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UROLOGICAL ONCOLOGY

Modern diagnostic and treatment regimens are needed to achieve the best cancer and quality of life control

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Penile cancer is a very rare disease, with incidence and mortality of 0.3% and 0.2% in Poland, respectively [1]. In 2010, 232 new cases were diagnosed (standardized rate 0.8/105) and 89 patients died from the disease (standardized rate 0.2/105). Most new cases and deaths were observed in men aged over 50, with a slight improvement in one– and five–year survival rates in the last 10 years [1].

The clinical symptoms of penile cancer are highly diverse (from erythematous plaques and indurations to more verrucous and exophytic lesions that may coalesce into an irregularly shaped mass). The initial abnormal changes may be difficult to recognize, both for the patient and the physician, particularly if the lesion is accompanied by phimosis. The risk factors of penile cancer include phimosis, lack of circumcision, chronic inflammatory conditions (poor hygiene), multiple sexual partners, history of smoking, HPV and HIV infections [2]. Psychological problems are still the most important reasons for the delay in reporting to the doctor. Shame, embarrassment, reluctance to undress in front of the doctor, and the threat of losing the attribute of masculinity associated with a potential surgical treatment are significant barriers to an early contact with the doctor.

Despite a large effort made to build a health–conscious society and raising awareness of the relationship between risk factors and diseases, e.g. bladder cancer and smoking, there seems to be a great need for discussion in the community about cancer of the penis, as well as testicular cancer. Most likely, a leading role in the education and diagnosis should be played by urologists, who are perfectly familiar with the natural course of these rare cancers.

Another important aspect to consider is the quality of life (QoL) of patients during the treatment process. Health related quality of life is defined as a subjective assessment of one's position in life made during the illness and treatment, which is not the same as health [3]. QoL is a functional effect of the disease and its treatment, as experienced by the patient. Psychooncology considers QoL, in addition to the survival rate, to be a main factor defining the quality of cancer diagnostic and care.

The authors of the study "Metastatic penile carcinoma – an update on the current diagnosis and treatment options" published in this issue of CEJU, accurately show what modern effective diagnostics should look like [4]. Careful medical history taking and physical examination, the use of appropriate diagnostic techniques, e.g. 18F–FDG–PET/CT or dynamic sentinel node biopsy (DSNB) in selected patients is crucial for the correct clinical staging.

The choice of a therapeutic method for penile cancer patients depends on the clinical and pathological stage. The scope of the treatment may range from conservative management (topical cream), the use of minimally invasive techniques (e.g. laser, Mohs procedure) to different types of surgical procedures (from partial to total penectomy). Depending on the extent of damage to the penis, we observe a negative impact on the sexual function, psychological well–being, the quality of life, and the occurrence of possible post–traumatic stress disorder [5]. Because the majority of patients will have a long 5– and 10–year disease specific survival, the mutilating treatment of the penis should be limited to a minimum [6]. Unfortunately, there are no available standardized tools or interventional pathways to properly measure and identify the psychological and sexual dysfunction in this group of patients. Well–designed multicentre studies are needed to enable the identification of patients who require intervention [7].

Chemotherapy is becoming an important part of multimodality treatment of penile cancer. Yet, as underlined in the article of Barski et al. [4], experience with chemotherapy in this particular malignancy is limited due to small and inhomogeneous

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groups of patients included in clinical analyses. Cytotoxic treatment is used in neoadjuvant, adjuvant or metastatic setting [8]. Neoadjuvant chemotherapy is supposed to downstage the tumor to enable surgical resection and prevent microscopic spread; this usually refers to bulky unresectable inguinal lymph nodes or pelvic lymph nodes involvement. The most effective chemotherapy regimen is still under debate but cisplatin is clearly considered the cornerstone of the treatment. Recently, four cycles of TIP (paclitaxel, ifosfamide, cisplatin) have been recommended by many authors as the optimal regimen in patients fit for cisplatin (overall response rate 50%, stable disease 30%, progressive disease 20%) [9]. Another triplet, TPF (paclitaxel, cisplatin, 5–fluorouracil) has been advocated by others. Combination treatment offers a higher response rate at the cost of significant or even unacceptable toxicity. Although supported by less evidence, adjuvant chemotherapy is recommended in resected pN2–N3 patients.

Disseminated disease is unfortunately incurable and chemotherapy in this setting is aimed to modestly prolong survival and time to progression or alleviate disease–related symptoms. Yet, the prognosis remains poor. The most common regimens include: PF (cisplatin, 5–fluorouracil), TIP (paclitaxel, ifosfamide, cisplatin), PG (cisplatin, gemcitabine) or cisplatin with irinotecan [8]. In most analyses, partial remission can be achieved in 20–33% of patients. Due to older age and comorbidities (kidney insufficiency, cardiovascular diseases, inability to tolerate long intravenous hydration) many patients are unfit for cisplatin. Such patients can be challenged with paclitaxel–carboplatin doublet or monotherapy (paclitaxel, methotrexate). It should be stressed that regimens containing bleomycin should now be avoided in view of a high risk of lung toxicity in this patient population (older age, present or former smokers, often compromised lung capacity).

Barski at al. agree that more high–volume multicenter trials are urgently needed to better understand the role of chemotherapy in penile cancer patients and to improve the level of evidence available [4]. The following issues may be of further interest in this disease:

- Chemoradiotherapy with cisplatin, as it proved active in other squamous cell carcinomas, e.g. cervical cancer or head and neck tumors;
- Direct comparison of different regimens;
- Epidermal growth factor receptor (EGFR)–targeted therapy, e.g. cetuximab, already approved in head and neck carcinomas [10].

The paper of Barski et al. [4] fully summarizes the role of proper diagnosis (clinical examinations imaging and invasive diagnostics) as well as treatment (surgical and chemotherapy) in penile cancer patients and outlines the issues for the future.

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