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Anal canal cancers

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ABSTRACT

Although anal canal cancer is rare, its incidence has increased in the last 30 years, especially in young men. The most common pathological type is squamous cell carcinoma. Definitive histopathological diagnosis is made by biopsy. "American Joint Committee on Cancer" (AJCC) TNM staging is used for staging. The standard approach in treatment is radiochemotherapy, and surgery is applied in persistent or recurrent failure.

Keywords: Anal canal cancers, surgery, radiotherapy, chemotherapy

INTRODUCTION

Anal canal cancers are rare and constitute approximately 3% of all gastrointestinal malignancies. Human immunodeficiency virus is considered as the most important risk factor. Due to the increasing prevalence of (HIV) and Human papilloma virus, there is an increase in the diagnosis of anal canal cancer (1-3). Cervical dysplasia, transplant recipients, autoimmune disorders, number of sexual partners, anal intercourse status and smoking are also risk factors.

Male gender, T3-T4 and node positivity, HPV negativity, smoking, presence of anemia and HIV positivity are bad prognostic factors in anal canal cancers. As of 2019, the number of newly diagnosed patients is approximately 8300 annually (4). Its incidence is 1/100,000 for women, 0.5-0.8/100,000 for men, and it is usually seen between the ages of 60-65 (5).

Tumors from the anal verge to 2 cm beyond the linea dentata are defined as anal cancer, and tumors beyond 2 cm are defined as rectal cancer. The average length of the anal canal is 3.5-4 cm, and it is defined as surgical and anatomical anal canal. The anatomical anal canal is between the anal verge and the dentate line, and the surgical anal canal is the 3-4 cm section between the anal verge and the anorectal ring (6).

Anal canal cancers are mostly squamous cell cancers (60%), followed by transitional cell (25%) and adenocancers (7%). Malignant melanoma, small cell cancers and basoloid cell cancers, which have a high risk of metastasis, are also rarely encountered (7).

DIAGNOSIS

Patients with anal cancer often present with a variety of symptoms that can be hard to distinguish from benign anorectal disease, often hemorrhoids. Rectal bleeding, straining during defecation, pain and itching around the anus are the most common symptoms. In addition, they can occur as a mass, non-healing ulcer, discharge, fecal incontinence and fistula. Anal cancers usually give symptoms in the early period.

In general, the initial evaluation of a patient with suspected anal canal cancer requires a detailed history and physical examination, including anal verge inspection, digital rectal examination, inguinal lymph node palpation. The biopsy required for diagnosis is usually taken during a rectal examination under anesthesia and endoscopic evaluation of the colon. Computed tomography of the thorax, abdomen, and pelvis for clinical staging, magnetic resonance imaging of the pelvis to evaluate local invasion of the tumor and pelvic/inguinal lymph nodes are used fort he diagnosis. In recent years, fluodeoxyglucose-positron emission tomography is also used to evaluate treatment response in terms of better evaluation of nodal status and distant metastases.

STAGING

American Joint Committee on Cancer (AJCC) TNM staging is used for anal cancers. According to the 8th edition of AJCC, the definitions of N2 and N3 nodal stages were removed, and the N1 category was divided into three subcategories as N1a, N1b and N1c. Tis high, defined as

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carcinoma in situ, Bowen's disease, anal intraepithelial neoplasia II-III, high grade anal intraepithelial neoplasia Grade squamous was defined as squamous intraepithelial. In addition, with new staging, perianal skin cancers in the anoderm region between the anal inlet and the intersphincteric groove; the skin is staged and treated like anal canal cancers, not squamous cell cancer. Anal canal TNM staging is summarized in **Table 1** and anatomical staging is summarized in **Table 2** (7).

Table 1. TNM staging in anal cancer (AJCC 8th edition)

Primary tumor (T)	
T	T criteria
TX	Primary tumor unspecified
T0	No evidence of primary tumor
Tis	High grade squamous squamous intraepithelial lesion
T1	Tumor ≤2 cm
T2	Tumor >2 cm but ≤5 cm
T3	Tumor >5 cm
T4	Tumor of any size but adjacent organ or organs (such as vagina, urethra, bladder) invaded
Regional lymph nodes (N)	
N	N criteria
NX	Regional lymph nodes cannot be evaluated
N0	No regional lymph node metastases
N1	Metastasis to inguinal, mesorectal, internal iliac, or external iliac lymph nodes
N1a	Metastasis to inguinal, mesorectal, internal iliac lymph nodes
N1b	Metastasis to external iliac lymph nodes
N1c	Metastasis to external iliac lymph nodes + one N1a lymph node metastasis to the node
Distant metastasis (M)	
M	M criteria
M0	No distant metastases
M1	There is distant metastasis

Table 2. AJCC Anatomical staging

Anatomical Stage Groups			
T	N	M	Stage
Tis	N0	M0	Stage 0
T1	N0	M0	Stage 1
T2	N0	M0	Stage 2A
T3	N0	M0	Stage 2B
T1-2	N1	M0	Stage 3A
T4	N0	M0	Stage 3B
T3-T4	N1	M0	Stage 3C
Any T	Any N	M1	Stage 4

