and the advanced group were 41 months (95% CI 31.5-50.5 months) and 17.6 months (95% CI 3.4-31.8 months) respectively, the median DFS were not reached and 10 months (95% CI 0-31.5 months) (**Figure 1**). In univariate analysis there was a significant statistic difference between the two groups (P_{os}=0.03, P_{DFS}=0.006) but there was an opposite result in multivariate analysis (P_{os}=0.407, P_{DFS}=0.547) (**Tables 2** and **3**). Despite of the difference this suggested FIGO stage might be a prognostic factor indicate early stage patients had a better outcome than advanced ones. In addition we found that the median DFS of cases with or without lymph node involvement were 29 months and not reached respectively. There was difference between the two groups in univariate analysis (P=0.031) but failed to obtain the similar result in multivariate analysis (P=0.193). Parametrial involvement was an unfavorable prognostic factor for OS (P=0.003, HR=14.555, **Table 2**;

Table 3. Univariate and multivariate analysis of DFS based on clinicopathological factors

	Univariate analysis	Multivariate analysis		
	P	P	HR	95% CI
Stage	0.006[a]	0.547		
Age	0.352	0.265		
PM	0.000[a]	0.003[a]	15.258	2.493-93.401
HP	0.079	0.627		
LN	0.031[a]	0.193		
LVSI	0.066	0.125		
Size	0.308	0.699		
DOI	0.469	0.938		
RT	0.193	0.103		

[a]Statistically significant difference.

Figure 2) and DFS (P=0.000, HR=15.258, **Table 3**; **Figure 2**). We also analyzed age at diagnosis (< 50 years vs. > 50 years), tumor size (< 4 cm vs. ≥ 4 cm), depth of stromal invasion (< 1/2 vs. ≥ 1/2), LVSI, histopathologic type (pure vs. mix) and adjuvant radiotherapy (RT), but unfortunately it seemed that there was no association between these factors and survival outcome.

Discussion

Small cell neuroendocrine carcinoma occurs in different organs and tissues such as lung, digestive tract, breast and female tract. In female tract carcinoma it is rare and occurs mostly in the uterine cervix. Chen reported the incidence of SNCUC was 0.06 per 100,000 women. At the same time SCC was 6.6 and ACC was 1.2 respectively [2]. SNCUC makes up 0.68%-0.8% of all cervical cancer [1, 3]. The pathogenesis of SNCUC is undefined. HPV infection, especially HPV-18, perhaps is related to SNCUC. Wang reported 17 of 31 cases were HPV-18 positive and 1 case was HPV-16 positive [5]. Abeler showed in 25 cases 40% involved HPV18 and 28% involved HPV16 [6]. One study revealed TP53 gene mutations in SNCUC cases [7]. Other abnormal genetic types that could induce SNCUC included Rb [8], p21Cip1/Waf1 and p27Kip1 [9].

The symptoms of SNCUC are nonspecific and consist of abnormal vaginal bleeding or leucorrhea, hypogastralgia, abdominal mass and so on. So the biopsy, especially that led by the colposcope, was important in helping the clinical diagnosis. In our research 17 (65.4%) cases were diagnosed as SNCUC before surgery with biopsy specimens. The other 9 (34.6%) cases were diagnosed as poorly or moderately differentiated ACC (19.2%) and SCC (15.4%). This might be caused by little size of biopsy specimen. In histopathologic diagnosis morphology of the tissue is important. Though IHC staining was not recommended by WHO [10] it is commonly used in the clinic. The most commonly used markers included synaptophysin, chromogranin A, neuron-specific enolase, Ki67 and CD56. But neuron-specific enolase sometimes has non-specific staining [11]. So it was considered synaptophysin, chromogranin A and Ki67 the most appropriate markers to help diagnosis [12]. In our study the above markers all had more than 50% positive staining rate. We also found some cases exhibited a typical morphology character, but negative IHC staining.

