Carcinomas and sarcomas of Bartholin gland. A report of nine cases and review of the literature

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Summary

The greater vestibular gland, also called Bartholin's gland after the Danish anatomist Caspar Bartholin the Younger who first described it in the 17th century, is the site of tumours arising from different types of epithelium and characterized by a different clinical course. In the years 1980-2009, 1,296 patients with vulvar carcinoma were treated at the Oncology Centre in Warsaw, Poland and nine of them had carcinoma of Bartholin's gland, including three patients with squamous cell carcinoma (SCC), three patients with adenoid cystic carcinoma (ACC) and three patients with sarcoma. In this paper the authors present the signs and symptoms, clinical course, treatment outcomes, and recurrence of these three malignant tumours of different histopathology. Own observations and evaluation of treatment results are compared with published reports from other centres. Interestingly, there is no consensus regarding diagnostic criteria or a uniform approach to management. Relatively poor knowledge of malignant tumours of Bartholin's gland seems to be responsible for delays in proper diagnosis and hence optimal management. When instituted, the treatment is usually aggressive and involves adjuvant radio- and chemotherapy, while the chances of longer disease-free survival after treatment may be compromised. *Conclusion:* Bartholin sarcomas grow fast and invasive, SCC, and ACC infiltrate slowly and systematic. All types are curable at high interest rates if they are originally from the surgically removed lymph nodes on both sides and irradiated.

Key words: Squamous cell carcinoma of Bartholin's gland; Malignant tumours of Bartholin's gland; Vulvar carcinoma; Adenoid cystic carcinoma; Leiomyosarcoma of Bartholin's gland.

Introduction

The greater vestibular gland was named Bartholin's gland after the Dutch anatomist Caspar Bartholin the Younger who first described its anatomical position in 1675. Some 190 years later, in 1864, J.M. Klob was the first to report a case of a patient with a malignant tumour arising from the Bartholin's gland. The structure of the gland was first described by T.S. Cullen in 1905.

The two Bartholin glands are the largest compound tubuloalveolar glands located on either side of the posterior part of the vestibule of the vagina below the bulbocavernous muscle inside the perineum. The secretory duct of the gland, which is two cm in length, runs diagonally and superiorly and opens below the urethra near the vaginal introitus. The duct is lined with the transitional epithelium and then the glandular epithelium with low columnar epithelium. In the alveoli of the gland, high columnar epithelium is found. Myoepithelial cells constitute the basal cell layer of the glandular epithelium and they are capable of multidirectional differentiation. Glandular cells, both low and high columnar cells, secrete mucus [1-4].

Malignant tumours of Bartholin's gland are extremely rare as they are thought to account for less than one percent of all vulvar malignancies. These are predominantly primary cancers arising from the epithelium lining the opening of the gland duct. Like vulvar cancer, they are keratinizing or non-keratinizing squamous cell carcinomas (SCCs). To date, approximately 300 cases have been reported. The peak incidence of SCC is after menopause. The tumours develop along the duct of the gland and deeply infiltrate the adjacent tissue. They grow slowly and do not cause any pain or other symptoms. They may achieve a considerable size, are located in the orifice, and very rarely cause overlying skin ulceration [1-3, 5-7].

Adenocarcinomas originate in the cells of tubules and alveoli of Bartholin's gland or in the glandular cells of the ducts and tend to grow deep into the perineal tissues along the nerves. Adenocarcinomas are rare and they include adenoid cystic carcinoma (ACC), papillary carcinoma originating in transitional epithelium, and mucus-secreting carcinomas like mucoepidermoid carcinoma or mucinous adenocarcinoma [1,4]. Adenocarcinoma presents as a firm solid tumour, which forms a bulge in the skin of the labium, is frequently cyst-like, and contains mucoid material.

ACC is a specific variant of adenocarcinoma and was first recognized in 1853. Initially it was described in salivary glands but subsequently other locations were identified such as breast, skin, and lung. In women, ACC is most commonly found in the cervix. To date, 64 cases of ACC found in Bartholin's gland have been reported. This variant of carcinoma usually occurs in middle-aged women, the median age at presentation being 49 years. ACC often presents as pain or pruritus which may precede the actual tumour. ACC is a slow-growing tumour, which resembles inflammation or abscess and accordingly in most cases is

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Table 1. — Summaries of patients with malignant tumours of the Bartholin gland treated in the years 1980-2009.

