

實證醫學報告

報告者：婦產部 R2 邱廣通

指導：陳渝潔 VS

報告日期：97年07月28日

Patient Profile

- Name: 劉X英
- Sex: female
- Age: 66 years old
- Chart No: 24659669
- Date of admission: 2008/07/17
- Date of discharge: 2008/07/23

Chief complaint

- Cervical cancer stage IVb was told at 小港 hospital.

Present Illness

- This 66 years old female was a case of cervical cancer diagnosed at 小港 hospital. After cancer survey done, pelvic CT reported as preliminary cancer stage IV (T2b N1 M1); colofibroscope reported as colon polyps & mild internal hemorrhoid; abdominal sonography reported as mild chronic liver disease. Lab data showed CEA 7.49 ng/ml, SCC 0.2 ng/ml, and cervical biopsy reported as squamous cell carcinoma. Because of above reasons, she was referred to 高醫 for further radiotherapy.
- Tracing back her history, she suffered from bloody urine with painful sensation for half a year. Dysuria was first noted 8~9 months ago, and bloody urine passage occurred at this year (6 months ago). Mild abdominal pain was also complained, but she didn't keep in mind and let it be recovered by itself. However, she felt severe abdominal pain in recent days, then she went to 關山慈濟 hospital for help. She visited GYN and Uro OPD, while this showed UTI and that found vaginal bleeding. She was then transferred to 小港 hospital where cancer survey was performed for suspected cervical cancer.

Past History

- 1. Hypertension (+) with medical control
- 2. Diabetes Mellitus (+) with medical control
- 3. Asthma: denied
- 4. Heart disease: denied
- 5. Smoking/alcohol: denied
- 6. Drug allergy: denied
- 7. Operation history: left total knee replacement (2007-03)
- left cataract S/P OP at several years ago

- <GYN/OBS History>
- 1. Married, G4P4A0 (NSD x 4)
- 2. Menopause at 48 y/o

Physical Examination

- Consciousness: alert, E4V5M6
- Vital sign: BP: 167/79 mmHg, PR: 74 bpm, RR: 18 cpm, BT: 37.2 °C
- General appearance: fair
- HEENT
- Conjunctiva: mild pale, Sclera: not icteric
- Neck: supple, LAP(+) left neck
- Chest: symmetric expansion
- Breath Sound: Bil. clear
- Heart Sound: regular heart beat, no murmur
- Abdomen: soft, no tenderness
- Bowel Sound: normoactive
- Liver/spleen: impalpable
- Extremity
- freely movable, no pitting edema

- <PV> cervix: necrosis with easy contact bleeding
- parametrium: involved (+)
- vaginal invasion (+) upper third vagina

Further Survey

- 97-7-21: whole body bone scan: high probability of bone metastasis from uterine cervical cancer to spine and acetabulum
- 97-7-21: Cystoscopy: external compression from bladder base & right lateral wall without bladder mucosal lesion.

Fine needle biopsy

- 病理編號: KMH-08-03747
- Specimen: Lymph node (neck, left).
- Diagnosis: Positive.
- Specimen description: 2 slides.
- Specimen adequacy: Satisfactory.
- Cytological features:
 - ● Background: (neutrophils and lymphocytes mainly), bloody.
 - ● Cellular arrangement: Flat sheets.
 - ● Cellular characteristics of positive cells.
 - Nuclear-cytoplasmic ratio: increased.
 - Nuclear membrane: irregular.
 - Nuclear pleomorphism: moderate.
 - Chromatin: coarsely granular.
 - Nucleoli: present. (i. Small).
- Comment: The picture suggests: metastatic carcinoma.