The SNCUC is thought to have the characteristic of high aggression and poor prognosis. The 5-year survival is 14-39% [13-16]. However SCC and ACC were 60.5% and 69.7% respectively [2]. Lee reported the median OS of early stage patients (I-IIA) and advanced patients were 40.7 months and 21.4 months respectively. The median time to progression was 22.3 months and 13.3 months respectively [17]. Peng's study showed the median OS and DFS were 18 months and 6 months respectively [3]. In our study all cases had a median OS 19.3 month, which was similar to the previous studies. However the median DFS was 16.6 months, which was similar to Lee but better than Peng's study. The reason, perhaps, lies in the limited case number and the different CT regime. Peng's regimen mainly was cisplatin plus etoposide (PE). But no further evidence could be provided.

Researchers analyzed prognostic factors. Lymph nodes metastasis was found in 36% early stage patients and LVSI in 90% [2]. Some other studies revealed lymph nodes positive indicated a poor prognosis [13, 16, 18, 19]. We had similar results that 78.6% and 58.3% early stage cases had LVSI and positive lymph nodes respectively. However in our study, although difference of DFS in univariate analysis was obtained (P=0.031) which suggested a trend towards a high risk of death among patients with lymph node involvement, there was no sta-

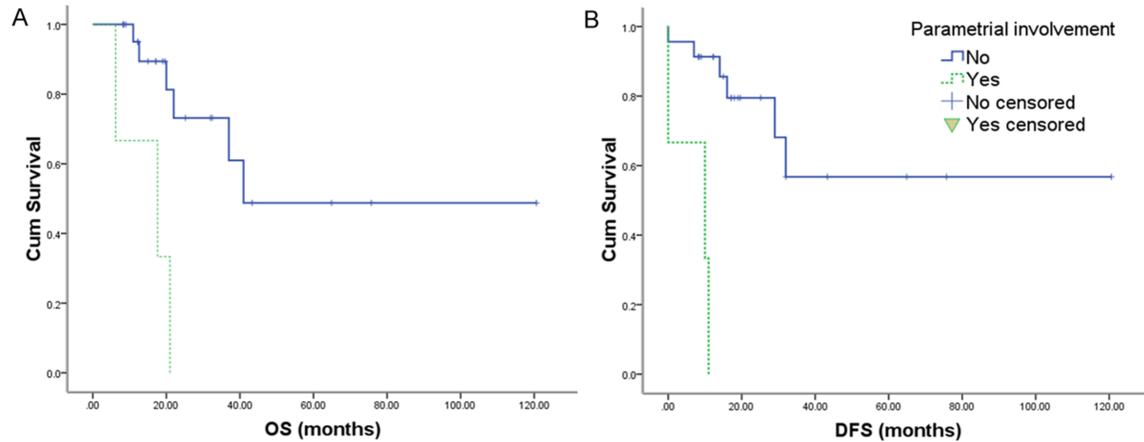

Figure 2. OS (A) and DFS (B) outcomes according to parametrial involvement. The OS and DFS were different (P=0.001 and P=0.000 respectively) between SNCUC with or without parametrial involvement.

tistical difference of OS and DFS between patients with lymph node metastasis and without it in multivariate analysis. This was consistent to some studies [15, 20].

According to Abeler's study, age of SNCUC patients was younger than that of SCC patients [6]. Studies had shown decreased survival followed increasing age [2, 15, 19-21]. Hoskins reported age exceeds 50 years was a prognostic factor (P=0.020) [22]. Regardless of the stages, patients whose age over 60 years had a worse overall survival than those under the age of 50 years (P<0.01) [20]. However in our study, older age was not associated with a poorer outcome.

In our study early stage patients had a better OS and DFS than advanced (P=0.030 and 0.006, respectively) in univariate analysis but failed in multivariate analysis (P=0.407 and 0.547, respectively). Limited cases in our study might be the reason for this difference. Conclusion of stage as a prognostic factor was obtained in previous studies [2, 14, 15, 21]. One study revealed that 7.4 times higher risk of death of patients with stage IV than stage IIB [20]. These conclusions prompted treatment of early stage patients can achieve better survival.