	Patient first treated in year	Patient's age lesion observation	Side	Lesion size and appearance	Primary treatment	Histopathology	Stage	Adjuvant treatment Recurrence treatment	Treatment outcome Follow-up
1.	BR** 1980	57 14 months	R+L	4 cm; rectovaginal fistula, ulceration	RV+BGND	Infiltrating macrocellular carcinoma	T3N2M0	**Excision … 1983, 1985. 1989	NED 13 13 years
2.	BE** 1988	75 24 months	R	5 cm; Ulceration, infiltration	RV	Squamous cell carcinoma	T4N2M0	**Excision	DOD 3 years Local recurrence
3.	GU** 2000	42 20 months	L	Ca. 6 cm in diameter; nodule, no ulceration	EX	Squamous cell carcinoma	T3N0M0	RV+BGND	NED 6 years
4.	EB 1991	20 6 months	R	15x8 cm; ulcerated lesion penetrating to bone	EX	Embryonal small-cell rhabdomyosarcoma	T3N2M0	**Chth+ RV+BGND RT 38 Gy Recurrence 1999 Chth*	DOD 9 years Lung metastases
5.	GA 1991	32 3 months	R	3 cm; raised nodule, no ulceration	EX	Leiomyosarcoma G1	T2N0M0	RT 60 Gy + RV+BGND Lobectomy 1993 9th rib	DOD 4 years Lung and bone metastases
6.	SH 2000	43 3 months	R	3x4 cm; discoid, non-ulcerated tumour	EX	Leiomyosarcoma G2	T3N0M0	RV+BGND	NED 7 years
7.	KW 1999	58 12 months	R	c. 10 cm; overlying skin ulceration	EX+BGND	Adenoid cystic carcinoma	T4N1M0	RT 50 Gy	NED 13 years
8.	KL 2006	51 9 months	R+L	c. 6 cm in diameter overlying skin	EX	Adenoid cystic carcinoma	T4N0M1 Lung metastasis	**Tumour resection + Chth CAP x 6	NED 32 months
9.	PE 1995	50 8 months	R	c. 5 cm in diameter; ulcerated	RV+BGND	Adenoid cystic carcinoma	T2N2M0	RT 48 Gy *** 1999 Uterine Cancer IC/ adenocarcinoma G2	DOD 11 years Disseminated disease

EX – local excision; RV – radical vulvectomy; BGND – bilateral groin node dissection; Chth – chemotherapy; RT – radiotherapy; DOD – dead of disease; NED – no evidence of disease; Chth* CYVADIC; * - recurrence treatment, ** - earlier reported cases [5]; *** another malignancy treated with surgery and EBRT.

initially treated by incision and drainage of the "abscess". The tumour invades deep tissues and spreads along the nerves causing pain, which becomes more severe as the tumour grows. Immunochemistry studies have demonstrated that the tumour cells produce keratins, carcinoembryonic antigen, lysozyme, and lactoferrin while steroid receptors are present in the tumour tissue [1, 3, 8, 9].

Sarcomas develop from the Bartholin gland's mesoderm. Depending on their differentiation and morphology, they may form solid tumours, with well or poorly defined borders, e.g. leimyosarcoma which is derived from smooth muscle. Another malignant neoplasm of Bartholin's gland is rhabdomyosarcoma which is poorly differentiated and derived from striated muscle. It has features of a germ cell tumour of muscle origin with considerable invasiveness [2]. Epithelioid sarcomas with the location in Bartholin's gland have also been reported. Sarcomas are diagnosed in young women and may develop during pregnancy [10-12]. Initially sarcomas are considered benign lesions but are rapidly growing tumours and may be soon over five cm in diameter with overlying skin ulceration and metastases to the inguinal, femoral, and pelvic lymph nodes. There are some slight differences between particular types of sarcoma concerning incidence but virtually no differences in their clinical course [2, 10-13].

Bartholin's gland is also the location where lymphomas, melanoma, neuroendocrine tumours, vascular tumours, transitional cell carcinoma and other, even less common, malignancies may develop [14-17].

Since malignant tumours of the Bartholin's gland are so rare, it has been difficult to develop the criteria for their recognition, differential diagnosis, and management [9, 18-20].

The diagnostic criteria for differentiating Bartholin's gland carcinoma from vulvar carcinoma were established by Honan in 1897. In 1972, they were modified by D.L. Chamlian and H.B. Taylor from the Armed Forces Institute of Pathology and are currently in use worldwide. Microscopic evaluation of the specimen must demonstrate some normal gland tissue and tumour tissue. In patients with Bartholin's gland tumour, it is necessary to exclude any other tumour with a similar microscopic structure. Frequently this is very difficult as distinguishing the Bartholin gland structure in

Table 2. — The effect of risk factors on recurrence and survival.

