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Cervical Cancer with Bulky Tumor: A Case Report

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ABSTRACT

Introduction: Cervical cancer is a malignancy originating from the cervix and represents one of the most common cancers affecting women both globally and in Indonesia. Meanwhile, bulky tumor is defined as a lesion measuring ≥4 cm in diameter. Neoadjuvant chemotherapy followed by radical surgery (NACT-RS) has emerged as a viable treatment option for stages IB3 and IIA2 cervical cancer, especially in settings where radiotherapy resources are limited or unavailable.

Case Report: A 28-year-old female was presented with abnormal vaginal bleeding persisting for four months. The bleeding was bright red and foul-smelling. The patient also reported postcoital bleeding beginning seven months prior to presentation. A cervical biopsy was performed, and histopathological analysis confirmed a diagnosis of non-keratinizing squamous cell carcinoma. Due to the large tumor size, the patient underwent three cycles of chemotherapy prior to radical hysterectomy as part of her treatment plan.

Conclusion: In patients with bulky cervical tumors, neoadjuvant chemotherapy followed by radical hysterectomy can offer favorable perioperative outcomes and remains a critical treatment approach.

Keywords

Cervical cancer, Bulky tumor, Neoadjuvant chemotherapy

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INTRODUCTION

Cervical cancer is the fourth most common malignancy among women, with an estimated 570,000 new cases reported in 2018 alone. It accounts for approximately 6.6% of all cancer-related deaths among women worldwide [1]. Approximately 90% of cervical cancer-related deaths occur in low- and middle-income countries (LMICs). In 2010, the estimated incidence of cervical cancer was 454,000. The age-standardised incidence rate in developed countries was 5.2 per 100,000 women in 2020. Among these patients, approximately 40% were diagnosed with locally advanced cervical cancer (LACC), as defined by the International Federation of Gynecology and Obstetrics (FIGO) staging system as stages IB3, IIA2, IIB, IIIA, IIIB, IIIC, and IVA, with a 5-year relative survival rate of 58% [2,3].

Cervical cancer typically progresses slowly from pre-invasive cervical intraepithelial neoplasia (CIN) to invasive cancer. Macroscopic enlargement of the lesion, commonly referred to as a "bulky tumor" is generally characterised by a tumour size ≥ 4 cm on imaging. Large cervical tumours are associated with a poor prognosis and reduced local control rates [2,4].

The recommended standard treatment involves external beam radiation therapy (EBRT) administered concurrently with platinum-based chemotherapy, followed by an intracavitary brachytherapy. According to the most recent guidelines from the National Comprehensive Cancer Network, the recommended total radiation dose is >85 Gy to point A. Given the high recurrence rate post-chemoradiation (up to 40.2 %), radical hysterectomy is performed in certain institutions [5]. Tumour size is one of the most significant prognostic

factors and is directly correlated with treatment failure. Several strategies have been proposed to address these challenges, including the introduction of neoadjuvant chemotherapy as a therapeutic approach for various malignancies, including advanced-stage cervical cancer [1,6].

CASE REPORT

On 3 June 2023 a 28-year-old woman presented with a chief complaint of vaginal bleeding persisting for the past four months. The bleeding was described as bright red and foul-smelling and required changing sanitary pads 2–3 times daily. The patient also reported postcoital bleeding that had persisted for seven months. She experienced abnormal vaginal discharge, which became foul-smelling. Abdominal distension was not observed. The patient underwent cervical biopsy, and histopathological examination revealed non-keratinising squamous cell carcinoma. A radical hysterectomy was planned following three cycles of chemotherapy because of the tumour's large size. She had received the first cycle of chemotherapy in February but refused to continue treatment, citing worsening general condition following chemotherapy, including greyish-brown skin discoloration, dryness, and burning sensations. Urination and defaecation were within the normal limits. The patient reported unintentional weight loss of approximately 6 kg over two months.