Chan reported the histopathologic subtype could affect the outcome of SNCUC patients. In his study univariate analysis showed a pure histologic pattern had poorer prognosis than a mixed pattern (P=0.044) [14]. But in multivariate analysis it failed to be a independent prognostic factor. Other authors found there was no relationship between histologic feature and survival [16, 20, 23]. This was consistent with our study.

Intaraphet reported patients with deep stromal invasion (outer one third) had 2.9 times higher risk of death (P=0.011) [20]. But similar to our study, some authors thought deep stromal invasion had no statistical difference for indicating a worse survival [3, 4, 18].

Patients with smaller tumors size (less than 4 cm) have better 5-year survival than larger ones (P=0.05) [16]. Another study demonstrated 11 of 13 patients with tumor size > 2 cm died of the disease while 2 of 8 patients who had a tumor of less than 2 cm died [14]. McCann had the similar results for small tumors [23]. Our findings did not provide any evidence of a relationship between tumor size and survival. Perhaps the limited number cases in our study affected the results.

Other factors such as race [2], smoking [14], parametrial invasion [24] and margin status [14] had been analyzed and found to relate to prognostic. In our study PM was an unfavorable prognostic factors for OS and DFS. Unfortunately other factors were failed to reveal difference in the study.

At present there were no therapeutic standard of SNCUC. Viswanathan reported 56% of cases underwent only RT and 40% underwent only

surgery finally recurred [13]. This result indicated solo modality therapy could not control the disease. Referring to therapeutic guidelines of other cervical cancer multimodality therapy, including surgery plus CT or/and RT for early stage disease (I-IIA) and CCRT for advanced stage patients, have been implemented [6, 13, 14, 25, 26]. NACT could be used if the tumor size is greater than 4cm or if metastasis is found by ultrasound, Computed Tomography or Magnetic Resonance Imaging. According to the treatment of small cell lung cancer (SCLC), the most commonly used adjuvant CT regimen consists of PE which provided some benefit in previous studies [19-21]. However, some authors reported that its efficacy was limited [14, 26]. Carboplatin/cisplatin combined paclitaxel (TC/PT) was another common protocol. Yuan analyzed 38 early stage SNCUC cases and found patients who underwent TC regimen after radical surgery had better 2- and 5-year survival than those with non-TC regimen (respectively 72.6% and 65.3% vs. 21.8% and 0) [24]. Furthermore the 2-year recurrence of the TC and the non-TC group were 27.3% and 74.3% respectively. Results of univariate and multivariate analysis of DFS and OS demonstrated there was a significant difference between the TC and non-TC protocol (P=0.002 and 0.006). Hoskins studied 31 cases of which 17 patients underwent CT regime of PE plus RT and 14 patients underwent PT plus RT. That author found the effect of the two protocols to be equivalent [22]. However the PT regimen was less toxicity. A similar conclusion was found in another study [20]. In our study TC/PT were the most frequently implemented protocols. In comparison to surgery and CT, adjuvant RT was only implemented only for patients who had a risk factor, such as pelvic lymph nodes metastasis, parametrial invasion. Although some authors showed adjuvant RT or CCRT could not improve survival in comparison to adjuvant CT alone [20, 25], more suggested multimodality, including RT, should been implemented to reduce pelvic recurrence in accordance with treatment of SCLC [3, 6, 13, 18, 22]. In our study 7 cases suffered recurrence, of which 4 had pelvic metastasis. How to reduce local relapse is important. McCann reported the use of triple-modality therapy in his study [23]. Patients with large size tumor or/and lymph node involvement did not suffer recurrence after surgery plus CT and RT. This, perhaps, prompted the future treatment trends.

However, due to the rarity of SNCUC and this single institute study, a limited number of cases were brought into our study and a short follow-up period was analyzed. The outcome needed further study. It was difficult to implement randomized controlled trials to analyze prognostic factors and different therapeutic protocols affected outcome. However multicenter cooperation in collecting cases for retrospective analysis could be planned and carried out.