Patient	Para	Family history of cancer	Pain at the tumour site	Lymph node involvement Blood vessels involvement	Margins after primary resection	Recurrence	Survival
1. B.R.	1	Negative	No pain	Bilaterally involved groin lymph nodes Blood vessels NAD	Neg.	Recurrence occurred three times in the 3, 5, 8 year of observation	13 years
2. B.E.	1	Father: colon cancer	Pain +	Bilaterally involved groin lymph nodes Blood vessels NAD	Pos.+	Recurrence occurred once in the three years of observation	3 years
3. G.U.	1	Negative	No pain	Lymph nodes neg. Blood vessels NAD	Neg.	No recurrence	6 years dead of cancer-unrelated disease
4. E.B.	0	Negative	Very severe pain +++	Bilaterally involved groin lymph nodes. Blood vessels pos.	Neg.	Recurrence occurred two times in the 8 months, and 8 years of observation	9 years
5. G.A.	2*	Negative	Severe pain ++	Lymph nodes neg. Blood vessels pos.	Neg.	No recurrence (double distant metastases)	4 years
6. S.H.	1	Negative	Severe pain ++	Lymph nodes neg. Blood vessels neg.	Pos.	5 months	7 years
7. K.W.	5	Mother: stomach cancer Father: bladder	Pain + stinging, burning, increasing in intensity	Unilaterally involved lymph nodes. Blood vessels neg.	Pos. +	No recurrence	13 years
8. K.L.	2	Both grandmothers: cervical cancer	Pain + prickling, throbbing, increasing in intensity	Lymph nodes neg. Blood vessels neg.	Pos. +	No recurrence	32 months
9. P.E.	1	Sister: breast cancer	Pain + burning, increasing at night	Bilaterally involved groin lymph nodes. Blood vessels neg.	Pos. +	No recurrence	11 years dead of cancer-unrelated disease

*The only patient in the group who had used oral contraceptives for five years prior to onset of the disease.

cases of diffuse invasion may be not feasible. Both sets of criteria rely on the subjective evaluation by the pathologist and gynaecologist. At present, a new classification could be established based on more objective molecular criteria, such as p53 protein expression, the presence of Ca 19-9 as a cancer marker or the use of immunohistochemistry methods to demonstrate desmin, actin or vimentin. Molecular methods could be used for precise and reliable differential diagnosis of vulvar malignancies [7, 18-23].

Materials and Methods

The study was based on the retrospective review of the medical records of patients treated at the present institution. All data concerning the patients are summarized in two tables. Table 1 presents such patient data as treatment duration, age, follow-up time, lesion size, type of tumour infiltration, histopathology findings, and primary treatment and its outcome. Table 2 summarizes the impact of risk factors on tumour recurrence and patient survival.

In the years 1980-2009, 1,296 patients were treated for vulvar carcinoma at the Oncology Centre in Warsaw. Three patients had SCC of Bartholin's gland [5], three had sarcoma (proximal-type epithelioid sarcoma (PES) in two patients, and malignant rhabdoid tumour (MRT) in one patient, and three had ACC.

Results

The patients' ages ranged from 20 to 75 years. The lesions were followed up for three to 24 months. In all patients, the primary treatment was surgical. Vulvectomy was performed in three patients and radical vulvectomy with bilateral inguinal lymph node dissection in two patients. The tumour size was described as T2 in two patients, as T3 in three patients, and as T4 in four patients. Primarily involved lymph nodes were found in five patients and in none was tumour dissemination identified. Of those five patients, four were subsequently treated with adjuvant radiotherapy and one underwent radical vulvectomy with lymph node dissection. During the follow-up, disease recurred in four patients within five months to three years of the primary treatment. In one patient, metastases to the

Table 3. — *Differentiating features of most common malignant tumours of Bartholin gland (based on the literature and own material).*