There was no family history of hypertension, asthma, cardiac disease, or diabetes. The patient experienced menarche at age 12 years with regular menstrual cycles lasting 6–7 days, changing pads 3–4 times daily, and no dysmenorrhoea. She was married at the age of 24 and had two pregnancies, both of which were delivered via caesarean section. She was receiving monthly injectable contraception.

Physical examination revealed a conscious patient with moderate general condition. The vital signs were as follows: blood pressure, 110/70 mmHg; pulse rate, 86 beats/min; respiratory rate, 20 breaths/min; and body temperature, 36.6°C. Head inspection revealed normocephaly, with no anaemia or icterus. Cardiovascular examination revealed regular S1 and S2 heart sounds without murmurs or gallops. Respiratory examination was unremarkable, with no wheezing or rhonchi. Abdominal examination revealed a soft, non-tender abdomen, with no signs of ascites or palpable masses; bowel sounds were present. The extremities were warm without pitting oedema.

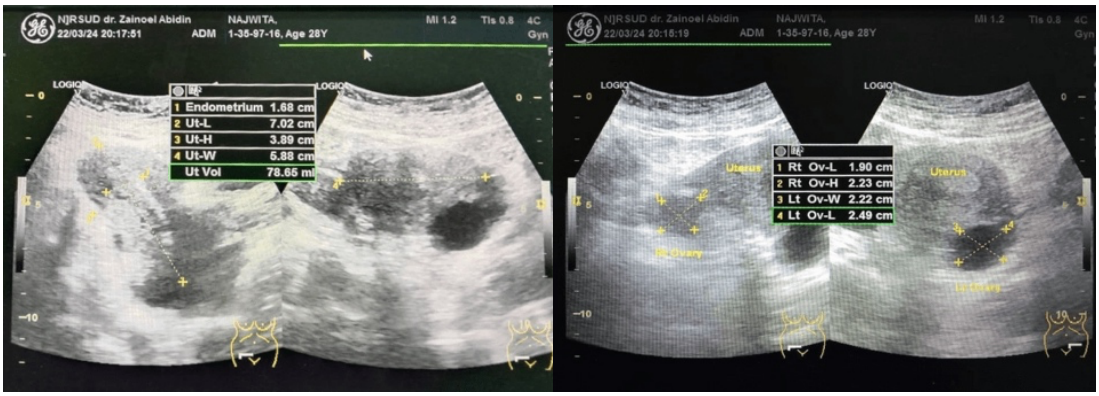

Figure 1. USG Imagery

Gynaecological examination revealed no vaginal bleeding. Speculum examination revealed a nodular cervix with a visible cervical mass approximately 5 cm in size and positive for abnormal discharge. Bimanual examination confirmed a 5 cm friable cervical mass involving the anterior third of the vagina. The uterine cavity was not enlarged, no adnexal masses were palpated, the pouch of Douglas was not prominent, and the parametrium was freely movable.

Hematological findings included hemoglobin 9.9 g/dL, hematocrit 31%, platelets 355,000/mm^3, leukocytes 11.75 x10^3/mm^3, SGOT/SGPT 17/20 U/L, and BUN/Creatinine 17/0.73 mg/dL. Transabdominal ultrasonography revealed an anteflexed uterus measuring 7.02 × 3.89 × 5.88 cm with an endometrial thickness of 1.2 cm, homogeneous myometrium, right ovary 2.10 × 2.23 cm, left ovary 2.22 × 3.49 cm, and no free fluid.

Impression: Stable gynaecological findings. Cervical biopsy confirmed nonkeratinizing squamous cell carcinoma.

Based on the clinical history, physical examination, and supporting investigations, the patient was diagnosed with Stage IIA2 cervical cancer with a bulky tumour. Management included patient stabilisation, chemotherapy using the Fancopac and Carboplatin regimen, and preparation for radical hysterectomy via laparotomy. Postoperative diagnosis: post-radical hysterectomy via laparotomy, bilateral salpingo-oophorectomy, and bilateral pelvic lymphadenectomy for Stage IIA2 cervical cancer with a bulky tumour and a history of two caesarean sections.