Lab Data

SCC	CEA	TPA	AFP	CA125
0.3	6.88	462.9	< 2.8	39
CA199	Ccr	DPL	WBC	Hb
62.4	59 ml/min	610 mg/day	6400	10.3
PLT	HBsAg	HBeAg	HCV IgG	Cr
209000	(-)	(-)	(-)	1.09

Impression

- 1. Cervical cancer (squamous cell carcinoma) stage IVb
- 2. Diabetes mellitus with drug control
- 3. Hypertension with medical control

Asking an answerable question

使用concurrent chemoradiotherapy (CCRT)
有較佳的預後

Patient: Cervical cancer IVb

Intervention: CCRT

Comparison: R/T

Outcome: Better prognosis

Chemoradiotherapy for uterine cancer: current status and perspectives

Int J Clin Oncol (2004) 9:458–470

Review article

A gynecologic oncology group (GOG) trial (1993)

- 296 patients with stage IIB to IVA disease
- Hydroxyurea (HU) or misonidazole
- Concurrently with RT
- 5-year DFS was higher in patients who received HU, but the difference was not statistically significant.

Tseng et al. (1997)

- 122 patients with IIB to IIIB disease
- RT + PVB versus RT alone
- Response rate: CCRT : RT (77% vs 61%)
- 3-year survival: CCRT : RT (61.7% vs 64.5%)

Colombo et al. (1997)

- 56 patients with stage IB2 to IVA disease
- RT + FJ(5-FU + carboplatin) vs RT alone
- 5-year survival: CCRT : RT (66% vs 70%)

Thomas et al. (1998)

- 234 patients with stage IB2 to IVA disease
- (1) standard RT (2) standard RT + 5-FU (3) hyperfractionated RT (4) hyperfractionated RT + 5-FU
- A trend toward higher response rates and 5-year DFS in the CCRT arms compared with the RT arms.
- A subgroup analysis by disease stage (IB2 to IIB):
 - 5-year DFS: RT + 5-FU (n=61) vs RT (n=45) (61% vs 45%; P=0.05)

Results of large randomized controlled studies of CCRT using CDDP-based regimens (1999)

- Whitney et al. (GOG 85 trial) 1999
- Rose et al. (GOG 120 trial) 1999
- Keys et al. (GOG 123 trial) 1999
- Morris et al. (RTGO 90-01 trial) 1999
- Peters et al. (SWOG 8797 trial) 2000

Whitney et al. (GOG 85 trial) 1999

- Paraaortic lymph node (PAN)-negative stage IB to IVA disease
- PF (cisplatin + 5-FU) or HU (hydroxyurea) concurrently with RT
- At a median follow-up of 7 years, DFS was significantly higher in patients who received PF (55% vs 43%; $P=0.0018$)

Rose et al. (GOG 120 trial) 1999

- PAN-negative stage IIB to IVA disease
- (1) RT with concurrent weekly CDDP (2) RT with concurrent PF plus HU (3) RT with concurrent HU
- 3-year survival rate was significantly higher in the two arms using CDDP-based regimens, i.e., the weekly CDDP and PF + HU arms, (66% and 67%, respectively) than in the HU arm (50%; $P=0.004$ and $P=0.002$, respectively)

Keys et al. (GOG 123 trial) 1999

- PAN-negative stage IB2 disease
- (1) RT + weekly CDDP + adjuvant hysterectomy (2) RT alone + adjuvant hysterectomy
- 3-year survival rate was significantly higher in the CCRT arm (83% vs 74%; $P=0.008$)

Morris et al. (RTGO 90-01 trial) 1999

- Patients with stage IB to IVA disease (stage IB/IIA with lymph node involvement or tumors 5 cm or greater, and stage IIB-IVA)
- CCRT, using PF, versus RT alone
- CCRT was associated with significantly higher 5-year OS (83% vs 58%; P 0.004) and 5-year DFS (67% vs 40%; P 0.001), as well as significantly lower distant and local recurrence rates (P 0.001)

Peters et al. (SWOG 8797 trial) 2000

- postoperative adjuvant setting in stage IA2 to IIA patients who were found to have poor prognostic factors (lymph node involvement, parametrial involvement, and/or positive surgical margins of the vagina)
- CCRT using PF vs RT alone
- The 4-year DFS was significantly higher in the CCRT arm (81% vs 71%; P 0.007).