	Squamous cells carcinoma	Adenoid cystic carcinoma	Sarcoma (epithelioid PES and rhabdoid MRT)
Incidence rate (of all malignant tumours of Bartholin gland)	ca. 80%	ca. 15%	ca. 2%
When first reported in the literature	In 1864 by J.M. Klob	In 1853 first reported in the salivary glands	In 1970 by F.M. Eninzer
Peak incidence	After menopause	Median age 49 years	Young adult women, menstruating
Pain	No pain initially, then pain increasing in intensity	Severe from onset, burning	No pain initially
Lesion	Inflammatory lesion deeply infiltrating surrounding tissues, often ulcerated	Along the nerves, cyst-like with diffuse infiltration of the surrounding tissues	Large tumour which soon becomes ulcerated
Growth rate	Variable, 3 to 70 weeks reported	Slow, constant	Rapid, constant
Predominant clinical features based on the literature	Lesion progressively increasing in size with late ulceration and involvement of lymph nodes	Very frequent recurrences: – following 68% of vulvar-sparing surgery procedures – following 43% of radical surgery procedures	Frequent puncture and incision of "abscess" does not yield any material. Early local recurrences and distant metastases
Treatment of choice	Radical surgery with bilateral femoral and inguinal lymph node dissection. RT+CHTH when margins positive and metastases present, RT + CHTH	Local excision in early stages, in advanced stages radical dissection and RT to prevent local cancer recurrence	Radical surgery with a wide margin excision (2 cm) followed by RT (recurrence rate of 71% without RT vs. 14% when RT used)
Outcome	Local recurrence after non-radical treatment. 5-year survival; 33-84% of patients Recurrence rate: 25% at 30 years	Frequent distant metastases treated with CHTH	Shorter survival when tumour > 5 cm on diagnosis; cancer cells in blood vessels; distant metastases in 50% of patients, recurrence in 85%.

lungs were diagnosed two years after treatment and to the ribs after four years. Another patient suffered lung metastases and recurrence after eight years. Both patients with the disseminated disease were initially diagnosed with Bartholin gland sarcoma. In one patient, another malignant tumour, adenocarcinoma of the endometrium, was diagnosed four years after treatment for Bartholin gland carcinoma. The second malignancy was treated with surgery and adjuvant radiotherapy. Overall, the survival ranged from three to thirteen years.

Evaluation of the risk factors and their impact on the recurrence and treatment outcome are presented in Table 2. In the group of nine patients, one was nulliparous and the others had from one to five children. Four patients had a positive family history of cancer (three patients with ACC and one patient with SCC of Bartholin's gland). Three patients with diagnosed sarcoma reported severe or very severe continuous pain. Increasing pain described as burning, itching, or stinging sensation was experienced by patients with ACC.

Bilateral lymph node involvement was found in four patients and unilateral involvement in one patient. In only one of these patients were cancer cells found in the blood vessels. In the other patients with cancer cells in the blood vessel lumen, there were no metastases to the lymph nodes. Resection margins of the first operation were positive in five of the patients. Despite these unfavourable prognostic features, the survival ranged from three to 13 years.

Discussion

Malignant tumours of Bartholin's gland are rare conditions. This paper presents cases of three different types of Bartholin gland malignancies i.e. SCC, adenocarcinoma, and sarcoma. SCC accounts for ca. 80% of all malignant tumours of the Bartholin gland, adenocarcinoma for ca. 15%, and sarcoma for ca. 2%. The reports of cases published in the literature are equally few. Up-to-date approximately 300 cases of SCC of Bartholin gland have been reported, 64 cases of ACC, and only single case of sarcoma [2, 3,5-7,21,22,24-26].

Slow development of the tumour and absence of characteristic symptoms of malignancy often delay the correct diagnosis. Not infrequently, gynaecologists do not suspect any malignancy and manage all lesions of Bartholin's gland as inflammation or abscess.

It is a well-known fact that an early diagnosis makes early treatment possible with the relief of the troublesome symptoms and improved chance of enduring cure. When a malignant tumour of Bartholin gland is not differentiated from its abscess or vulvar carcinoma, treatment is delayed, which may affect its outcome.

The management of patients with vulvar carcinoma must be prompt and aggressive using very radical methods. A long period of observation before the treatment is instituted may produce a less successful outcome. Initially, malignant

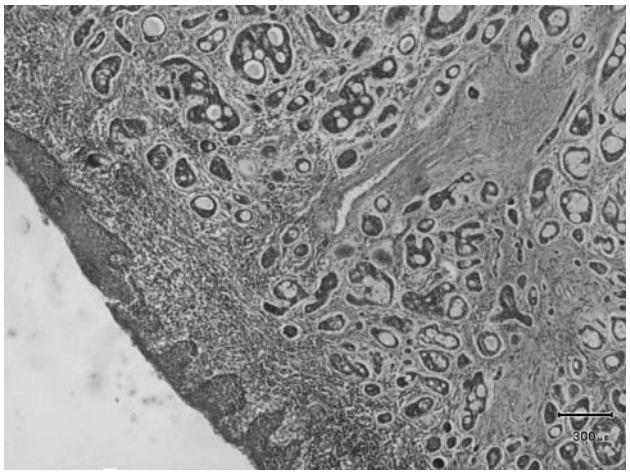

Figure 1. — Adenoid cystic carcinoma (HE x5).

