

# Primary plasmacytoma of the uterine cervix treated with three-dimensional conformal radiotherapy

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## ABSTRACT

Primary plasmacytoma of the uterine cervix is a rare neoplasm with limited known data, and only several cases sporadically reported in the published literature. Radiotherapy might have a role in the treatment of plasmacytoma of the uterine cervix. We describe primary plasmacytoma of the uterine cervix in a 45-year-old woman treated with three-dimensional conformal radiotherapy, and also reviewed the literature to evaluate the treatment modality and therapeutic outcome of this rare disease.

**Keywords:** cervical plasmacytoma, cervical tumour, primary plasmacytoma, three-dimensional conformal radiotherapy, uterine cervix

*Singapore Med J 2008;49(12):e361-e364*

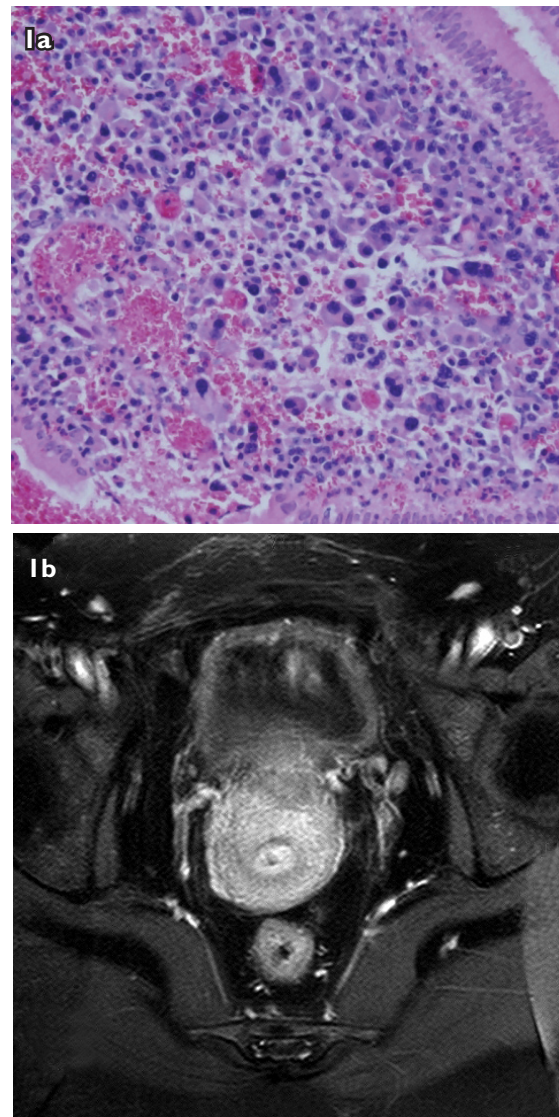
## INTRODUCTION

Primary plasmacytoma of the uterine cervix is a rare neoplasm. To our knowledge, there have only been seven cases reported in the published literature.<sup>(1-7)</sup> Here we described primary plasmacytoma at the uterine cervix of a 45-year-old woman treated with three-dimensional conformal radiotherapy, and reviewed the literature of this rare disease.

## CASE REPORT

A 45-year-old woman who presented for a routine health examination was in her usual healthy status without any vaginal infection or sexually-transmitted disease. Since March 2005, she had constitutional symptoms of soreness over the left lower quadrant abdomen, and ultrasonography showed uterine myoma. She was then on regular follow-up at the Department of Gynaecology outpatient clinic. The previous routine Pap smears were negative for malignancy; however, a Pap smear in September 2006 showed carcinoma. Vaginal examination revealed an unremarkable finding of the uterine cervix, and showed no parametrium nor vagina abnormality. Physical examination showed no bony tenderness or palpable neck lymph node.

The biopsy was suggested by the physician, and the final pathological report of conisation revealed



**Fig. 1** (a) Photomicrograph shows the plasmacytoma of the uterine cervix, comprising a dense aggregate of atypical plasma cells with pleomorphic nuclei, binucleation and amphophilic cytoplasm (Haematoxylin & eosin, x 100). (b) Contrast-enhanced axial T1-W MR image of the pelvis shows a mildly-enhanced mucosa at the cervical endocervical region.

plasma cell myeloma (Fig. 1). The conisation tissues showed a dense aggregate of atypical plasma cells with pleomorphic nuclei, binucleation and amphophilic cytoplasm. Bizarre giant cells were also seen. Immunohistochemical stain revealed cytokeratin(-), CD10(-), oestrogen receptor(-), progesterone receptor(-), CD138(+), EMA(+), vimentin(+),  $\lambda$ -light chain(+) and  $\kappa$ -light chain(-). Magnetic resonance (MR)

