CHAPTER 4

DISCUSSION

The pattern of p53 protein expression in cervical cancer

Most of p53 immunoreactivity was observed exclusively in the nucleus. In cervical carcinoma, the presence of the p53 protein in the nucleus of neoplasmic cells is infrequent and heterogenously. The level of intensity varied from cell to cell (Figure 18). This could imply several things: the intensity of staining may depend on the level of p53 protein in the nucleus of tumor cells, p53 may be mutated in many tumor cells, but accumulates to a detectable level in only a small number of cells, or detected p53 may be normal p53 that is somehow abnormally increased or stabilized in amount. Sometimes cytoplasmic staining was found in scattered cells (Figure 19). Thus, it may be involving the background staining, may be involving the regulation of p53 cellular localization that depends on several factor, such as, MDM2, one of the most important protein which influence p53 nuclear import and export.[8]

For the correlation of p53 expression with histologic type, several studied reported that p53 protein expression is more frequent in squamous cell carcinomas than in adenocarcinomas.[2,9,11] In this study, squamous cell carcinoma showed a higher percentage of cases with p53 protein expression (91.67% in cases group vs 89.29% in controls group) when compared to the case of adenocarcinoma(8.33% in cases group vs 10.17% in controls group) and adenosquamous carcinoma(3.57% in controls group) respectively. This result showed that p53 expression may be the prognostic indicator for cervical cancer, especially in squamous lesion.

The comparison of positive p53 protein expression

The proportion of p53 protein expression in controls group was slightly higher than in cases group, with mean value of 8.83% and 7.71% respectively. In patients without tumor recurrence, the p53 expression have trend higher than in those with tumor recurrence. This result showed that the proportion of p53 expression in cervical cancer patients who underwent RDH in those with tumor recurrence is not different from the proportion in those without tumor recurrence. There are several factors that have confounded the results of p53 studies in patients with cervical carcinoma. The first factor is the type of tissue which analyzed by mean immunohistochemistry technique. Most of studies have used paraffin tissue block.[2,9,11,13,20,25] Using frozen tissue in these studies were still available. The importance of the type of tissue base on the fact that frozen tissue has better preservation of the p53 protein.[12] From this result, if the type of tissue interfere the expression of antigen, it is difficult to detect p53 expression in patients who cervical cancer were studied by analysis of paraffin sections. However, the antigen retreival method could be solve this problem. There are three antibodies that have been used when analyzing p53 immunostaining in patients with cervical carcinoma: pAb 1801[19,20], CM-1[31] and DO-7.[2,9,11,13,25] In paraffin embedded tissue, monoclonal antibody p53 DO-7 detected more positive cases than p53 pAb 1801 when the paraffin sections were pretreated by using antigen retrieval method.[31] In this study, p53 immunoreactivity was detected only in a small proportion of cells. This could imply using paraffin tissue blocks that were kept for a long time before they were brought for immunostaining(between 1992 to 1997).[61]

The correlation between p53 protein expression, clinicopathological variables in cervical cancer

The correlation between p53 protein expression and clinicopathological variables in patients underwent RAD and PLD and have negative pelvic node were studied. In this study, the p53 expression was demonstrated to be a significant prognostic factor in histologic type of cervical carcinoma, especially in squamous cell carcinoma(p=0.036)(Table 5). For the relationship of p53 expression with histologic type, the same observation was reported in one study.[13] Many investigators showed the various prognostic factors that have been relate to recurrence in cervical cancer patients that treated by RDH and PLD, including FIGO stage[13], histologic type[13], depth of invasion[29,39] and parametrial involvement.[24] For tumor characteristics, the p53 expression have trend associated with the exophytic lesion more than other lesion *(p=0.168)* (Table 5). Moreover, the p53 protein expression also have trend related to high tumor grade, especially grade II *(p= 0.080),* even though there was no any significant correlation between expression of p53 and tumor grade. However, no significant correlation between p53 protein expression and other clinicopathological variables for cervical cancer were found in this study. [including, FIGO staging (p=0.082) , tumor characteristics (p= 0.168 vs 0.697), LVSI (p= 0.345), depth of invasion (p= 0.464) and tumor grade (p= 0.265 vs 0.080)] This could be imply that the limitation of time and the rarity of the case. In this study, the patients who operated before 1992 were not recruit, because the hospital kept the paraffin blocks for only ten years. The 5-year follow up period was performed to define cases and controls. From this result, the patients who were operated after 1997 also were not recruit. In addition, tumor recurrence in early stage cervical cancer patients, who treated by RDH and have negative pelvic node is not common.