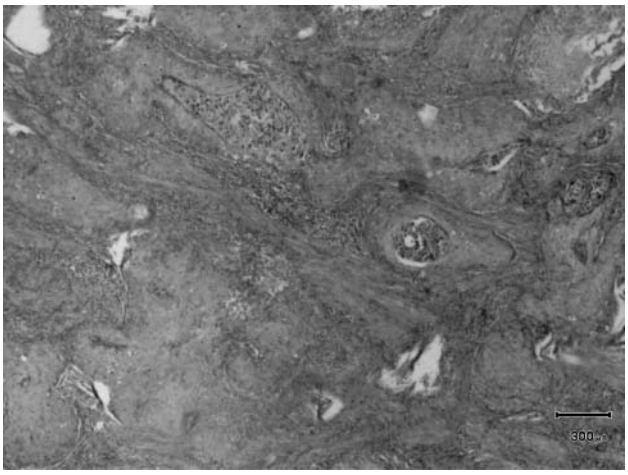

Figure 2. — Squamous cell carcinoma (HE x10).

tumours of the Bartholin gland – SCC, ACC or sarcoma – run a slower course than vulvar carcinoma, while their radical surgery and adjuvant radiotherapy may result in longer disease-free survival than in vulvar carcinoma.

The clinical courses of three types of malignant tumours of Bartholin's gland described in this paper demonstrate their distinct clinical features and require to employ special treatment. Only small series of cases are reported in the literature and drawing definite conclusions is often difficult. As there are no universally recognized diagnostic and management standards, the present authors evaluated the cases with the aim of proposing appropriate management. The characteristic features which allow the differentiation of the three types of Bartholin's gland malignancies are presented in Table 3 which summarises these differentiating features.

Initially, the tumour develops slowly and in the described patient group the duration of presenting symptoms, i.e. the interval from the reported onset of symptoms to the appropriate diagnosis was three to 24 months, which is also reported by other authors. The age at onset ranged from young adulthood in patients with a sarcoma of Bartholin's gland to premenopausal women in their forties with ACC to postmenopausal patients with SCC [3, 5-7, 27].

SCCs often present as long and slowly, growing tumours with features of inflammation. After reaching a larger size, the tumours become ulcerated with pain and metastases to the lymph nodes [5-7].

Symptoms such as itchiness and burning are reported by patients with ACC only. These symptoms are associated with the infiltration by the tumour spreading along the nerves from the onset of the disease and increase in intensity with the tumour development, although they may occur before the Bartholin gland begins to enlarge. The gland enlargement produces a continuous pain which becomes increasingly severe. Ulceration and deep penetration into the surrounding tissues are commonly observed. Initially, the pain is described as nagging and troublesome rather than severe and it is seldom relieved by analgesics. Patients with ACC require wide vulvectomy with bilateral dissection of the inguinal and femoral lymph nodes. Adjuvant radiotherapy is mandatory in all patients whether there are any cancer cells in the dissection line/resection margins or not. The patients should undergo a general evaluation as ACC may produce distant metastases, mostly to bones and lungs before the regional lymph nodes become involved. In such cases chemotherapy is recommended. A five-year progress-free interval is 43% and overall five-year survival rate is 71%, the corresponding rates being 38% and 50% at ten years and 13% and 51% at fifteen years [6-11, 28-30].

Bartholin gland sarcomas rapidly infiltrate the surrounding tissues and become ulcerated. The lesions are diagnosed as abscesses, not malignancies and repeated incisions are performed. Pain is reported only when the malignancy involves a large area of the surrounding tissues. The tumour size on diagnosis is an important predictive factor since some authors have reported worse treatment outcomes and more frequent distant metastases with lesions over five cm in diameter. Leiomyosarcoma occurred during pregnancy and steroid receptors for estrogens and progesterone were found in the tumour tissue and that is why its etiology was linked to hormone therapy [12, 24, 27]. In this study, only one patient used oral contraceptives.