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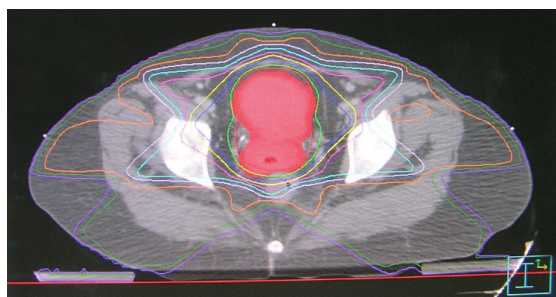
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**Fig. 2** Axial CT image shows the three-dimensional conformal radiotherapy plan. The prescribed radiation dose was 50 Gy to the 95% isodose line.

imaging of the pelvis showed a mildly-enhanced mucosa on the cervical endocervical region (Fig. 1). The serum immunoglobulin levels were IgG 1,809 mg/dL (normal range 700–1,600 mg/dL), IgA 289 mg/dL (normal range 70–400 mg/dL), and IgM 52 mg/dL (normal range 40–230 mg/dL). The immunofixative electrophoresis revealed monoclonal gammopathy of IgG- $\kappa$  type. Bone marrow biopsy revealed that the immunohistochemical study for CD138 demonstrated less than 5% of plasma cells with reversed  $\kappa/\lambda$  light chain ratio, and no further skeletal survey was arranged. Chest radiograph was unremarkable.

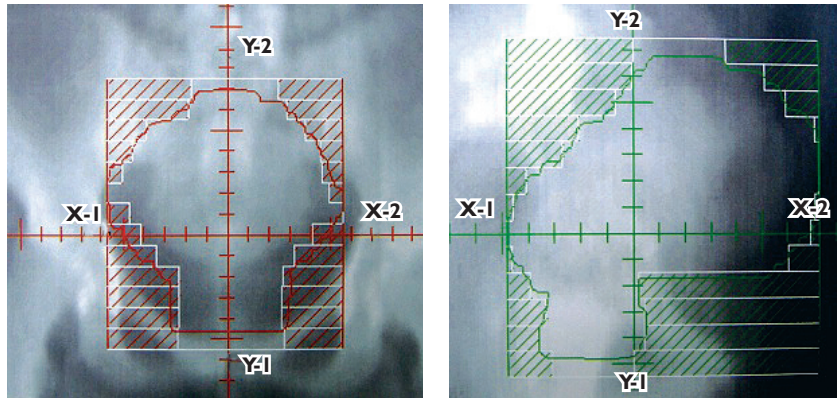
The patient was then referred to the Department of Radiation Oncology for radiotherapy. Irradiation was delivered using three-dimensional conformal radiotherapy. Linear accelerator with computer-controlled autosequencing multileaf collimator (Siemens Medical Systems, Concord, CA, USA) was used to deliver radiotherapy with the Pinnacle-3 Treatment Planning System (ADAC Laboratories, Milpitas, CA, USA). The clinical target volume (CTV) included the uterine cervix, uterine corpus and bilateral pelvic lymph nodes. The beam energies used were 6 MV and 15 MV photons. The prescribed radiation dose was 50 Gy to the 95% isodose line (Figs. 2 & 3). The fractionation size was 2 Gy daily, five days a week. The patient completed radiotherapy in December 2006, after which the IgG level returned to the upper limit of the normal range with 1,703 mg/dL (normal range 700–1,600 mg/dL). The patient then received thalidomide 100 mg per day for the following 12 months. The level of IgG was 1,407 mg/dL in October 2007. Follow-up pelvis MR imaging in December 2007 showed a mildly-enhanced mucosa on the cervical endocervical region, and no change in size of the intramural myoma. The patient was kept on follow-up. The IgG was examined each month, and the latest level of IgG was 1,486 mg/dL in March 2008.

## DISCUSSION

Plasmacytomas are localised, usually focal, plasma cell neoplasms that occur in visceral structures, soft tissue, or bone.<sup>(1)</sup> Less than 5% of patients with a plasma cell dyscrasia present with a single bone (SBP) or extramedullary plasmacytoma (EMP) without evidence of systemic disease.<sup>(8)</sup> In contrast to SPB, EMP represents a rare category of plasma cell tumours, and it may originate at any site, but occurs predominantly in the upper respiratory tract.<sup>(9–11)</sup> Plasmacytomas of the uterine cervix are extremely rare. There is few data available and only several cases sporadically reported in the published literature. Based on the literature review on primary plasmacytoma of the uterine cervix, the median age at diagnosis is 34 years, and the presenting symptoms are contact vaginal bleeding, vaginal discharge, and pelvic pain.<sup>(1–7)</sup> The diagnosis of primary plasmacytoma of the uterine cervix is identical to the diagnosis of EMP, which requires biopsy confirmation of a monoclonal plasma cell infiltrate from a single site, with no evidence of bone destruction or occult disease elsewhere, and this plasma cell tumour has less than 5% bone marrow plasma cells.<sup>(8,12)</sup> The lesion is histopathologically characterised by infiltrates of plasma cells of diverse maturity and by their monoclonal immunoglobulin products.<sup>(11)</sup>