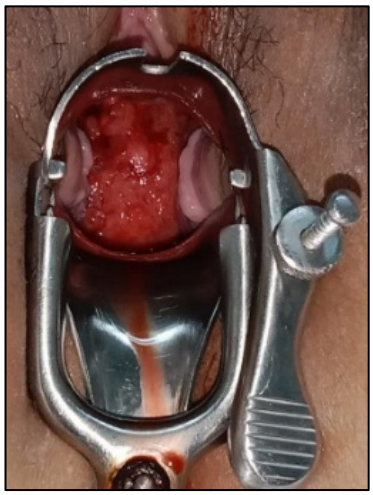

Figure 2. Stage IIA2 cervical cancer with bulky tumor

DISCUSSION

Cervical cancer is a malignancy that originates in the cervix. The cervix constitutes the lower third of the uterus, has a cylindrical and protruding shape, and connects to the vagina via the external ostium uteri externum [1]. In terms of size, the term "bulky" refers to a mass that is large relative to its weight or too large to be easily grasped. Although there is no universally accepted definition of a "bulky tumor" in gynaecologic malignancies, it generally refers to a tumour measuring ≥4 cm in diameter [2,3]. Locally advanced cervical cancer (LACC) commonly refers to FIGO 2009 stages IB2–IVA cervical cancer, whereas a narrower definition of LACC typically refers to stages IB2 and IIA2 [4].

According to the Global Cancer Observatory 2020, cervical cancer is the fourth most frequently diagnosed cancer among women worldwide and the second most common cancer in low- and middle-income countries (LMICs). In the United States, recent statistics estimate 13,800 new cases of cervical carcinoma with 4,290 associated deaths [5]. A 2020 study by Nam Hoang Dang Phan et al. reported 315,346 new cases of cervical cancer in Asia, with 168,411 deaths. Southeast Asia ranked third in Asia in terms of new cases (62,456) and deaths (35,738). In 2020, Southeast Asia ranked seventh globally for incidence and sixth for mortality [6]. According to GLOBOCAN 2018, cervical cancer ranks second in cancer incidence in Indonesia, with 32,469 new cases, and third in cancer-related mortality, with 18,729 deaths. According to IARC's GLOBOCAN 2020 data, cervical cancer cases in Indonesia increased to 36,633 (17.2%) with 23,451 deaths. Approximately 80% of new cases and 85% of deaths occur in developing countries, with over 70% diagnosed at locally advanced stages [7,8].

Numerous studies have shown that the risk of acquiring genital HPV infection and cervical cancer is closely associated with sexual activity. Individuals are at greater risk if they have multiple sexual partners or a partner with a history of multiple sexual partners. Early initiation of sexual activity increases the risk of HPV infection, as does a history of sexually transmitted infections, genital warts, abnormal Pap smears, or personal or partner history of penile cancer [9].

All sexually active women are at risk of developing cervical cancer or its precancerous stages, irrespective of age or lifestyle. Owing to the pathophysiology of HPV infection, women who initiate sexual

activity at a younger age are at a higher risk, as the columnar epithelium of the cervix is more susceptible to metaplastic transformation. Women who have sexual intercourse before the age of 18 years are five times more likely to develop cervical cancer [10]. Typically, cervical mucosal cells mature after 20 years of age. Before the age of 16, these mucosal cells are immature and vulnerable to stimuli, including chemical substances in semen, which can trigger a malignant transformation. Cancer cells proliferate uncontrollably and fail to undergo programmed cell death (apoptosis), leading to tumour formation. In contrast, women engaging in sexual activity after the age of 20 years are less susceptible due to the maturation of cervical epithelial cells [11,12].