To date, nine cases of epithelioid sarcoma have been reported in the international literature. The tumour presents as a painful abscess or ulceration with central necrosis or, at times, as multinodular ulceration. In eight of the nine patients, recurrence was observed after the excision of the primary lesion and in five distant metastases [12, 26, 27]. All types of sarcomas reported so far required radical vulvectomy combined with dissection of the inguinal and femoral nodes in patients with metastases to the lymph nodes. Prog-

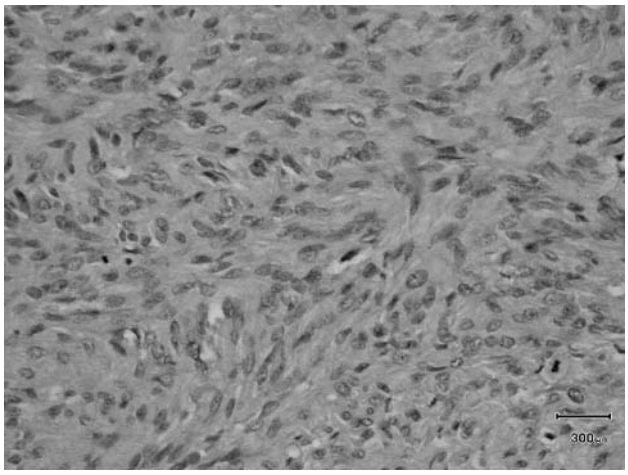

Figure 3. — Leiomyosarcoma (HE x20).

nosis continues to be poor with recurrence in 77% of the patients and distant metastases in 55% [12, 31-33].

All of the patients, in whom malignancy was diagnosed in the excision line of the primary surgery underwent another surgery (Patients 2, 6 and 8) or adjuvant radiotherapy (Patients 7 and 9). One (Patient 2) died despite the treatment and the other patients survived for 16 months to 11 years.

Involvement of the lymph nodes is an important predictive factor in malignant tumours of Bartholin gland. Cases of contralateral lymph node involvement have been reported [3,34]. According to many authors, metastases to lymph nodes are found in most patients (55%) [7]. In a series of 11 cases of Bartholin gland carcinoma, nine patients had bilateral metastases to the lymph nodes. The author advises bilateral dissection of the lymph nodes [30, 35]. However, there is no consensus concerning dissection of lymph nodes, especially in cases of early-diagnosed lesions. Monika Hampel, who analysed metastases of vulvar carcinoma to the sentinel nodes, found that bilateral involvement was associated with the location of the primary lesion on the vulva as midline tumours spread bilaterally. Considering the position of Bartholin's gland, its malignant tumour is likely to spread bilaterally, especially as the vulvar region is characterized by a considerable anatomical variety in the course of the lymphatic channels [36, 37].

Based on the reports in the literature, the best treatment outcomes with the highest rates of recurrence-free survival in all types of Bartholin gland malignancies are observed with radical excision of the tumour (in cases of sarcoma the margin must be at least two cm) and bilateral dissection of the lymph nodes, followed by radio and chemotherapy.

Chemotherapy is proposed as the treatment for metastases in cases of adenocarcinoma and sarcoma. Hormone therapy is justified solely when estrogen and progesterone receptors are found in the tumour tissue. Vulvar-conserving surgery may be advised in early stages of the disease only. Reported survival rates in different types of Bartholin carcinomas are fairly satisfactory and in none of the groups death was reported within two years after primary treatment. Prognosis was adversely affected by recurrence or metastasis [38-40].

Proposed management of patients with malignant tumours of Bartholin's gland:

1. Prompt microscopic evaluation of the affected Bartholin gland which enlarges in size, even in cases of diffuse edema in the area spreading towards the anal canal, without pain or ulceration;
2. Radical surgery of tumours of Bartholin's gland with bilateral dissection of the lymph nodes;
3. When microscopic examination of the removed tumour tissue finds cancer cells in blood vessels, positive margins or metastases to the lymph nodes, radio and chemotherapy must be instituted and high-dose-rate brachytherapy considered;
4. The patient must be carefully monitored beyond the standard five years, including lymph node status;
5. Recurrence must be treated surgically or with brachytherapy. Distant metastases should be treated by chemotherapy when Hypertrehalosemic hormone (HTH) receptors are positive.

The proposed management based on the latest scientific and clinical knowledge offers a chance of cure for patients with Bartholin gland carcinoma.

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References

[1] Berstein S.G., Voet R.L., Lifshitz S.: "Adenoid cystic carcinoma of Bartholin's gland". *J. Obstet. Gynecol*., 1983, *15*, 385.

[2] Klasa-Mazurkiewicz D., Emerich J., Milczanek T., Ciach K.: "Pierwotny rak gruczołu Bartholina". *Ginekol. Pol*., 2003, *74*, 220.