TREATMENT

The curative treatment of anal canal cancers was abdominoperineal resection (APR) before sphincter-sparing treatments. The rates of locoregional recurrence after APR were 27-50% and the 5-year overall survival (GSC) rate was 24-62%. Today, APR is used in cases where chemoradiotherapy cannot be performed or in relapses after chemoradiotherapy (8,9)

Although the number of patients suitable for curative local excision is small, local excision; it can be applied for curative purposes in stage 1, smaller than 2 cm in diameter, superficial, only submucosal, mobile and well-differentiated squamous anal cancers. Local recurrence after local excision is 20-78%, and 5-year GCI is 45-85% (10,11).

In a small number of case series in anal canal squamous cancers treated only with radiotherapy, 5-year local control was reported as 100% for tumors 2 cm and below. Local recurrence is 44-51% in these series, with tumor diameter over 2 cm (12,13).

For the first time in 1972, Nigro et al. (14) applied neoadjuvant chemoradiotherapy (5-Fluorouracil (5-FU) and combined RT with Mitomycin C) in the treatment of anal canal squamous cancers. When abdomino-perineal resection pieces were examined, it was found that complete response was obtained in most of the cases.

In the following years, curative radiochemotherapy has been accepted as the main treatment method for stage 1-3 anal canal squamous cancers, as a result of the detection of radiochemotherapy causing a significant increase in local regional control in studies including adjustments of radiation doses and chemotherapy doses (15).

In the results of prospective randomized studies comparing only radiotherapy and radiochemotherapy in anal canal cancer, it was determined that radiochemotherapy significantly increased local control of the locus(16). The most commonly used agents for chemotherapy are Mitomycin C and 5-Flurouracil (5-FU). Bleomycin, cisplatin and doxorubucin can also be given for the same purpose (17-19).

In concomitant therapy, Mitomycin C 12 mg/m² on day 1 of RT 5-FU 1000 mg/m² on days 1 to 4 and days 29 to 32 of RT, or Mitomycin C is administered on days 1 and 29 of 10mg/m² RT, and from days 1 to 4 and days 29 to 32 of 5-FU 1000 mg/m² RT.

As a result of studies investigating effective chemotherapy agents in concomitant chemotherapy, it was concluded that survival and local control without colostomy are better with Mitomycin C, Mitomycin C is more effective than cisplatin, and prolonged chemotherapy does not provide benefit (20,21).

Palliative radiotherapy, palliative chemotherapy, chemoradiotherapy are used in the treatment of stage IV anal cancer. If the patient has received palliative radiotherapy before, one of the abdominoperineal excision options can be applied (22).

Anal canal region radiotherapy is complex due to irregularity of target volumes and proximity to critical dose-sensitive structures such as the small intestine, femoral heads, perineum and external genitalia. Early complications of radiochemotherapy include dermatitis, diarrhea, cystitis, urgent need for defecation, fatigue, and bone marrow suppression. Late complications are proctitis, rectal bleeding, fecal incontinence, narrowing of the small intestine and malabsorption. Rarely, the need for colostomy arises due to worsening of rectal functions (23). In retrospective series, recurrences of 35-46% in the pelvic lymph nodes and 13-16% in the inguinal lymph nodes after surgery revealed the necessity of including the pelvic and inguinal lymph nodes in the radiotherapy area (24,25). After intensity modulated radiotherapy technique (IMRT) and volumetric arc therapy (VMAT), side effects were found to be less than after conventional radiotherapy technique, resulting in better quality of life and less treatment interruption rates. Reduction in gastrointestinal and skin toxicities and 2-year local regional control was reported as 80% after treatment, and IMRT/VMAT, which are more conformal techniques, is recommended in radiotherapy planning.

The optimal radiotherapy dose and scheme in the treatment of anal canal squamous cancer is still being investigated, and the recommended total radiation dose is usually 50-54 Gy. The results of using higher doses are uncertain and studies are ongoing.

In anal canal tumors, regression is slow after chemoradiotherapy and a response is observed in an average of 3 months, this period is 12 months for some patients. After simultaneous chemoradiotherapy, rectal examination and inguinal lymph node examination are performed 8-12 weeks after the completion of treatment. Since magnetic resonance imaging is not beneficial in the early period, it is not recommended. In patients with residual disease, examination should be continued once a month, and biopsy should not be performed if no progression is observed at 8-12 weeks. Biopsy should be postponed until progressive disease is detected by physical examination (26). After a complete response, patients are treated every 3 months for the first two years, and every 2 years for 5 years.

CONCLUSION

Anal canal cancer is a rare cancer, and the main goal in treatment is to maintain local regional disease control and to preserve anal functions to improve quality of life. Curative radiochemotherapy is the main treatment modality. Surgery is recommended in persistent or recurrent disease. Today, radiotherapy doses and schemes continue to achieve a more effective response.

ETHICAL DECLARATIONS

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