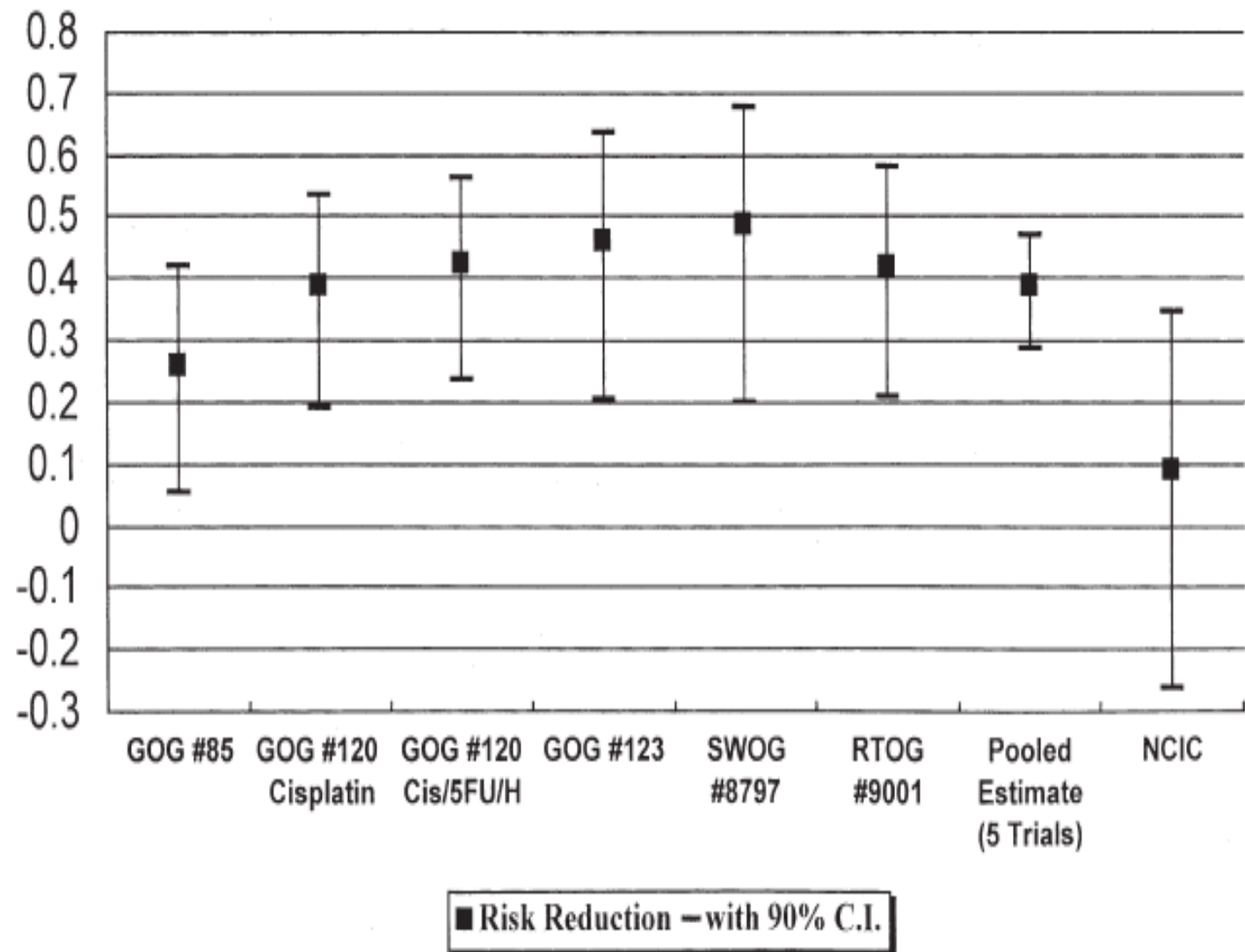
Table 3. Large randomized studies of concurrent chemoradiotherapy in cervical cancer