[3] Yang S.Y., Lee J.W., Kim W.S., Jung K.L., Lee S.J., Lee J.H. *et al*.: "Adenoid cystic carcinoma of the Bartholin's gland; report of two cases and review of the literature". *Gynecol. Oncol*., 2006, *100*, 422. Epub 2005 Sep 27.

[4] Sikorowa L.: "Histogeneza i patomorfologia nowotworów złośliwych narządów kobiecych". In: L. Tarłowska (ed). *Ginekologia Onkologiczna*, PZWL 1983. INCOMPLETE: CITY? PUBLISHER?

[5] Kozakiewicz B.: "Rak płaskonabłonkowy gruczołu Bartholina. Raport 3 przypadków". *Current Gynecol. Oncol*., 2010, *8*, 51.

[6] Cardosi R.J., Speighs A., Fiorica J.V., Grendys E.C., Hakam A., Hoffman M.S.: "Bartholin's gland carcinoma: a 15 year experience". *Gynecol. Oncol*., 2001, *82*, 247.

[7] Wheelock J.B., Goplerud D.R., Dunn L.J., Oates J.F.: "Primary carcinoma of Bartholin gland: A report of ten cases". *Obstet. Gynecol*., 1984, *63*, 820.

[8] Ozono S., Onozuka M., Sato K., Ito Y.: "Immunohistochemical localization of estradiol, progesterone, and progesterone receptor in human salivary glands and salivary adenoid cystic carcinomas". *Cell Struct. Funct*.,1992, *17*, 169.
[9] Azumi N., Battifora H.: "The cellular composition of adenoid cystic carcinoma: an immunohistochemical study". *Cancer*, 1987, *60*, 1589.
[10] Ulbright T.M., Brokaw S.A., Stehman F.B., Roth L.M.: "Epithelioid sarcoma of vulva. Evidence suggesting a more aggressive behavior than extra-genital epithelioid sarcoma". *Cancer*, 1983, *52*, 1462.
[11] Emerich J., Konefka T., Dudziak M., Stankowska B.: "Przypadek mięsaka nabłonkowatokomórkowego gruczołu Bartholina". *Gin. Pol*., 1995, *66*, 188.
[12] Nielson G.P., Rosenberg A.E., Koerner F.C., Young R.H., Scully R.E.: "Smooth-muscle tumors of vulva. A clinico-pathological study 25 cases of review of the literature". *Am. J. Surg. Pathol*., 1996, *86*, 272.
[13] Gilio A.R., Resta C.G., Carriero L., loizzi V., Paeisi A.M., Selvaggi L.: "Rapid growth of myxoidleiomyosarcoma of the vulva during pregnancy: a case report". *Int. J. Gynecol. Cancer*, 2004, *14*, 172.
[14] Sieiński W., Bobkiewicz P.: "Bartholin's gland mixed carcinoma predominantly of the transitional cell type following radiotherapy for a cervical carcinoma". *Zentralblallg. Pathol. Pathol. Anat*.,1990, *3*, 265.
[15] Khoury-Collado F., Elliot K.S., Lee Y.C., Chen P.C., Abulafia O.: "Merkel cell carcinoma of the Bartholin's gland". *Gynecol. Oncol*., 2005, *97*, 928.
[16] Tjalma W.A.A., Van de Velde A.L.R., Schroyens W.A.M.: "Primary non-Hodkin's lymphoma in Bartholin's gland". *Gynecol. Oncol*., 2002, *87*, 308.
[17] Lim K.C.K., Thomson I.W., Wiener J.J.: "A case of clear cell adenocarcinoma of Bartholin's gland". *Int. J. Obstet. Gynecol*., 2002, *109*, 1305.
[18] Tatsuya O., Nakano T., Abe A., Sano T., Niibe Y., Kuniyuki O.: "Mucinous Adenocarcinoma of Bartholin Gland Treated with Radiation Therapy : a Case Report". *Jpn. J. Clin. Oncol.,* 2001, *31*, 226.
[19] Sośnik H., Sośnik K., Hałoń A.: "The pathomorphology of Bartholin's gland. Analysis of surgical data". *Pol. J. Pathol*., 2007, *58*, 99.
[20] Scinicariello F., Raday P., Hannigan E., Dinh T.V., Tyring S.K.: "Case report. Human papillomavirus type 16 found in primary transitional cell carcinoma of the Bartholin's gland and lymph node metastasis". *Gynecol. Oncol.,* 1992, *47*, 263.
[21] Copeland L.J., Sneige N., Gershenson D.M., Karim F., Rutledge F.N.: "Bartholin gland carcinoma". *Obstet. Gynecol*., 1986, *67*, 794.