In summary, SNCUC is a rare type of female genital tract malignant tumor and is characterized by high aggression and poor outcome. Sometimes it depends mainly on histopathologic diagnosis including morphology and IHC staining. The involvement of lymph nodes and LVSI could appear in the early stage. Multimodality treatment could be implemented in the clinic although no standard therapeutic methods have been presented. The factors, such as age, stage, histological component, tumor size, LVSI, pelvic lymph node invasion, infiltration to deep stroma or parametrium, might influence outcome of patients.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Yuan Qing Yao, Department of Obstetrics and Gynecology, No. 28 Fuxing Road, Beijing 100853, China. Tel: +86 1066938043; E-mail: yqyao_301@163.com

References

[1] Tsunoda S, Jobo T, Arai M, Imai M, Kanai T, Tamura T, Watanabe J, Obokata A, Kuramoto H. Small-cell carcinoma of the uterine cervix: a clinicopathologic study of 11 cases. Int J Gynecol Cancer 2005; 15: 295-300.

[2] Chen J, Macdonald OK, Gaffney DK. Incidence, mortality, and prognostic factors of small cell carcinoma of the cervix. Obstet Gynecol 2008; 111: 1394-1402.

[3] Peng P, Ming W, Jiaxin Y, Keng S. Neuroendocrine tumor of the uterine cervix: a clinicopathologic study of 14 cases. Arch Gynecol Obstet 2012; 286: 1247-1253.

[4] Atienza-Amores M, Guerini-Rocco E, Soslow RA, Park KJ, Weigelt B. Small cell carcinoma of the gynecologic tract: a multifaceted spectrum of lesions. Gynecol Oncol 2014; 134: 410-418.

[5] Wang KL, Yang YC, Wang TY, Chen JR, Chen TC, Chen HS, Su TH, Wang KG. Neuroendocrine carcinoma of the uterine cervix: a clinicopathologic retrospective study of 31 cases with prog-