In addition to sexual activity, age is a significant determinant of the risk of HPV infection. Most cervical cancers arise at the squamocolumnar junction between the endocervical columnar epithelium and the ectocervical squamous epithelium. This site undergoes continuous metaplastic activity and presents the highest risk of HPV infection, especially during puberty and early pregnancy, with reduced susceptibility post-menopause. HPV prevalence peaked among individuals aged 18–30 years and declined with age. Up to 46% of college-aged women may have genital HPV infections, although cervical cancer predominantly affects women over the age of 35. Having multiple or promiscuous sexual partners increases the risk of sexually transmitted diseases, including HPV infection. Women with six or more lifetime sexual partners have a tenfold increased risk of developing cervical cancer compared with those with a single partner [13,14].

Premalignant cervical lesions are often asymptomatic and self-resolve. When the disease progresses to invasive cancer, the most common symptoms are abnormal vaginal bleeding (e.g. postcoital bleeding) and leucorrhoea. In advanced stages, symptoms may progress to lower abdominal or flank pain due to pelvic tumour compression, leading to ureteral obstruction and potentially oliguria or anuria. Large tumours are often secondarily infected, resulting in foul-smelling discharge that may precede overt bleeding. In very advanced cases, patients may present with pelvic pain, bowel or bladder pressure symptoms, and occasionally, passage of urine or faeces through the vagina [1,5].

A comprehensive physical examination should include lymph node palpation, particularly of the supraclavicular and inguinal nodes, to rule out metastatic disease. On speculum examination, primary cervical lesions may appear exophytic, endophytic, ulcerative, or polypoid in nature. If the tumour originates beneath the epithelium or within the endocervical canal, the ectocervix may appear macroscopically normal. Vaginal extension is typically evident, but subepithelial invasion may be suspected only by the loss of vaginal fornices or the presence of apical stenosis. On bimanual palpation, the cervix typically feels firm (except during pregnancy) and is often enlarged. Cervical size is best assessed via rectal examination, which also helps evaluate the potential extension into the parametria [1].

Clinical evaluation includes cytology, colposcopy, cervical biopsy, cystoscopy, rectoscopy, ultrasonography (USG), intravenous pyelography (IVP), chest radiography, bone scan, computed tomography (CT) scan or magnetic resonance imaging (MRI), and positron emission tomography (PET) scan [1]. The presence of malignant cells in necrotic tissue, blood, and inflammatory cells is characteristic of invasive carcinomas. Differentiation between squamous and glandular cells is usually possible, unless the lesion is poorly differentiated. Pap smears are primarily screening tests for asymptomatic women, with false-negative rates for invasive cervical cancer reaching up to 50% [1].

Any apparent tumour growth or ulceration should undergo an office punch biopsy or loop excision for histopathological confirmation. A cervix that appears indurated or enlarged should also be biopsied, and endocervical curettage should be performed. If the cervix appears normal but symptoms or abnormal Pap smear results are present, colposcopy is indicated for further evaluation. If invasive carcinoma cannot be definitively diagnosed by biopsy, diagnostic conization may be required [1].

CONCLUSION

Cervical cancer is a common malignancy among women, ranking as the fourth most prevalent cancer worldwide, with Indonesia having the second highest incidence rate. Cervical cancer progresses through stages I to IV. The pathogenesis of cervical cancer begins with a precancerous lesion known as Cervical

Intraepithelial Neoplasia (CIN), which marks the initial transformation toward invasive cervical cancer. These precancerous lesions are characterised by abnormal cellular structural changes that can lead to cancer. Cervical cancer is primarily caused by infection with oncogenic types of Human Papillomavirus (HPV), particularly those involving the viral oncogenes E6 and E7. Other contributing risk factors include exposure to mutagenic agents, hormonal influences, cigarette smoking, multiple sexual partners, and contraceptive use. Radical hysterectomy following neoadjuvant chemotherapy (NACT) in patients with bulky cervical tumours has been shown to improve perioperative outcomes.

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T.M.H. conceptualised the study, collected the data, wrote the manuscript, and approved the final version. H. contributed to the data analysis, edited the manuscript, and approved the final version. Both authors contributed equally to the design, execution, and preparation of the manuscript.

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