Interestingly, in our patient, immunohistochemical stain of the cervix biopsy revealed  $\lambda$ -light chain (+) and  $\kappa$ -light chain (–), while the immunofixative electrophoresis of serum revealed monoclonal gammopathy of the IgG- $\kappa$  type. Differential diagnosis other than solitary plasmacytoma of the uterine cervix should be considered. The first consideration was that there could be two colonies; one colony was cervical plasmacytoma, while the other was monoclonal gammopathy of unknown significance. The second consideration was a rare presentation of separate solitary plasmacytoma with two colonies. Computer tomography (CT) or MR imaging is required to document the extent of the solitary lesion.<sup>(8)</sup> In solitary extramedullary plasmacytoma, CT may show masses or infiltrative lesions with soft-tissue attenuation, and these lesions may be isointense and hyperintense on T1- and T2-weighted MR images, respectively.<sup>(13–15)</sup>

Because EMP is a highly radiosensitive tumour, surgical procedures of the head and neck are not recommended, but surgery may be considered for other sites of the disease, such as the gastrointestinal tract.<sup>(8)</sup> However, due to the paucity of patient data, there is no experience of surgery in plasmacytoma of the uterine cervix. Radiotherapy might have a role in the treatment of plasmacytoma of the uterine cervix, and the



**Fig. 3** The beam's eye view radiographs of the three-dimensional conformal radiotherapy plan.

standard treatment of EMP is local radiation therapy.<sup>(10)</sup> Considering the high cure rate of EMP with radiotherapy and the lack of published data regarding the use of adjuvant chemotherapy, use of adjuvant chemotherapy is not justified outside a clinical trial.<sup>(8)</sup> The treatment of radiotherapy is given with curative intent.<sup>(8)</sup> In our literature review of seven cases of plasmacytoma of the uterine cervix, two patients received only conisation, two had a hysterectomy, two received radiotherapy, and one patient was treated with tumour excision followed by radiotherapy and chemotherapy.<sup>(1-7)</sup> For EMP, the irradiation dose is usually 40–65 Gy, with median daily dose of 2 Gy.<sup>(8)</sup> However, with little known experience about radiotherapy of plasmacytoma of the uterine cervix, there is no standard or optimal irradiation dose that has ever been described.

In most reports on EMP, nearly all patients successfully achieve local control of 80%–100%, and approximately 50%–65% of patients remain free of disease longer than ten years. The ten-year disease-free status and overall survival ranges from 50% to 80%.<sup>(10)</sup> About 30%–50% of patients develop disease progression to myeloma, with a median period of two years.<sup>(8)</sup> As for plasmacytoma of the uterine cervix, our review of the literature revealed that the clinical follow-up in these patients ranges from three months to three years.<sup>(1-7)</sup> The first patient underwent simple vaginal hysterectomy four months after her initial presentation. There was no clinical evidence of recurrence at her nine-month postoperative evaluation. The second patient was treated with conisation, and no sign of local recurrence or generalised disease during a three-year follow-up period. The third patient received a surgical excision of the tumour with a dissection of the relevant lymph nodes. Although irradiation and chemotherapy were administered postoperatively, multiple bone metastasis

was found a month after the operation, and the patient died eight months later. The fourth patient had local irradiation to the tumour, and was alive with clinically detected residual lesions at the three-year follow-up. The fifth patient was treated by simple hysterectomy, but local recurrence in the vaginal vault was noted at the three-month follow-up. The sixth patient underwent conisation and vaginal hysterectomy for the tumour. There was no residual lesion in the hysterectomy specimen. The seventh patient received local irradiation to the tumour. At one-year follow-up, there was no abnormal finding in the pelvis, but two other plasmacytomas in the groin node and jaw were noted.<sup>(1-7)</sup>

Our patient was treated with three-dimensional conformal radiotherapy after conisation of the uterine cervix. The prescribed radiation dose was 50 Gy to the 95% isodose line. During the radiotherapy course, the patient had grade I diarrhoea, and the symptoms improved with medication. After completion of radiotherapy, her IgG returned to the upper limit of the normal range with a level from 1,809 mg/dL to 1,703 mg/dL (normal range 700–1,600 mg/dL). The patient then received thalidomide in the following 12 months, and the latest level of IgG returned to normal range at 1,486 mg/dL in March 2008. The IgG level of this patient at the initial presentation was borderline raised over the normal range, with a value of 1,809 mg/dL. During the follow-up period after treatment, the IgG level was checked monthly. Although there was no obvious decline in the level of the IgG in the first month after radiotherapy completion, the gradual decrease of IgG level was noted within the following months.

To our knowledge, this is the first case of primary plasmacytoma of the uterine cervix treated with three-dimensional conformal radiotherapy. Biological complete response of tumour was achieved with 50 Gy

of radiotherapy and treatment of thalidomide. Due to the paucity of published data on primary plasmacytoma of the uterine cervix, more cases and experience are required to evaluate the optimal treatment and prognosis of this rare disease.

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