nostic implications. J Chemother 2006; 18: 209-216.
[6] Abeler VM, Holm R, Nesland JM, Kjørstad KE. Small cell carcinoma of the cervix. A clinicopathologic study of 26 patients. Cancer 1994; 73: 672-677.
[7] Wistuba II, Thomas B, Behrens C, Onuki N, Lindberg G, Albores-Saavedra J, Gazdar AF. Molecular abnormalities associated with endocrine tumors of the uterine cervix. Gynecol Oncol 1999; 72: 3-9.
[8] Herrington CS, Graham D, Southern SA, Bramdev A, Chetty R. Loss of retinoblastoma protein expression is frequent in small cell neuroendocrine carcinoma of the cervix and is unrelated to HPV type. Hum Pathol 1999; 30: 906-910.
[9] Kataoka TR, Tsukamoto Y, Matsumura M, Miyake A, Kamiura S, Ishiguro S, Nishizawa Y. Expression of p21Cip1/Waf1 and p27Kip1 in small cell neuroendocrine carcinoma of the uterine cervix. Int J Surg Pathol 2008; 16: 11-15.
[10] Tavassoli FADP. World Health Organization classification of tumours. Pathology and genetics of tumours of the breast and female genital organs. Lyon: IARC Press; 2003.
[11] Rekhi B, Patil B, Deodhar KK, Maheshwari A, A Kerkar R, Gupta S, Tongaonkar HB, Shrivastava SK. Spectrum of neuroendocrine carcinomas of the uterine cervix, including histopathologic features, terminology, immunohistochemical profile, and clinical outcomes in a series of 50 cases from a single institution in India. Ann Diagn Pathol 2013; 17: 1-9.
[12] Slodkowska J, Zych J, Szturmowicz M, Demkow U, Rowinska-Zakrzewska E, Roszkowski-Sliz K. Neuroendocrine phenotype of non-small cell lung carcinoma: immunohistological evaluation and biochemical study. Int J Biol Markers 2005; 20: 217-226.
[13] Viswanathan AN, Deavers MT, Jhingran A, Ramirez PT, Levenback C, Eifel PJ. Small cell neuroendocrine carcinoma of the cervix: outcome and patterns of recurrence. Gynecol Oncol 2004; 93: 27-33.
[14] Chan JK, Loizzi V, Burger RA, Rutgers J, Monk BJ. Prognostic factors in neuroendocrine small cell cervical carcinoma: a multivariate analysis. Cancer 2003; 97: 568-574.
[15] Wang KL, Chang TC, Jung SM, Chen CH, Cheng YM, Wu HH, Liou WS, Hsu ST, Ou YC, Yeh LS, Lai HC, Huang CY, Chen TC, Chang CJ, Lai CH. Primary treatment and prognostic factors of small cell neuroendocrine carcinoma of the uterine cervix: a Taiwanese Gynecologic Oncology Group study. Eur J Cancer 2012; 48: 1484-1494.
[16] Bermúdez A, Vighi S, García A, Sardi J. Neuroendocrine cervical carcinoma: a diagnostic and therapeutic challenge. Gynecol Oncol 2001; 82: 32-39.
[17] Lee SW, Lim KT, Bae DS, Park SY, Kim YT, Kim KR, Nam JH. A multicenter study of the importance of systemic chemotherapy for patients with small-cell neuroendocrine carcinoma of the uterine cervix. Gynecol Obstet Invest 2015; 79: 172-178.
[18] Tian WJ, Zhang MQ, Shui RH. Prognostic factors and treatment comparison in early-stage small cell carcinoma of the uterine cervix. Oncol Lett 2012; 3: 125-130.
[19] Zivanovic O, Leitao MM Jr, Park KJ, Zhao H, Diaz JP, Konner J, Alektiar K, Chi DS, Abu-Rustum NR, Aghajanian C. Small cell neuroendocrine carcinoma of the cervix: analysis of outcome, recurrence pattern and the impact of platinum-based combination chemotherapy. Gynecol Oncol 2009; 112: 590-593.
[20] Intaraphet S, Kasatpibal N, Siriaunkgul S, Chandacham A, Sukpan K, Patumanond J. Prognostic factors for small cell neuroendocrine carcinoma of the uterine cervix an institutional experience. Int J Gynecol Cancer 2014; 24: 272-279.
[21] Cohen JG, Kapp DS, Shin JY, Urban R, Sherman AE, Chen LM, Osann K, Chan JK. Small cell carcinoma of the cervix: treatment and survival outcomes of 188 patients. Am J Obstet Gynecol 2011; 203: 347, e1-6.
[22] Hoskins PJ, Swenerton KD, Pike JA, Lim P, Aquino-Parsons C, Wong F, Lee N. Small-cell carcinoma of the cervix: fourteen years of experience at a single institution using a combined-modality regimen of involved-field irradiation and platinum-based combination chemotherapy. J Clin Oncol 2003; 21: 3495-3501.
[23] McCann GA, Boutsicaris CE, Preston MM, Backes FJ, Eisenhauer EL, Fowler JM, Cohn DE, Copeland LJ, Salani R, O'Malley DM. Neuroendocrine carcinoma of the uterine cervix the role of multimodality therapy in early-stage disease. Gynecol Oncol 2013; 129: 135-139.
[24] Yuan L, Jiang H, Lu Y, Guo SW, Liu X. Prognostic factors of surgically treated early-stage small cell neuroendocrine carcinoma of the cervix. Int J Gynecol Cancer 2015; 25: 1315-321.
[25] Boruta DM 2nd, Schorge JO, Duska LA, Crum CP, Castrillon DH, Sheets EE. Multimodality therapy in early-stage neuroendocrine carcinoma of the uterine cervix. Gynecol Oncol 2001; 81: 82-87.
[26] Lee SS, Lee JL, Ryu MH, Chang HM, Kim TW, Kim WK, Lee JS, Jang SJ, Khang SK, Kang YK. Extrapulmonary small cell carcinoma: single center experience with 61 patients. Acta Oncol 2007; 46: 846-851.