Author	Stage	Design	RT	CT (mg/m ² , except for HU)	No. of patients	Survival (%) CT/RT vs RT (follow-up)	<i>P</i>
Whitney, ²⁸ GOG 85, 1999	IIB-IVA PAN (-), Washing cytology (-)	WP+PF×3 vs WP+HU+PAN	IIB:40 Gy+Ra III,IVA:WP, 51 Gy+Ra III,IV:61 Gy	P:50/Day1 F:1000/Days2-5, q 4 Weeks HU:80 mg/kg/twice a Week	388	55 vs 43 (8.7 Years)	0.018
Rose, ²⁹ GOG 120, 1999	IIB-IVA PAN (-)	WP+P weekly vs WP+PF+HU vs WP+HU	IIB:40 Gy+Ra III,IVA:WP, 51 Gy+Ra III,IV:61 Gy	P:40/Week for 4 Weeks vs P:50/Day1 +F:1000/Days1-4+ HU:2000/2/Week, q 4 weeks vs HU:3000/2/Week for 6 Weeks	176	66 vs 67 vs 50 (3 Years) 81 vs 71 (4 Years)	0.004 0.002
Keys, ³⁰ GOG 123, 1999	IB ≥4 cm	WP+P weekly vs WP Adj ATH	WP:45 Gy+Ra	P:40/Week for 6 Weeks	369	83 vs 74 (3 Years)	0.008
Morris, ³¹ RTOG 90-01, 1999	IB-IVA > 5 cm or PAN (+)	WP+PF×3 vs WP+PAN	WP:45 Gy PAN:45 Gy	P:75/Day1 F:1000/Days2-5, q 3 Weeks	386	83 vs 58 (5 Years)	0.004
Peters, ³² SWOG 8797, 2000	IA2-IIA Postsurgical pN1/pT2b/ stump (+)	WP+PF×4 vs WP+PAN	WP:45 Gy WP+PAN	P:70/Day1 F:1000/Days1-4, q 3 Weeks	268	81 vs 71 (4 Years)	0.007

CT, chemotherapy; RT, radiotherapy; WP, whole pelvis; PAN, paraaortic lymph node; Adj, adjuvant; ATH, abdominal total hysterectomy; P, cisplatin; F, 5-FU; HU, hydroxyurea; Ra, radium therapy

five large studies demonstrated a significant survival benefit for patients treated with CCRT using a CDDP-based regimen, with a 28%–50% relative reduction in the risk of death

Fig. 1. Reduction in the risk (1-relative risk [RR]) of death in six clinical trials of chemoradiation in patients with cervical cancer. *GOG*, Gynecologic Oncology Group; *SWOG*, Southwest Oncology Group; *RTOG*, Radiation Therapy Oncology Group; *NCIC*, National Cancer Institute, of Canada; *5FU*, 5-fluorouracil; *H*, hydroxyurea; *CI*, confidence interval. From reference 34, with permission



Conclusion

- the following theoretical advantages of using concurrent CT have been suggested:
 - (1) CT inhibits the repair of RT-induced sublethal damage in tumor cells
 - (2) CT reduces tumor size directly by exerting its cytotoxic effect
 - (3) CT enhances the synchronization of tumor cells into a radiosensitive phase of the cell cycle and reduces the proportion of radioresistant hypoxic cells
 - (4) CT and RT target different phases of the cell cycle and, therefore, provide additive efficacy that increases tumor cell death without leading to delay of local therapy or prolongation of RT duration

Conclusion

- It has been demonstrated that CCRT improves the prognosis of cervical cancer patients compared with RT alone.
- CCRT is currently recommended as standard therapy for advanced cancer (stage III/IVA) in the United States

The guidelines published by the National Comprehensive Cancer Network (NCCN)

- For patients with stage IB1 or more advanced disease, primary RT should be combined with CDDP-containing CT
- For patients undergoing surgical staging and found to have positive pelvic nodes or positive parametrium, adjuvant CCRT, consisting of pelvic RT and CDDP-containing CT should be considered, regardless of postoperative tumor stage.

Thanks for your attention