[22] Chamilton D.L., Taylor H.B.: "Primary carcinoma of Bartholin's gland. A raport of 24 patients". *Obstet. Gynecol.,* 1972, *39*, 489.
[23] Leuchter R.S., Hacker N.F., Voet R.L., Berek J.S., Townsend D.E., Lagasse L.D.: "Primary carcinoma of Bartholin gland: A report of 14 cases and review of the literature". *Obstet. Gynecol*., 1982, *60*, 361.
[24] Tavassoli F.A., Norris H.J.: "Smooth muscle tumors of vulva". *Obstet. Gynecol*., 1979, *53*, 213.
[25] Nielson G.P., Rosenberg A.E., Koerner F.C., Young R.H., Scully RE.: "Smooth muscle tumors of vulva. A clinico-pathological study 25cases of review of the literature". *Am. J. Surg. Pathol.*, 1996, *86*, 296.
[26] Hajdu S.I., Shiu M.H., Fortner J.G.: "Tendosynovioma sarcoma. A clinicopathological study of 136 cases". *Cancer*, 1977, *39*, 1201.
[27] Nycum L.R., Farley J.H., Reed M.E., Taylor R.R.: "Case report Recurrent squamous cell carcinoma of Bartholin's duct treated with en bloc resection". *Gynecol. Oncol*., 1999, *75*, 282.
[28] Woida F.M.**,** Ribeiro-Silva A**.: "**Adenoid cystic carcinoma of the Bartholin's gland". *Arch. Med. Lab. Pathol*., 2007, 131, 796.
[29] Addison A., Parker R.T.: "Adenoid cystic carcinoma of the Bartholin's gland; A review of the literature of patient". *Gynecol. Oncol*., 1977, *5*, 196.
[30] Copeland L.J., Sneige N., Gershenson D.M., Karim F., Rutledge F.N.: "Adenoid cystic carcinoma of the Bartholin gland". *Obstet. Gynecol*., 1986, *67*, 794.
[31] Fried-Oginski W., Lovecchio J.L., Farahani G.: "Malignant myxoid sarcoma of the Bartholin gland in pregnancy". *Am. J. Obstet. Gynecol*., 1995, *173*, 1633.
[32] Finn M.A., Bevre G.: "Bartholin glans carcinoma, malignant melanoma and other rare tumors of the vulvae". *Best Pract. Res. Clin. Obstet. Gynecol*., 2003, *17*, 609.
[33] Konefka T., Senkus E., Emerlich J., Dudziak M.: "Epithelioid sarcoma of Bartholin's gland primary diagnosed as vulvar carcinoma". *Gynecol. Oncol*., 1994, *54*, 393.
[34] Mazouni C., Morice P., Duvilllard P., Bonnier P., Castaigne D.: "Contralateral groin recurrence in patients with stage I Bartholin's gland squamous cell carcinoma and ipsilateral nodes: report on two cases and implications for lymphadenectomy". *Gynecol. Oncol*., 2004, *94*, 843.
[35] Massad L.S., Geest K.D.: "Multimodality therapy of carcinoma of Bartholin gland". *Gynecol. Oncol*., 1999, *75*, 305.
[36] Hampel M., Hantschmann P., Michels W., Hillemanns P.: "German multicenter group, Validation of the accuracy of the sentinel lymph node procedure in patients with vulvar cancer: results of a multicenter study in Germany". *Gynecol. Obstet*., 2008, *111*, 282.
[37] Frumovitz M., Gayed I.W., Jhingram A., Euscher E.D., Coleman R.L., Ramirez P.T. *et al*.: "Lymphatic mapping and sentinel lymph node detection in women with vaginal cancer". *Gynecol. Oncol*. 2008, *108*, 478.
[38] Balat Ö., Edwards C.L., Delclos L.: "Advanced primary carcinoma of the Bartholin gland: report of 18 patients". *Eur. J. Gynecol. Oncol*., 2001, *59*, 47.
[39] Yamada T., Yanagawa S., Iwai H., Ishigaki T.: "High-dose interstitial brachytherapy of Bartholin's gland: a case report". *Gynecol. Oncol*., 2000, *77*, 193.
[40] Downs L.S., Ghosh K., Dusenbery K.E., Cosin J.A.: "Stage IV of Bartholin gland managed with primary chemoradiation". *Gynecol. Oncol*., 2002, *87*, 210.

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